Diagnostic Testing of Common Sexually Transmitted Infections

Policy Number: AHS – G2157 – Diagnostic Testing of Common Sexually Transmitted Infections	Effective Date: 11/01/2026

POLICY DESCRIPTION | INDICATIONS AND/OR LIMITATIONS OF COVERAGE | TABLE OF TERMINOLOGY | SCIENTIFIC BACKGROUND | GUIDELINES AND RECOMMENDATIONS | APPLICABLE STATE AND FEDERAL REGULATIONS | APPLICABLE CPT/HCPCS PROCEDURE CODES | EVIDENCE-BASED SCIENTIFIC REFERENCES | REVISION HISTORY

I. Policy Description

Sexually transmitted infections (STIs), often referred to as sexually transmitted diseases or STDs, include a variety of pathogenic bacteria, virus, and other microorganisms that are spread through sexual contact and can cause a multitude of complications if left untreated. Chlamydia and gonorrhea, caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, respectively, have high rates of occurrence in the United States and can cause pelvic inflammatory disease (PID), infertility, and pregnancy complications. The causative agent of syphilis is *Treponema pallidum*; if left untreated, syphilis can lead to serious cardiac and neurological conditions.[1] Human papillomavirus (HPV) is a double-stranded DNA virus that can be sexually transmitted and is associated with cervical cancer, vulvar/vaginal cancer, anal cancer, oropharyngeal cancer, penile cancer, and both genital and nongenital warts. "Globally, anogenital HPV is the most common sexually transmitted infection" with an estimated 80% of sexually active adults exposed to it at least once in their lifetime.[2] Herpes simplex virus (HSV) is a common STI where many individuals are asymptomatic. HSV infection has been linked to an increased risk of other infections, including human immunodeficiency virus (HIV), and in rare cases, can also result in HSV meningitis or proctitis.[3] In general, risk factors for STIs can include both behavioral elements, such as multiple sex partners, working in a sex trade, and inconsistent use of condoms when in non-monogamous relationships as well as demographic risks, including men who have sex with men (MSM), prior STI diagnosis, admission to correctional facilities, and lower socioeconomic status.[1]

This policy is limited to testing for *C. trachomatis*, *N. gonorrhoeae*, *T. pallidum*, *T. vaginalis* (for guidance on panel testing for *T. vaginalis* in vaginitis, see AHS-M2057-Diagnosis of Vaginitis), HSV, and HPV. The following conditions and/or tests are discussed in the corresponding policies:

- Human Immunodeficiency Virus: AHS-M2116
- Hepatitis B and C: AHS-G2036-Hepatitis Testing
- Pediatric Preventive Screening: AHS-G2042
- Cervical Cancer Screening: AHS-G2002
- Pathogen Panel Testing: AHS-G2149

For STI screening in pregnant individuals, please see AHS-G2035-Prenatal Screening (Nongenetic).

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

1) Antibody testing for syphilis infection **MEETS COVERAGE CRITERIA** in the following situations:

   a) For any asymptomatic person in a high-risk category (see Notes 1 & 2), once a year assessment using either a "standard" or "reverse" algorithm that includes initial and confirmatory tests for any initial positive test, such as:

      i) Treponemal Ig test **and**

      ii) Nontreponemal Ig test.

   b) For diagnosis of any person presenting with signs and/or symptoms of a syphilis infection (see Note 3).

   c) Once every three months for HIV-positive men or MSM.

   d) Treponemal Ig testing and nontreponemal testing (once prior to transplant) as a part of a pre-transplant assessment in both donors and recipients of an allogeneic hematopoietic stem cell transplantation (allo-HCT).

   e) When a nontreponemal test is used as a test of cure (TOC) for a positive syphilis infection.

2) For asymptomatic individuals NOT belonging to a high-risk category (see Notes 1 & 2), antibody screening for syphilis **MEETS COVERAGE CRITERIA** only in the following situations:

   a) For pregnant individuals as part of the first prenatal visit.

   b) As part of newborn screening.

   c) As part of follow-up in a victim of sexual assault.

   d) For sexually active individuals less than 18 years of age (annually).

3) For individuals who are currently diagnosed with a syphilis infection or who have a past history of a syphilis infection, treponemal Ig testing **DOES NOT MEET COVERAGE CRITERIA.**

4) Polymerase chain reaction (PCR) testing, nucleic acid amplification testing (NAAT), and antigen testing for syphilis **DO NOT MEET COVERAGE CRITERIA**.

5) Qualitative NAAT for chlamydia **MEETS COVERAGE CRITERIA** in the following situations:

   a) Once a year assessment for any asymptomatic person in a high-risk category (see Notes 1& 4).

   b) For diagnosis of any person presenting with signs and/or symptoms of a chlamydial infection (see Note 5).

   c) For the diagnosis of any person with suspected lymphogranuloma venereum (LGV).

   d) At least three months after initial chlamydial diagnosis as a TOC for non-pregnant individuals.

   e) At least four weeks after initial chlamydial diagnosis as a TOC for pregnant individuals.

6) For asymptomatic individuals NOT belonging to a high-risk category (see Notes 1 & 4), NAAT screening for chlamydia **MEETS COVERAGE CRITERIA** only in the following situations:

   a) For pregnant individuals 24 years of age or younger as part of the first prenatal visit.

   b) As part of newborn screening.

   c) As part of follow-up in a victim of sexual assault.

d) For sexually active individuals less than 18 years of age (annually).

7) Culture testing, antibody testing, and antigen testing for chlamydia or LGV **DO NOT MEET COVERAGE CRITERIA**.

8) Qualitative NAAT for gonorrhea **MEETS COVERAGE CRITERIA** in the following situations:
   a) Once a year assessment for any asymptomatic person in a high-risk category (see Notes 1 & 4).
   b) For diagnosis of any person presenting with signs and/or symptoms of a gonorrheal infection (see Note 6).
   c) At least three months after initial gonorrhea diagnosis as a TOC.

9) For an individual that does not respond to initial treatment, culture testing for *N. gonorrhoeae* to determine antimicrobial susceptibility **MEETS COVERAGE CRITERIA**.

10) For asymptomatic individuals NOT belonging to a high-risk category (see Notes 1 & 4), NAAT screening for gonorrhea **MEETS COVERAGE CRITERIA** only in the following situations:
   a) For pregnant individuals 24 years of age or younger as part of the first prenatal visit.
   b) As part of newborn screening.
   c) As part of follow-up in a victim of sexual assault.
   d) For sexually active individuals less than 18 years of age (annually).

11) Qualitative NAAT for *T. vaginalis* **MEETS COVERAGE CRITERIA** in the following situations:
   a) For symptomatic individuals (see Note 7).
   b) Follow up testing a minimum of three months after initial trichomoniasis diagnosis.
   c) Annual screening for asymptomatic individuals belonging to a high-risk group (see Note 8).
   d) Annual screening for asymptomatic individuals who have an HIV infection.
   e) As a part of follow-up in a victim of sexual assault.

12) Rapid identification of Trichomonas by enzyme immunoassay **DOES NOT MEET COVERAGE CRITERIA**.

13) For symptomatic individuals (see Note 9), testing for *Mycoplasma genitalium* using qualitative NAAT **MEETS COVERAGE CRITERIA**.

14) For asymptomatic individuals, screening for *M. genitalium* using NAAT **DOES NOT MEET COVERAGE CRITERIA**.

15) When an individual meets any of the conditions described above, multitarget PCR testing (targets limited to *C. trachomatis, N. gonorrhoeae, T. vaginalis*, and *M. genitalium*) **MEETS COVERAGE CRITERIA**.

16) For individuals with active genital ulcers or mucocutaneous lesions, qualitative NAAT for herpes simplex virus-1 (HSV-1) or herpes simplex virus-2 (HSV-2) **MEETS COVERAGE CRITERIA**.

17) Type-specific antibody testing for HSV-2 using a glycoprotein G2 (gG2) test **MEETS COVERAGE CRITERIA** in the following situations:

   a) Recurrent or atypical genital symptoms or lesions in individuals with a negative herpes simplex virus PCR or culture result.

   b) For the clinical diagnosis of genital herpes in individuals with a negative PCR or culture result or without laboratory confirmation.

   c) When an individual's partner has genital herpes.

18) Antibody and antigen testing for HSV-1 and and/or herpes simplex (non-specific type test) and antigen testing for HSV-2 **DO NOT MEET COVERAGE CRITERIA**.

19) In asymptomatic individuals, screening for HSV-1 or HSV-2 **DOES NOT MEET COVERAGE CRITERIA**.

20) In the diagnosis and/or assessment of cancer or cancer therapy (immunohistochemistry testing for p16 or NAAT testing for high-risk human papillomavirus [HR-HPV]), testing for HR-HPV **MEETS COVERAGE CRITERIA**.

21) Testing for HPV **DOES NOT MEET COVERAGE CRITERIA** in the following situations:

   a) To screen for oncogenic high-risk types, such as HPV-16 and HPV-18, as part of a general sexually transmitted disease (STD) or sexually transmitted infection (STI) screening process or panel for asymptomatic individuals.

   b) As part of the diagnosis of anogenital warts.

   c) Testing for low-risk types of HPV.

   d) In the general population, either as a part of a panel of tests or as an individual NAAT to determine HPV status.

22) Prior to beginning or while an individual is undergoing a preexposure prophylaxis (PrEP) regimen for HIV prevention, the following screens/tests for additional STIs **MEET COVERAGE CRITERIA**:

   a) Qualitative NAAT screening for gonorrhea and chlamydia:

      i) Once every three months for MSM.

      ii) Once every six months for sexually active individuals.

   b) Blood testing to screen for syphilis:

      i) Once every three months for MSM.

      ii) Once every six months for sexually active individuals.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

23) Nucleic acid testing to determine antimicrobial susceptibility in *N. gonorrhoeae* or macrolide resistance in *M. genitalium* **DOES NOT MEET COVERAGE CRITERIA**.

24) Direct probe detection and/or quantitative NAAT for the following microorganisms **DOES NOT MEET COVERAGE CRITERIA**:

a) *Chlamydia trachomatis*

b) *Neisseria gonorrhoeae*

c) Herpes Simplex Virus-1

d) Herpes Simplex Virus-2

e) *Treponema pallidum*

f) *Trichomonas vaginalis*

NOTES:

Note 1: For sexually active children and adolescents under the age of 18, risk factors for chlamydia, gonorrhea, and/or syphilis infection as defined by the CDC include: initiating sex early in adolescence; living in detention facilities; receiving services at STD clinics; being involved in commercial sex exploitation or exchanging sex for drugs, money, food, or housing; having multiple sex partners, having sequential sex partnerships of limited duration or concurrent partnerships; failing to use barrier protection consistently and correctly; having lower socioeconomic status, and facing numerous obstacles to accessing healthcare. At-risk individuals also include: males who have sex with males (YMSM); transgender youths; youths with disabilities, substance abuse, or mental health disorders.[4]

Note 2: <u>High-risk for Syphilis:</u>[5,6]

- Sexually active men who have sex with men (MSM)
- Sexually active individuals with an HIV-positive status
- Having a sexual partner recently diagnosed with a STI
- Exchanging sex for money or drugs
- Individuals in adult correctional facilities
- During pregnancy when the following risk factors are present:
  - Sexually active HIV-positive status
  - Sexually active with multiple partners
  - Sexually active in conjunction with drug use or transactional sex
  - Late entry to prenatal care (i.e., first visit during the second trimester or later) or no prenatal care
  - Methamphetamine or heroin use
  - Incarceration of the woman or her partner
  - Unstable housing or homelessness

Note 3: <u>Signs and Symptoms of a Syphilis Infection:</u>[5,7]

- Chancre
- Skin rash and/or mucous membrane lesions in mouth, vagina, anus, hands, and feet
- Condyloma lata
- Secondary symptomology can include fever, fatigue, sore throat, swollen lymph nodes, weight loss, muscle aches, headache, and hair loss

- Signs and symptoms of neurosyphilis can include severe headache, trouble with muscle movements, muscle weakness or paralysis (not being able to move certain parts of the body), numbness, and changes in mental status (trouble focusing, confusion, personality change) and/or dementia (problems with memory, thinking, and/or making decisions).
- Signs and symptoms of ocular syphilis can include eye pain or redness, floating spots in the field of vision ("floaters"), sensitivity to light, and changes in vision (blurry vision or even blindness).
- Signs and symptoms of otosyphilis may include hearing loss, ringing, buzzing, roaring, or hissing in the ears ("tinnitus"), balance difficulties, and dizziness or vertigo.
- Signs and symptoms of late/tertiary syphilis include inflammatory lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), and bone (e.g., osteitis).

Note 4: High-risk for Chlamydia and/or Gonorrhea:[8-11]

- Sexually active men who have sex with men (MSM)
- Sexually active individuals with an HIV-positive status
- Sexually active individuals with a cervix who are under the age of 25
- Individuals with a cervix who are 25 years of age or older and who have multiple sexual partners
- Having a sexual partner recently diagnosed with an STI
- Previous or concurrent STI
- Exchanging sex for money or drugs

Note 5: Signs and Symptoms of a Chlamydia Infection:[8,11]

- Genital symptoms, including "discharge, burning during urination, unusual sores, or rash"
- Pelvic Inflammatory Disease (PID), including "symptoms of abdominal and/or pelvic pain, along with signs of cervical motion tenderness, and uterine or adnexal tenderness on examination"
- Urethritis
- Pyuria
- Dysuria
- Increase in frequency in urination
- Epididymitis (with or without symptomatic urethritis) in men
- Proctitis
- Sexually acquired chlamydial conjunctivitis

Note 6: Signs and Symptoms of Gonorrhea:[10]

- Dysuria
- Urethral infection
- Urethral or vaginal discharge
- Epididymitis (Testicular or scrotal pain)
- Rectal infection symptoms include anal itching, discharge, rectal bleeding, and painful bowel movements

Note 7: Signs and Symptoms of Trichomoniasis:[12]

- Vaginal or penile discharge
- Itching, irritation, a burning sensation, or soreness of the genitalia

- Discomfort or burning sensation during/after urination and/or ejaculation
- Urethritis
- Epididymitis
- Prostatitis

Note 8: High-risk for Trichomoniasis:[13]

- Receiving care in high-prevalence settings (e.g., STI clinics, correctional facilities)
- Having multiple sexual partners
- Exchanging sex for money or drugs
- Having a previous or concurrent STI
- Drug misuse
- History of incarceration
- Sexually active individuals with an HIV-positive status

Note 9: Signs and Symptoms of *M. genitalium* Infection:[14]

- When present, typical symptoms of *Mgen*-urethritis in men include dysuria, urethral pruritus, and purulent or mucopurulent urethral discharge.
- When present, typical symptoms of *Mgen* cervicitis in women include vaginal discharge, vaginal itching, dysuria, and pelvic discomfort.
- When present, typical symptoms of PID due to *Mgen* include mild to severe pelvic pain, abdominal pain, abnormal vaginal discharge, and/or bleeding.

III. Table of Terminology

Term	Definition
AAP	American Academy of Pediatrics
AGIHO/DGHO	Infectious Diseases Working Party of the German Society for Hematology and Medical Oncology
AGW	Anogenital warts
AIDs	Acquired immune deficiency syndrome
AIN	Anal intraepithelial neoplasia
Allo-HCT	Allogeneic haematopoietic stem cell transplantation
Anti-HBc	Hepatitis B core antigen
ASCUS	Atypical squamous cells of undetermined significance
BASHH	British Association for Sexual Health and HIV
BD	Becton Dickinson
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CIA	Chemiluminescence immunoassay
CIN2+	Cervical intraepithelial neoplasia grade 2+
CIN3	Cervical intraepithelial neoplasia grade 3
CLIA	Chemiluminescent assay
CLIA ’88	Clinical Laboratory Improvement Amendments of 1988
CMIA	Chemiluminescence immunoassay
CMS	Centers for Medicare and Medicaid
CNS	Central nervous system

CPS	Canadian Paediatric Society
CSF	Cerebrospinal fluid
CT	*Chlamydia trachomatis*
DAG-KBT	German Working Group for Blood and Marrow Transplantation
DFE	Darkfield examination
DNA	Deoxyribonucleic acid
DRE	Digital rectal examination
E7-MPG	E7 multiplex genotyping
EBV	Epstein Barr virus
ED	Emergency department
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
FDA	Food and Drug Administration
FEMS	Federation of European Microbiological Societies
FIA	Fluorescence immunoassay
FNA	Fine needle aspiration
FTA	Fluorescent treponemal antibody
GC	Gonococcal
gG2	Glycoprotein G2
GP5+/6+	General primer 5+/6+
HBV	Hepatitis B
HBSAG	Hepatitis B surface antigen
HC2	Hybrid capture 2
hCG	Human chorionic gonadotropin
HIV	Human immunodeficiency virus
HIV-1	Human immunodeficiency virus-1
HPV	Human papillomavirus
HPV-16	Human papillomavirus type 16
HPV-18	Human papillomavirus type 18
HR-HPV	High risk or oncogenic HPV testing
HSIL	High-grade squamous intraepithelial lesion
HSV	Herpes simplex virus
HSV-1	Herpes simplex virus-1
HSV-2	Herpes simplex virus-2
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHC	Immunohistochemistry
IMCA	Immunochemiluminometric assay
ISH	In situ hybridization
ISVVD	The International Society for the Study of Vulvovaginal Disease
IUSTI	International Union Against Sexually Transmitted Infections
JAMA	Journal of the American Medical Association
LDTs	Laboratory-Developed Tests
LGSIL	Low grade squamous intraepithelial lesion on cytologic smear of anus
LGV	Lymphogranuloma venereum
LSIL	Low-grade squamous intraepithelial lesions

MG	*Mycoplasma genitalium*
Mgen	*Mycoplasma genitalium*
MHA-TP	Microhemagglutination Assay for *Treponema pallidum* antibodies
MLST	Multilocus sequence typing
mRNA	Messenger RNA
MSM	Men having sex with men
MTC	Male Training Center for Family Planning & Reproductive Health
NA	Not applicable
NAAT	Nucleic acid amplification testing
NCCN	National Comprehensive Cancer Network
NG	*Neisseria gonorrhoeae*
NGU	Nongonococcal urethritis
NICE	National Institute for Health and Care Excellence
NOS	Not otherwise specified
NTT	Nontreponemal test
ORPH-1	Oropharynx-1
OS	Overall survival
PCR	Polymerase chain reaction
PHAC	Public Health Agency of Canada
PID	Pelvic inflammatory disease
POC	Point-of-care
POCT	Point-of-care test
PrEP	Preexposure prophylaxis
PWID	People who inject drugs
RFLP	Restriction fragment length polymorphism
RNA	Ribonucleic acid
RPR	Rapid plasma reagin test
rRNA	Ribosomal ribonucleic acid
RT-PCR	Reverse transcription-polymerase chain reaction
SDA	Strand displacement amplification
STBBI	Sexually transmitted and blood-borne infections
STDs	Sexually transmitted diseases
STIs	Sexually transmitted infections
TMA	Transcription-mediated amplification
TOC	Test of cure
TPHA	*Treponema pallidum* hemagglutination
TP-IgA	*Treponema pallidum* IgA antibodies
TPPA	*Treponema pallidum* particle agglutination
TP-PA	*T. pallidum* passive particle agglutination
TSS	Type-specific serology
TT	Treponemal test
TV	Trichomonas vaginalis
USPSTF	United States Preventive Services Task Force
VDRL	Venereal disease research laboratory
VIN	Vulvar intraepithelial neoplasia
YMSM	Young men who have sex with men

IV. Scientific Background

Chlamydia

Chlamydia, caused by the bacterium *Chlamydia trachomatis*, is usually an asymptomatic sexually transmitted infection that can be passed to a newborn from an infected mother, potentially resulting in conjunctivitis and/or pneumonia. Symptomatic infections can include cervicitis, pelvic inflammatory disease (PID), and Fitzhugh-Curtis syndrome in women as well as epididymitis, prostatitis, and reactive arthritis triad in men. Both men and women can have proctitis, urethritis, conjunctivitis, pharyngitis, and genital lymphogranuloma venereum as a result of a chlamydial infection. Nucleic acid amplification testing (NAAT) for chlamydia is the gold standard due to high specificity and sensitivity instead of using culture testing, microscopy, or antigen detection.[15] In the U.S. alone, in 2024 over 1.5 million cases of chlamydia were reported to the CDC, but the CDC estimates that 2.86 million chlamydial infections occur annually.[8,16] This under-reporting is due to individuals who are asymptomatic and, therefore, do not seek treatment. Highest prevalence occurs among men who have sex with men (MSM) and young people. "It is estimated that 1 in 20 sexually active young women aged 14-24 years has chlamydia."[8]

Mycoplasma genitalium (Mgen) is a sexually transmitted infection that is strongly associated with urethritis symptoms, similar to *Chlamydia trachomatis* and *Neisseria gonorrhoeae.*[17] *Mgen* can infect the uterus, urethra, or rectum, and causes infections in all genders. In men, common symptoms of *Mgen*-urethritis include: dysuria, urethral pruritus, and purulent or mucopurulent urethral discharge. In women, common symptoms of Mgen cervicitis include: vaginal discharge, vaginal itching, dysuria, and pelvic discomfort. The prevalence of *Mgen* in the United States is estimated to be 1.7% among people aged 14 to 59 years. However, the prevalence of *Mgen* in clinical-based populations are higher; a multicenter study around diverse geographic regions of the United States found the prevalence of *Mgen* to be 10.3% in people seeking care.[14]

Gonorrhea

Gonorrhea is a sexually transmitted infection caused by the bacterium *Neisseria gonorrhoeae*. A gonorrheal infection can cause many of the same complications as chlamydia, including PID, cervicitis, and Fitzhugh-Curtis syndrome in women and epididymitis in men. Urethritis, pharyngitis, and proctitis can also occur; in fact, "*N. gonorrhoeae* can be isolated from the urethra in up to 90 percent of women with gonococcal cervicitis."[18] Like chlamydia, if left untreated, gonorrhea can be spread from mother to newborn, resulting in conjunctivitis. NAAT is the best method to diagnose gonorrhea, but culture testing is still used to determine antimicrobial susceptibility due to an increase in antibiotic resistance.[19] In 2024, the CDC reported a 19% decrease since 2019 in the number of cases of gonorrhea reported in the United States.[16] The CDC also reported 543,409 cases of gonorrhea in the United States in 2024.[16]

Syphilis

Syphilis is caused by the bacterium *Treponema pallidum*, and it progresses, if left untreated, through various stages—primary, secondary, early-latent, late-latent, and late-stage syphilis—until infecting the central nervous system. "Syphilis infection is associated with HIV infection and increases the risk for acquiring or spreading HIV."[6] Worldwide, the World Health Organization estimates that 8 million adults between 15 and 49 years old acquired syphilis in 2022.[20] The U.S. has reported an increase in the rate of syphilis between 2019 and 2024, with an increase by 42%. Of concern, there has also been an increased number of cases of primary and secondary syphilis in women by 50% in the past five years. In 2024, 3,941 cases of congenital syphilis were reported.[16]

Similar to other STIs, syphilis is often asymptomatic. For symptomatic syphilis, the signs and symptoms can vary, depending on the stage of disease. Primary syphilis can have a characteristic chancre, a skin lesion that is usually painless and often heals even in the absence of treatment. Secondary syphilis occurs weeks to months later and can be manifested by typical immunologic responses, such as fever, lethargy, and so on; adenopathy; rash; alopecia; hepatitis; gastrointestinal abnormalities; and even early symptoms of neurological infection, if left untreated. Later stages of syphilis can include cardiovascular abnormalities and progression of neurological syphilitic infection. Asymptomatic, latent syphilis can also occur; moreover, "pregnant women with latent syphilis can transmit *T. pallidum* to their fetus for up to four years after acquisition."[21]

The standard protocol for diagnosing a syphilis infection is to use a two-tiered serological testing algorithm of treponemal testing and nontreponemal testing. Treponemal testing is typically more complex than the latter, and they both rely upon the detection of specific treponemal antigens using enzyme immunoassay (EIA), particle agglutination assay, fluorescence, or chemiluminescence immunoassay (CIA). Nontreponemal testing methods, including the rapid plasma reagin test (RPR) and the venereal disease research laboratory (VDRL) test, "are based upon the reactivity of serum from infected patients to a cardiolipin-cholesterol-lecithin antigen."[22] Rapid serological testing using darkfield microscopy is not as universally used due to complexity and cost. NAAT has not been FDA-approved at this time and is not typically performed for genital syphilis. "There is no internationally approved PCR for *T. pallidum* and accordingly, it is crucial to select a strictly validated method and always use it with appropriate quality controls."[23]

Herpes Simplex Virus (HSV)

Herpes Simplex Virus-2 (HSV-2) is the common cause of most of genital herpes simplex infections worldwide with the CDC estimating that 50 million people in the U.S. were infected with HSV-2 in 2015.[24] In 2018, CDC estimates show there were 572,000 new genital herpes infections in the U.S. among people aged 14 to 49; moreover, HSV-1 genital herpes has increased in recent years. This trend is believed to be due to a decline in childhood oral HSV-1 infections that in the past increased immune resistance to genital HSV-1 infections.[25] Primary genital herpes infections can present with genital ulcers as well as other immunological responses, such as fever and lymphadenopathy; however, for some people, a primary genital herpes infection is asymptomatic. Nonprimary infections occur when a patient acquires HSV-1 with pre-existing HSV-2 antibodies or vice versa. Recurrent infections can be either symptomatic or asymptomatic, which can be referred as subclinical. A minority of HSV-positive patients can also present with meningitis and/or proctitis.[3] Vertical transmission from mother to newborn can occur during delivery, especially if the mother acquires a primary infection near the end of the pregnancy. This vertical transmission can occur even if the mother is asymptomatic.[26] Diagnosis of genital herpes infection can be performed by viral culture, NAAT, and serological testing. "Cell culture and PCR-based testing are the preferred tests for a patient presenting with active lesions, although PCR-based testing has the greatest overall sensitivity and specificity."[3]

Human Papillomavirus (HPV)

Anogenital HPV infection is the most common STI worldwide with an estimation that "almost all sexually active individuals will acquire HPV at some point in their lifetime."[2] This is due to the large number of different types of HPV known to infect the genital tract—at least 40 characterized to date—and the transitory nature of HPV infections. HPV is associated with a variety of cancers, including anal, penile, vulvar, vaginal, and oropharyngeal cancer; moreover, the carcinogenic effect of an HPV infection can be years after the initial diagnosis of HPV. Multiple HPV vaccinations have been approved for use in the

U.S., and the CDC recommends vaccination for HPV for all children ages 11 or 12.[27] HPV can be detected from swab samples and can be included in many routine cervical exams. High-risk oncogenic HPV testing is commercially available.[28]

HIV Preexposure Prophylaxis (PrEP)

An estimated 1.2 million people in the United States currently live with human immunodeficiency virus (HIV) and over 630,000 deaths were reports globally in 2024.[29-31] The U.S. Preventive Services Task Force (USPSTF) determined that HIV preexposure prophylaxis (PrEP) is beneficial in decreasing the risk of infection with HIV for individuals who have an elevated risk of acquiring an HIV infection (i.e., "sexually active adults and adolescents weighing at least 35 kg (77 lb) who report sexual behaviors that place them at substantial ongoing risk of HIV exposure and acquisition or who inject drugs and report injection practices that place them at substantial ongoing risk of HIV exposure and acquisition.")[30]

When evaluating patients for PrEP or during ongoing PrEP use, comprehensive STI screening is an essential component of care. The goal is to confirm the absence of HIV infection before initiating PrEP and to identify and manage other sexually transmitted infections that may be present. The CDC recommends laboratory-based antigen/antibody HIV testing within one week prior to starting or restarting PrEP to confirm a negative HIV status, hepatitis B testing prior to beginning PreP, and testing "to screen for chlamydia, gonorrhea, and syphilis are recommended for all sexually active adults before starting oral or injectable PrEP."[32] Ongoing monitoring is recommended every three to six months for individuals on PrEP, including repeated HIV testing and screening for bacterial STIs. This approach ensures early detection and treatment of infections, reduces transmission risk, and supports optimal sexual health alongside HIV prevention strategies.[32]

Proprietary Testing

BD Onclarity HPV Assay

The BD Onclarity HPV Assay, a qualitative in vitro assay of cervical swabs using PCR (i.e., a nucleic acid amplification test or NAAT), is offered by Becton, Dickinson and Company and is approved by the FDA. This test specifically identifies types 16, 18 and 45, while concurrently detecting the other high-risk (HR) HPV types (including 31, 51, 52, 33/58, 35/39/68, and 56/59/66). For HR-HPV 31, 51, 52, 33/58, 35/39/68, and 56/59/66, this is "the only FDA-approved assay to individually identify and report these genotype results."[33]

Becton, Dickinson and Company note that "the BD Onclarity HPV Assay is indicated: 1) In women 21 years and older with ASC-US (atypical squamous cells of undetermined significance) cervical cytology test results, the BD Onclarity HPV Assay can be used to determine the need for referral to colposcopy; 2) In women 21 years and older with ASC-US cervical cytology test results, the BD Onclarity HPV Assay can be used to detect high-risk HPV genotypes 16, 18 and 45. This information together with physicians assessment of screening history, other risk factors, and professional guidelines, may be used to guide patient management. The results of this test are not intended to prevent women from proceeding to colposcopy; 3) In women 30 years and older, the BD Onclarity HPV Assay can be used together with cervical cytology to adjunctively screen to detect high risk HPV types. This information, together with the physicians assessment of screening history, other factors, and professional guidelines, may be used to guide patient management; 4) In women 30 years and older, the BD Onclarity HPV Assay can be used to detect high-risk HPV genotypes 16, 18 and 45. This information, together with the physicians assessment of screening history, other factors, and professional guidelines, may be used to guide patient

management; and 5) In women 25 years and older, the BD Onclarity HPV Assay can be used as a first-line primary cervical cancer screening test to detect high risk HPV, including 16 and 18. Women who test negative for the high risk HPV types by the BD Onclarity HPV Assay should be followed up in accordance with the physicians assessment of screening and medical history, other risk factors, and professional guidelines. Women who test positive for HPV genotypes 16 and/or 18 by the BD Onclarity HPV Assay should be referred to colposcopy. Women who test high risk HPV positive and 16 and 18 negative by the BD Onclarity HPV Assay (12 other HR HPV Positive) should be evaluated by cervical cytology to determine the need for referral to colposcopy."[34]

Cepheid Xpert® CT/NG

Cepheid offers the Cepheid Xpert® CT/NG test, an FDA-approved nucleic acid amplification test to detect *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (NG) using urogenital specimens and extragenital specimens (pharynx and rectum).[35,36] It is performed using the GeneXpert® Instrument Systems with a qualitative *in vitro* real-time PCR "for the automated detection and differentiation of genomic DNA from Chlamydia trachomatis (CT) and/or Neisseria gonorrhoeae (NG)"[37,38] and is stated to provide results for up to 96 specimens in approximately 90 minutes.[39] The assay may be used to "test the following specimens from asymptomatic and symptomatic individuals: female and male urine, patient-collected vaginal swabs (collected in a clinical setting), clinician-collected endocervical swabs, and female and male pharyngeal and rectal swabs."[39] Sensitivity and specificity of this test are dependent on the manner in which samples were collected, with patient collected vaginal swab, endocervical swab, urine, and pharyngeal swab specimens showing sensitivity and specificity in the mid to high ninetieth percentile. Rectal swab specimens showed a lower sensitivity for both CT (86%) and NG (91.2%), but specificity in the 99th percentile, similar to the specificity of the other sample collection methods.[39]

Abbott Alinity™ m STI Assay

Abbott offers the Alinity™ m STI AMP Kit. The test is "an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for the direct, qualitative detection and differentiation of RNA from *Chlamydia trachomatis* (CT), *Trichomonas vaginalis* (TV), *Mycoplasma genitalium* (MG), and DNA from *Neisseria gonorrhoeae* (NG)." The test is a four in one multiplex assay that detects four reactions. The first result should appear in under 115 minutes. Abbott reports a sensitivity of 100% for all analytes and specificity with "no cross-activity observed with 148 organisms." The assay may be used to test the following specimens: "endocervical swab specimens, clinician-collected vaginal swab specimens, self-collected vaginal swab specimens (in a clinical setting), gynecological specimens collected in ThinPrep PreservCyt solution, female urine, and male urine."[40]

Goldstein, et al. (2021) performed an international, multicenter study to evaluate accuracy, reproducibility, and clinical performance of the Alinity™ m STI assay. The Alinity™ m STI assay was compared with commonly used STI assays. "The Alinity m STI assay identified accurately and precisely single and mixed pathogens from an analytical panel of specimens" and had "high overall agreement rates with comparator STI assays."[17]

Analytical Validity

A 2005 study by Cook, et al. (2005) reviewed the validity of NAAT for chlamydia and gonorrhea from urine samples as compared to swabs obtained directly from either the cervix or urethra. They reviewed 29 different studies and only included studies using collections of samples obtained from two anatomic

sites. Each test required either a secondary culture confirmation or a secondary NAAT-based confirmation. Over 20,000 different patients were included in the pooled study, and three different NAAT assays were monitored—polymerase chain reaction (PCR), transcription-mediated amplification, and strand displacement amplification (SDA).[42] "The pooled study specificities of each of the 3 assays exceeded 97% when urine samples were tested, for both chlamydial infection and gonorrhea and in both men and women." The use of PCR for gonorrheal testing, though, from female urine samples had only 55.6% specificity. The authors concluded the following: "Results of nucleic acid amplification tests for *C. trachomatis* on urine samples are nearly identical to those obtained on samples collected directly from the cervix or urethra. Although all 3 assays can also be used to test for *N. gonorrhoeae*, the sensitivity of the polymerase chain reaction assay in women is too low to recommend its routine use to test for gonorrhea in urine specimens."[41]

Due to an increase in demand for enzyme immunoassay-based testing of syphilis, Wong, et al. (2011) evaluated the validity of such testing—using the Trep-Sure EIA test—to that of the documented Venereal Disease Research Laboratory (VDRL) test and Treponema pallidum particle agglutination (TPPA) assay. Their research included 674 samples. The EIA-based test had a sensitivity of 98.0% and a specificity of 98.6%.[6] The authors conclude that "an IgM/IgG sensitive EIA would be an effective alternative to VDRL for syphilis screening."[43] An earlier study using another EIA-based assay, the Trep-Check IgG EIA test, conducted at the National Microbiology Laboratory of Canada did not report as positive results as the Wong study. This research consisted of 604 samples submitted from local or provincial hospitals for confirmation of local testing.[44] Their findings were that the Trep-Check IgG EIA had a sensitivity of 85.3% and specificity of 95.6%, but they also report a positive predictive value of 53.7% as compared to the positive predictive value of 98.4% of the Trep-Sure EIA test.[6,43] These results can be compared to the published results of the accuracy of the TPPA assay of 87.1% sensitivity, 100% specificity, and 100% positive predictive value—albeit in a smaller sample size (n = 198).[6,45]

The U.S. Preventive Services Task Force (USPSTF) conducted a systematic review of the use of serologic screening for genital herpes and published their findings in 2016. Their extensive review consisted of 17 different studies, ranging from 24 to 3,290 participants, in 19 different publications. Reviewing only the serological testing of HSV-2, they note that the "pooled estimates of sensitivity and specificity of the most commonly used test at the manufacturer's cutpoint were 99% (95% CI, 97%-100%) and 81% (95% CI, 68%-98%), respectively." However, they also note that "use of this test at the manufacturer's cutpoint in a population of 100 000 with a prevalence of HSV-2 of 16% (the seroprevalence in US adults with unknown symptom status) would result in 15 840 true-positive results and 15,960 false-positive results (positive predictive value, 50%)." They note the potential psychosocial harm due to false-positive results. The authors conclude, "Serologic screening for genital herpes is associate with a high rate of false-positive test results and psychosocial harms."[46]

In 2021, the US Preventive Services Task Force issued a brief update on genital herpes simplex diagnostics. Their assessment found that viral culture continues to be the gold standard for HSV infections. For central nervous system infections of HSV, PCR continues to be the gold standard, because of the assay's sensitivity of 80% to 90% for lesion specimens. They also indicated that serological tests are used to detect previous infections of herpes simplex in asymptomatic patients, specifying the Western blot assay as the most validated method. In addition, they noted: "two type-specific glycoprotein G serological tests are commercially available in the United States. Sensitivity and specificity of these tests are comparable to the Western blot assay."[47] The ATHENA study conducted in 2008-2009 and published in Lancet in 2011 consisted of more than 40,000 women in the U.S. aged 25 or over in 61 different clinical centers. The goal was to assess high-risk HPV16 and HPV18 testing versus

traditional methods. Their results show that "in women who had colposcopy, the Cobas HPV test was more sensitive than liquid-based cytology for detection of CIN3 [cervical intraepithelial neoplasia grade 3] or worse" with 92.0% versus 53.3% for liquid cytology. "Addition of liquid-based cytology to HPV testing increased sensitivity for CIN3 or worse to 96.7%...but increased the number of screen positives by 35.2%." The authors conclude, "HPV testing with separate HPV16 and HPV18 detection could provide an alternative, more sensitive, and efficient strategy for cervical cancer screening than do methods based solely on cytology."[48] Guenat and colleagues report a coefficient of variation of less than 8% for repeatability and reproducibility when using the Novaprep HQ+ medium in liquid-based cytology for HPV.[49] Another study comparing the validity of using urine samples in comparison with cervical samples for monitoring HPV in women over the age of 30 shows that the sensitivity of the urine testing varies considerably depending on the NAAT assay used. The multiplex type-specific PCR (E7-MPG) assay had a sensitivity of 80% and specificity of only 61% whereas the GP5+/6+ PCR assay resulted in 58% and 89%, respectively, for sensitivity and specificity as compared to the gold standard cervical swabs.[50]

A study by Golden, et al. (2019) compared the sensitivity of syphilis serological testing using the rapid plasma reagin (RPR) test and an experimental 23S rRNA *Treponema pallidum* real-time transcription-mediated amplification assay.[42] This study included 545 men who have sex with men (MSM); a total of 506 pharyngeal specimens and 410 rectal specimens were provided for this study. Twenty-two men were diagnosed with syphilis based on serological testing results; further, two more men were diagnosed based on TMA testing results. The authors report that "At least 1 specimen was TMA positive for 12 of 24 men with syphilis (sensitivity, 50% [95% confidence interval [CI], 29 to 71%]). RPR testing and clinical diagnosis were 92% sensitive (95% CI, 73 to 99%) in identifying infected men."[42] A combinatory approach of mucosal TMA testing and serological testing may improve the sensitivity of syphilis screening.

Pham, et al. (2020) reported on a new prototype point-of-care test (POCT) based on detecting IgA antibodies for *Treponema pallidum* (TP-IgA), which is a new biomarker for active syphilis. Using "458 pre-characterised stored plasma in China… and 503 venous blood samples collected from pregnant/postpartum in South Africa," the performance of the POCT was compared against TPHA and RPR tests. In the sub-study group from China, the index test had a sensitivity of 96.1% (95% confidence interval 91.7%-98.5%) and specificity of 84.7% (95% confidence interval 80.1%-88.6%) for "identification of active syphilis," (TPHA positive, RPR positive) and identified 71% samples of past-treated syphilis, defined as a TPHA positive but RPR negative test. In the sub-study group from South Africa, the index test had a 100% sensitivity (95% confidence interval 59%-100%) for active syphilis, and "correctly identified all nine women with past syphilis." The researchers cite that in comparison to other POCTs on the market, this new test can "identify past syphilis whilst maintaining a high sensitivity for active syphilis infections," and "support[s] the global effort in prevention of mother to child transmission and elimination of congenital syphilis in settings where laboratory capacity is limited."[51]

In 2019, Bristow, et al. (2019) compared the use of the Xpert® CT/NG test on extragenital samples to the already FDA-approved APTIMA transcription mediated amplification Combo 2 assay. They found the Xpert® CT/NG test performed similarly, but with a faster turnaround time and increased potential for same-day treatment. Their results demonstrated that "the pooled positive and negative percent agreement for detection of CT in rectal specimens was 89.72% (95% CI: 84.97%, 93.64%) and 99.23% (95% CI: 98.74%, 99.60%), and in pharyngeal specimens, they were 89.96% (95% CI: 66.38%, 99.72%) and 99.62% (95% CI: 98.95%, 99.95%) respectively. For NG detection in rectal specimens, the pooled positive and negative per cent agreement was 92.75% (95% CI: 87.91%, 96.46%) and 99.75% (95% CI:

99.46%, 99.93%), and in pharyngeal specimens, they were 92.51% (95% CI: 85.84%, 97.18%) and 98.56% (95% CI: 97.69%, 99.23%) respectively."[52]

A separate study done earlier by Cosentino, et al. (2017) also compared APTIMA's transcription mediated Combo 2 assay with the Xpert® CT/NG assay and found that "For *C. trachomatis*, neither system was >95% sensitive from the rectum, though both were >99.5% specific. For *N. gonorrhoeae*, Xpert had higher sensitivity than Aptima, but with more false positives from pharyngeal samples."[53]

Clinical Validity and Utility

A 2017 review of POCTs versus near-patient NAAT for chlamydia reviewed 11 different studies consisting of a combined total of more than 13,000 patients. The pooled results show that POCTs have a sensitivity of only 53%, 37%, and 63% for cervical swabs, vaginal swabs, and male urine, respectively, but that the specificity for each ranged from 97-99%. The near-patient NAAT has a sensitivity of >98% regardless of sample with a specificity of 99.4%. "The systematic reviews show that antigen detection POCTs for CT [*C. trachomatis*], although easy to use, lacked sufficient sensitivity to be recommended as a screening test. A near-patient NAAT shows acceptable performance as a screening or diagnostic test but requires electricity, takes 90 min and is costly."[54] Likewise, a review of five POCTs and one near-patient NAAT for gonorrhea in 2017 show that POTC immunochromatographic tests and optical immunoassays had sensitivities ranging from 12.5% to 70% compared to laboratory NAAT for cervical and vaginal swab samples. The specificities of the near-patient NAATs were >99.8% with sensitivities >95%.[55]

A 2018 review of laboratory testing for *T. pallidum* in Australia compared the clinical value of PCR testing for syphilis as compared to the traditional serological testing using RPR, agglutination, and/or chemiluminescence immunoassay (CMIA).[56] This review covered all testing at the Australian lab from 2010 to 2017. They show that 19% of PCR results were positive for syphilis with 97% of those patients also showing positive serological results. The *T. pallidum* PCR had a sensitivity of 68% and specificity of 99% as compared to the serology testing sensitivity of 97% and 88% specificity. "Our results show that most patients with positive *T. pallidum* PCR results also had positive syphilis serology. Therefore, *T. pallidum* PCR adds little clinical value over serology for the diagnosis of syphilis in certain clinical settings."[56] A 2015 Chinese study does show that the CMIA screening is not as specific as the TPPA agglutination assay for syphilis with 18 of the 149 CMIA-positive samples being false-positive results.[57]

The 2016 USPSTF review of genital herpes serological testing included a review of the HerpeSelect serological test consisting of the data from ten studies with a combined total of 6537 participants. The pooled, combined results show a sensitivity of 99% and specificity of 81%. Four additional studies they reviewed used the biokit HSV-2 Rapid Test assay. These studies had a combined total of 1512 participants. The sensitivity is considerably lower (84%), but the specificity was higher than the HerpeSelect assay (95%).[29]

A study by Liu, et al. (2014) evaluated the clinical performance of the QuantiVirus HPV E6/E7 mRNA with respect to identifying ≥Grade 2 cervical intraepithelial neoplasia. Approximately 40.3% of the 335 female patients tested positive for high-risk HPV. They note that "the positivity rate of HPV E6/E7 mRNA increased with the severity of cytological and histological evaluation…a high specificity and a low positivity rate of E6/E7 mRNA testing as a triage test in HPV DNA-positive women can be translated into a low referral for colposcopy."[58] Another study of the QuantiVirus system in 2017 of 404 HPV-positive women show no statistical difference between QuantiVirus and cytological testing in sensitivity, specificity, positive predictive value, and negative predictive value for predicting high-grade squamous intraepithelial lesion (HSIL).[59] "HPV E6/E7 mRNA detection in cervical exfoliated cells shows the same

performance as Pap triage for HSIL identification for HPV-positive women. Detection of HPV E6/E7 mRNA may be used as a new triage option for HPV-positive women."[59] A review by Arbyn and colleagues concerning the efficacy of repeat cytology versus HPV testing for atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesions (LSIL) demonstrated that the pooled sensitivity of the Hybrid Capture 2 (HC2) assay for the high-risk HPV types was significantly higher than performing repeat cytology (relative sensitivity of 1.27 and 1.23, respectively) for detecting CIN2+ but was significantly lower than repeat cytology for LSIL. "HPV-triage with HC2 can be recommended to triage women with ASCUS because it has higher accuracy…than repeat cytology. When triaging women with LSIL, an HC2 test yields a significantly higher sensitivity, but a significantly lower specificity, compared to repeat cytology. Therefore, practice recommendations for management of women with LSIL should be balanced, taking local circumstances into account."[60]

A study by Gaydos, et al. (2019) showed that, for women in the emergency department (ED), the use of rapid diagnostic tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections can improve clinical management. This randomized clinical trial was composed of 254 women undergoing pelvic examinations for both *C. trachomatis* and *N. gonorrhoeae* testing; the women were split into control and rapid test groups. For the rapid test group, the GeneXpert rapid test was used. The authors report that "Undertreatment for both *C trachomatis* and *N gonorrhoeae* in the ED was 0% for the rapid test group and 43.8% for the control standard-of-care group. Clinicians overtreated 46.5% of uninfected standard-of-care control patients for *C trachomatis* compared with 23.1% of uninfected rapid test patients. For patients uninfected with *N gonorrhoeae*, clinicians overtreated 46.7% of standard-of-care control patients compared with 25.4% of rapid test patients."[61] These results show that rapid testing of *C. trachomatis* and *N. gonorrhoeae* led to a significant reduction in overtreatment compared to the control group.

V. Guidelines and Recommendations

National Comprehensive Cancer Network (NCCN)

Anal Carcinoma: HPV, especially high-risk types HPV-16 and HPV-18, are linked to anal carcinoma. The NCCN refers to a study that detected HPV in 84% of anal carcinoma samples and 0% in rectal cancer samples, and they state that "the prevalence of HPV-16/18 to be 72% in patients with invasive anal cancer."[62] Precursor high-grade anal intraepithelial neoplasia "can be identified by cytology, HPV testing, digital rectal examination, high-resolution anoscopy, and/or biopsy."[63] They also state that "data suggest that HPV- and/or p16-positivity are prognostic for improved OS [overall survival] in patients with anal carcinoma." For females, the NCCN also recommends a gynecologic examination, including cervical cancer screening, due to the link between HPV and anal carcinoma.

Cervical Cancer: "Persistent human papillomavirus (HPV) infection is the most important factor in the development of cervical cancer. The incidence of cervical cancer appears to be related to the prevalence of HPV in the population…. Screening methods using HPV testing may increase detection of adenocarcinoma." The NCCN lists chronic, persistent HPV infection along with persistently abnormal Pap tests as criteria to be considered for women contemplating hysterectomy after the completion of child-bearing.[64]

Head and Neck Cancers: The NCCN in the Head and Neck Cancers guidelines now specifically states, "Tumor human papillomavirus (HPV) testing by p16 immunohistochemistry (IHC) required" in their workup for cancer of the oropharynx because the p16 status dictates the treatment options to be

considered (per the ORPH-1 workup). This version of the guidelines also includes a page on the "Principles of P16 Testing for HPV-Mediated Oropharyngeal Cancer" where they state the following:

- "P16 expression correlates with HPV status in geographic regions where HPV is etiologically responsible for a high proportion of cancers. Confirmatory HPV direct testing is recommended, especially for clinical trials. Clinical centers are recommended to ascertain concordance rate of p16 and direct HPV testing, as this may vary by region, if considering use of p16 IHC alone as a surrogate.
- Distinguishing p16+ patients by HPV tumor status informs prognosis. Patients with p16+ and HPV+ tumors have an improved prognosis compared to patients with p16+ and HPV-negative tumors.
- Direct HPV confirmatory tests include polymerase chain reaction (PCR) and RNA in situ hybridization (ISH).
- PCR may provide additional sensitivity while ISH provides increased specificity.
- Sufficient pathologic material for HPV testing can be obtained through FNA.
- A small proportion of tumors at non-oropharyngeal sites (eg, paranasal sinus, oral cavity, larynx) are HPV-related. However, given the small proportion and lack of consistent evidence in support of prognostic significance, routine HPV testing or p16 testing of non-oropharyngeal cancers is not recommended.
- Guidelines for testing are available from the College of American Pathologists.
- When using p16, the 70% cutoff with nuclear and cytoplasmic expression with at least moderate to strong intensity is recommended."[65]

Occult Primary Cancers: The NCCN now lists HPV to be tested for Occult Primary cancers. The NCCN also states that for squamous cell carcinoma with a clinical presentation in the head and neck nodes, "Check results of p16 immunohistochemistry/human papillomavirus (HPV) in situ hybridization (ISH) and Epstein-Barr virus (EBV) (ISH); positive results can help localize primary site." Further, the guidelines note that HPV can be used as a potential immunohistochemistry marker for unknown primary cancers, including tumors identified in the cervix, vulva, vagina, penis, anal, oropharynx; a nuclear (DNA ISH) or nuclear/cytoplasmic (RNA ISH) staining pattern is recommended.[66]

Penile Cancer: "Overall, approximately 45% to 80% of penile cancers are related to HPV, with a strong correlation with types 16, 6 and 18." Discerning whether a penile cancer lesion is infected with HPV is important for laser ablation therapy as noted in the section titled "Principles of Penile Organ-Sparing Approaches." "HPV and HIV status should also be assessed, as HPV or HIV positivity has prognostic significance, could prompt screening for sexual partners, and may be considered in treatment decision making."[67]

Vulvar Cancer: "Risk factors for the development of vulvar neoplasia include increasing age, infection with human papillomavirus (HPV), cigarette smoking, inflammatory conditions affecting the vulva, and immunodeficiency…. Usual-type VIN [vulvar intraepithelial neoplasia] was linked to persistent infection with carcinogenic strains of HPV, while differentiated VIN was commonly associated with vulvar dermatologic conditions such as lichen sclerosus. In 2015, the ISVVD updated the description to three classes of vulvar lesions: 1) low-grade squamous intraepithelial lesion (LSIL) due to flat condyloma or HPV effect; 2) high-grade squamous intraepithelial lesions (HSIL, formerly considered usual-type VIN); and 3) differentiated VIN." The NCCN notes that 80-90% of HSIL cases have HPV infections, and that between 30%-69% of all vulvar cancers are believed to be "attributable to HPV infection." In the "Diagnosis and Workup" section, they state, "Appropriate patients should receive smoking cessation counseling, cervical HPV testing, and cytology testing." The guidelines also note for the surveillance of

vulvar cancer: “Annual cervical/vaginal cytology tests, which may include HPV testing, can be considered as indicated for detection of lower genital tract dysplasia, although its value in detecting recurrent cancers is limited and the likelihood of detecting asymptomatic recurrence is low.” Regarding pathologic assessment for squamous cell carcinoma the NCCN recommends “ancillary testing to determine HPV status either by p16 IHC or RNA sequencing or HPV in situ hybridization (ISH) if available, or DNA sequencing.”[68]

U.S. Preventive Services Task Force (USPSTF)

Screening for Chlamydia and Gonorrhea: The USPSTF recommends (Grade B) to screen for chlamydia and gonorrhea in “sexually active females aged 24 years or younger and in women 25 years or older who are at increased risk for infection.” They also conclude (an “I” statement) “that the current evidence is insufficient to assess the balance of benefits and harms of screening for chlamydia and gonorrhea in men.” Besides age, “women 25 years or older are at increased risk for infection if they have a new sex partner, more than 1 sex partner, a sex partner with concurrent partners, or a sex partner who has an STI; practice inconsistent condom use when not in a mutually monogamous relationship; or have a previous or coexisting STI. Exchanging sex for money or drugs and history of incarceration also are associated with increased risk.” For pregnant individuals, the USPSTF recommends screening for chlamydia and gonorrhea in all sexually active [individuals] 24 years or younger and in [individuals] 25 years or older who are at increased risk for infection.(Grade B).[69] They clearly state that both chlamydia and gonorrhea should be tested using NAATs.[70]

Screening for Oral Cancer: Given the link between HPV infection and oral cancers, the USPSTF released their findings concerning the screening of asymptomatic patients. “The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults.” They also state the following: “Although there is interest in screening for oral HPV infection, medical and dental organizations do not recommend it. Currently, no screening test for oral HPV infection has been approved by the U.S. Food and Drug Administration (FDA). Evaluating the accuracy of tests that detect oral HPV infection is a potentially promising area of research.”[71]

Serological Screening for Genital Herpes: HSV-2 is the primary causative agent of genital herpes, and HSV-2 infection during pregnancy can cause fetal morbidity and mortality. Due to its prevalence in the U.S. and the possible consequences of a genital herpes infection, the USPSTF researched the validity and practicality of HSV-2 screening in asymptomatic patients. They conclude that “serologic screening for genital herpes is associated with a high rate of false-positive test results and potential psychosocial harms. Evidence from RCTs [randomized clinical trials] does not establish whether preventive antiviral medication for asymptomatic HSV-2 infection has benefit.” Overall, the USPSTF “recommends against routine serologic screening for genital herpes simplex virus infection in asymptomatic adolescents and adults, including pregnant persons.”[29]

Screening for Syphilis: Previously, in 2004, the USPSTF “recommended routine screening for syphilis in asymptomatic men and nonpregnant women at increased risk of infection (A recommendation) and recommended against routine screening for those not at increased risk (D recommendation).” The previous study did not address the frequency of repeat testing.[6]

The current 2016 study adds to the previous recommendations. “Screening HIV-positive men or MSM for syphilis every 3-months is associated with improved syphilis detection. Treponemal or nontreponemal tests are accurate screening tests but require confirmation. Research is needed on the

effect of screening on clinical outcomes; effective screening strategies, including reverse sequence screening, in various patient populations; and harms of screening."[6]

In 2022 these recommendations were reaffirmed with the additional recommendation that "screening for syphilis infection in persons who are at increased risk for risk for infection" includes "Asymptomatic, nonpregnant adolescents and adults who are at increased risk for syphilis infection."[72] In their most recent update "The USPSTF recommends early, universal screening for syphilis infection during pregnancy; if an individual is not screened early in pregnancy, the USPSTF recommends screening at the first available opportunity."[73]

Centers for Disease Control and Prevention (CDC)

Diseases Characterized by Genital, Anal, or Perianal Ulcers: "…all persons who have genital, anal, or perianal ulcers should be evaluated; . . . Specific evaluation of genital, anal, or perianal ulcers includes syphilis serology tests and darkfield examination from lesion exudate or tissue, or NAAT if available; NAAT or culture for genital herpes type 1 or 2; and serologic testing for type-specific HSV antibody. In settings where chancroid is prevalent, a NAAT or culture for Haemophilus ducreyi should be performed." Later, in the section specifically focused on genital HSV infections, the CDC states, "Both type-specific virologic and type-specific serologic tests for HSV should be available in clinical settings that provide care to persons with or at risk for STIs." They stress that the patient's prognosis does depend on the type of HSV infection, especially since "recurrences and subclinical shedding are much more frequent for genital HSV-2 infection than for genital HSV-1 infection." Regarding testing, "HSV NAAT assays are the most sensitive tests because they detect HSV from genital ulcers or other mucocutaneous lesions; these tests are increasingly available."[11] NAATs are more sensitive than viral culture testing. On the CDC's detailed fact sheet about genital herpes, they state, "Routine serologic HSV screening of pregnant women is not recommended."[25]

In guidance on serology, the CDC states in 2021 that "type-specific HSV-2 serologic assays for diagnosing HSV-2 are useful in the following scenarios: recurrent or atypical genital symptoms or lesions with a negative HSV PCR or culture result, clinical diagnosis of genital herpes without laboratory confirmation, and a patient's partner has genital herpes. HSV-2 serologic screening among the general population is not recommended. Patients who are at higher risk for infection (e.g., those presenting for an STI evaluation, especially for persons with ≥10 lifetime sex partners, and persons with HIV infection) might need to be assessed for a history of genital herpes symptoms, followed by type-specific HSV serologic assays to diagnose genital herpes for those with genital symptoms."[11] These recommendations were reaffirmed in 2025.[74] In addition, the CDC notes that while a "direct immunofluorescence assay using fluorescein-labeled monoclonal antibodies is also available for detecting HSV antigen from genital specimens, this assay lacks sensitivity and is not recommended."[75]

Syphilis: Darkfield examinations and molecular tests for detecting *T. pallidum* lesion cells, fluid, or tissue are the gold standard methods for diagnosing early syphilis and congenital syphilis. According to the CDC, "Although no *T. pallidum* direct detection molecular NAATs are commercially available, certain laboratories provide locally developed and validated PCR tests for detecting *T. pallidum* DNA. A presumptive diagnosis of syphilis requires use of two laboratory serologic tests: a nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR] test) and a treponemal test (i.e., the T. pallidum passive particle agglutination [TP-PA] assay, various EIAs, chemiluminescence immunoassays [CIAs] and immunoblots, or rapid treponemal assays) … Use of only one type of serologic test (nontreponemal or treponemal) is insufficient for diagnosis and can result in false-negative results among persons tested during primary syphilis and false-positive results among persons without syphilis

or previously treated syphilis." If a patient shows signs and symptoms of neurosyphilis, including "cranial nerve dysfunction, auditory or ophthalmic abnormalities, meningitis, stroke, acute or chronic altered mental status, and loss of vibration sense," further testing is required-CSF cell count or protein and a reactive CSF-VDRL.[11] In 2024, the CDC reaffirmed its 2021 guidance in a comprehensive update to its laboratory recommendations for syphilis testing. The following recommendations reflect current best practices:

- "Serologic tests that measure antibodies to both nontreponemal (lipoidal) and treponemal antigens related to syphilitic infections should be used in combination, when the primary test is reactive, to aid in the diagnosis of syphilis.
- Nontreponemal (lipoidal antigen) and treponemal tests should be interpreted in the same manner regardless of pregnancy status.
- Nontreponemal (lipoidal antigen) and treponemal tests should be interpreted in the same manner regardless of HIV status.
- Darkfield microscopy should be maintained if already in use or established in sexually transmitted diseases clinics where a point-of-care test for primary or secondary syphilis diagnosis would be beneficial for timely patient treatment."[76]

"Patients who receive a diagnosis of syphilis and have neurologic, ocular, and/or otologic symptoms should be evaluated for neurosyphilis, ocular syphilis, or otosyphilis according to their clinical presentation. Patients who have syphilis and symptoms or signs suggestive of neurologic disease (e.g., cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, or motor or sensory deficits) should have an evaluation that includes CSF analysis before treatment. Patients with syphilis who have symptoms or signs of ocular syphilis (e.g., uveitis, iritis, neuroretinitis, or optic neuritis) should have a full ocular slit-lamp and ophthalmologic examination, including a thorough cranial nerve evaluation; if cranial nerve dysfunction is present, CSF examination is indicated."[77] The CDC also recommends that, prior to donating, prospective hematopoietic stem cell transplant donors should be tested for syphilis.[78]

While treponemal tests are clinically useful to confirm results of a reactive nontreponemal tests and are also clinically useful in evaluating patients with early signs suggestive of syphilis when nontreponemal antibodies may not yet be reactive, it is important to note that antibodies detected in treponemal tests typically persist for life despite treatment. Only approximately 15-25% of patients treated early in the course of infection can revert to nonreactive treponemal tests within two to three years after treatment and "no patients treated for secondary syphilis or stages of longer duration of infection seroreverted the reactive treponemal test."[76]

Chlamydial Infections: "Annual screening of all sexually active women aged <25 years is recommended, as is screening of older women at increased risk for infection (e.g., those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has a sexually transmitted infection…screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional facilities, or STD specialty clinics) or for populations with a high burden of infection (e.g., MSM)."[11] The CDC notes that anatomy-based screening recommendations cover gender-diverse individuals with a cervix, under the same guidelines as cisgender women for annual screening if <25 years or at increased risk.[13]

NAAT testing of first-catch urine or swab specimens is recommended. In the diagnostic considerations section of chlamydial infections, the CDC does not address any differences between symptomatic or

asymptomatic screening, and they do not mention any specific diagnostic considerations of patients showing signs or symptoms of a chlamydial infection. In the 2014 CDC guide for laboratory testing of chlamydia and gonorrhea, they, too, recommend using NAATs and not the older nonculture or non-NAAT testing methods. For extragenital infections such as rectal and oropharyngeal infections, the CDC recommends testing at the anatomic exposure site. NAATs demonstrate improved sensitivity and specificity in comparison to culture for extragenital infection. In addition, newly available molecular point-of-care (POC) tests for asymptomatic persons can help with faster, more efficient treatment. With symptomatic cases these POC tests can also "optimize treatment by limiting unnecessary presumptive treatment at the time of clinical decision-making and improve antimicrobial stewardship. Thus, using a POC test will likely be a cost-effective diagnostic strategy for *C. trachomatis* infection… newer NAAT-based POC tests have promising performance and are becoming commercially available."[11] While serological testing and culture are available tests for chlamydia, the CDC notes that serological testing lacks specificity and requires multiple patient visits in a time sensitive sampling manner and culture is only performed in reference laboratories, is time consuming, is not optimal for treatment decisions, and requires confirmation by an additional test such as NAAT.[79]

Gonococcal Infections: The CDC recommendation concerning gonococcal screening is similar to that of chlamydia—sexually active women aged <25 years and older women and men in high-risk categories. "Screening for gonorrhea in men and older women who are at low risk for infection is not recommended."[11] The CDC notes that anatomy-based screening recommendations cover gender-diverse individuals with a cervix, under the same guidelines as cisgender women for annual screening if <25 years or at increased risk.[13] For testing genitourinary infection with N. gonorrhoeae, "culture, NAAT, and POC NAAT, such as GeneXpert (Cepheid), are available." NAAT allows for best testing of genitourinary infection.

Gonorrhea has developed resistance to nearly all the antibiotics used for its treatment, creating a need for research into identifying genetic mutations in the pathogen that are contributing to the antibiotic resistance. However, according to the CDC "currently, there is no well-studied, reliable technology that allows for antibiotic susceptibility testing from nonculture specimens. Increased laboratory culture capacity is needed."[80] CDC recommends that all state and local health department labs maintain or develop the capacity to perform gonorrhea culture, or form partnerships with experienced laboratories that can perform this type of testing. All laboratories serving as part of surveillance or public health response are recommended to maintain culture capabilities, especially for urethral, cervical, ocular, pharyngeal, or rectal specimens.[81]

For rectal, oropharyngeal, and conjunctival infections, culture is available. The CDC states that "NAATs and POC NAATs allow for the widest variety of FDA-cleared specimen types, including endocervical and vaginal swabs and urine for women, urethral swabs and urine for men, and rectal swabs and pharyngeal swabs for men and women. However, product inserts for each NAAT manufacturer should be consulted carefully because collection methods and specimen types vary. Certain NAATs that have been demonstrated to detect commensal Neisseria species might have comparable low specificity when testing oropharyngeal specimens for N. gonorrhoeae. NAAT sensitivity for detecting N. gonorrhoeae from urogenital and nongenital anatomic sites is superior to culture but varies by NAAT type. NAAT testing of rectal and/or oropharyngeal swab specimens can be performed in certain laboratories that have met CLIA requirements even though the testing methodology has not been FDA-approved."[11] Follow-up testing post-treatment for urogenital or rectal gonorrhea is not necessary, but NAAT testing should be performed 14 days after treatment for pharyngeal gonorrhea. Vaginitis is the most common symptom of infection in preadolescent girls."[24]

In the 2014 laboratory guide, the CDC states that "*N. gonorrhoeae* culture capacity is still needed for evaluating suspected cases of treatment failure and monitoring antimicrobial susceptibility." They also state, "*C. trachomatis* and *N. gonorrhoeae* culture capacity might still be needed in instances of child sexual assault in boys and extragenital infections in girls."[82]

Mycoplasma genitalium Infections: The CDC recommends that men with recurrent nongonococcal urethritis (NGU) should be tested for *M. genitalium* using an FDA-cleared NAAT. The CDC also recommends that women with recurrent cervicitis should be tested for *M. genitalium,* while testing should be considered in women with PID. For both, resistance testing is recommended if testing is available. The CDC notes that screening of asymptomatic "*M. genitalium* infection among women and men or extragenital testing for *M. genitalium* is not recommended. In clinical practice, if testing is unavailable, *M. genitalium* should be suspected in cases of persistent or recurrent urethritis or cervicitis and considered for PID."[14]

"*M. genitalium* is an extremely slow-growing organism. Culture can take up to 6 months, and technical laboratory capacity is limited to research settings. NAAT for *M. genitalium* is FDA cleared for use with urine and urethral, penile meatal, endocervical, and vaginal swab samples . . . Molecular tests for macrolide (i.e., azithromycin) or quinolone (i.e., moxifloxacin) resistance markers are not commercially available in the United States. However, molecular assays that incorporate detection of mutations associated with macrolide resistance are under evaluation."[14] The CDC then goes on to add, if available, men with recurrent NGU should be tested for *M. genitalium* using an FDA-cleared NAAT, resistance testing should be performed, and the results used to guide therapy. Women with recurrent cervicitis should be tested for *M. genitalium*, and testing should be considered among women with PID. Testing should be accompanied with resistance testing.[14]

Human Papillomavirus Infections: Even though testing for oncogenic HPV variants exists, the CDC states, "These tests should not be used for male partners of women with HPV or women aged <25 years, for diagnosis of genital warts, or as a general STI test." For patients showing signs and symptoms of anogenital warts, the CDC states, "HPV testing is not recommended for anogenital wart diagnosis, because test results are not confirmatory and do not guide genital wart management." For cervical screening, "For persons aged 30–65 years, a cytology test every 3 years, an HPV test alone every 5 years, or a cytology test plus an HPV test (cotest) every 5 years is recommended."[11]

The CDC (2025) also notes that "Routine screening for women aged 21 to 65 years old can prevent cervical cancer"; further, "There are HPV tests that can be used to screen for cervical cancer. Healthcare providers only use these tests for screening in women aged 30 years and older. HPV tests are not recommended to screen men, adolescents, or women under the age of 30 years."[74]

Finally, the CDC (2019) states that "there is currently no approved test for HPV in men. CDC does not recommend routine testing (also called 'screening') for HPV in men. CDC also does not recommend routine testing for diseases from HPV before there are signs or symptoms in men. Some healthcare providers offer anal Pap tests to men who may be at greater risk for anal cancer. This includes men with HIV or men who receive anal sex. If you have symptoms and are concerned about cancer, please see a healthcare provider."[83]

Trichomoniasis: For the evaluation of trichomoniasis, the CDC recommends: "Diagnostic testing for *T. vaginalis* should be performed for women seeking care for vaginal discharge. Annual screening might be considered for persons receiving care in high-prevalence settings (e.g., STD clinics and correctional facilities) and for asymptomatic women at high risk for infection (e.g., multiple sex partners,

transactional sex, drug misuse, or a history of STIs or incarceration). . . Routine annual screening for T. vaginalis among asymptomatic women with HIV infection is recommended because of these adverse events associated with trichomoniasis and HIV infection. . .Wet-mount microscopy traditionally has been used as the preferred diagnostic test for *T. vaginalis* among women because it is inexpensive and can be performed at the POC; however, it has low sensitivity (44%–68%) compared with culture. . . More highly sensitive and specific molecular diagnostic options are available, which should be used in conjunction with a negative wet mount when possible. NAATs are highly sensitive, detecting more *T. vaginalis* infections than wet-mount microscopy among women. . . The Solana trichomonas assay (Quidel) is another rapid test for the qualitative detection of *T. vaginalis* DNA and can yield results <40 minutes after specimen collection. . . The Amplivue trichomonas assay (Quidel) is another rapid test providing qualitative detection of *T. vaginalis* that has been FDA cleared for vaginal specimens from symptomatic and asymptomatic women."[84]

For follow-up testing after treatment, the CDC recommends: "Because of the high rate of reinfection among women treated for trichomoniasis, retesting for T. vaginalis is recommended for all sexually active women approximately 3 months after initial treatment regardless of whether they believe their sex partners were treated. If retesting at 3 months is not possible, clinicians should retest whenever persons next seek medical care <12 months after initial treatment. Data are insufficient to support retesting men after treatment."[84]

In the updated Sexually Transmitted Infections Treatment Guidelines, the CDC also mentions the FDA-cleared Aptima *T. vaginalis* assay that may be used for detection of *T. vaginalis* from symptomatic or asymptomatic women.[84]

The CDC recommends screening for high-risk asymptomatic individuals: "Consider screening for women receiving care in high-prevalence settings (e.g., STI clinics and correctional facilities) and for asymptomatic women at high risk for infection (e.g., women with multiple sex partners, transactional sex, drug misuse, or a history of STI or incarceration) ." For individuals with HIV, the CDC recommends "for sexually active women at entry to care and at least annually thereafter."[13]

"Trichomoniasis, BV, gonorrhea, and chlamydia are the most frequently diagnosed infections among women who have been sexually assaulted. Such conditions are prevalent among the population, and detection of these infections after an assault does not necessarily imply acquisition during the assault. However, a postassault examination presents an important opportunity for identifying or preventing an STI."[85]

Pregnancy

The Centers for Disease Control and Prevention (CDC) recommends:[13]

Disease	Recommendations for Pregnant Individuals
Chlamydia	All pregnant individuals under 25 years of age Pregnant individuals 25 years of age and older if at increased risk* Retest during the 3rd trimester for individuals under 25 years of age or at risk Pregnant individuals with chlamydial infection should have a test of cure 4 weeks after treatment and be retested within 3 months
Gonorrhea	All pregnant individuals under 25 years of age, and those 25 and older if at increased risk* Retest during the 3rd trimester for individuals under 25 years of age or at risk

	Pregnant individuals with gonorrhea should be retested within 3 months
Syphilis	All pregnant individuals at the first prenatal visit Retest at 28 weeks gestation and at delivery if at increased risk due to geography or personal risk (substance use, STIs during pregnancy, multiple partners, a new partner, partner with STIs
Herpes†	Routine HSV-2 serologic screening among asymptomatic pregnant individuals is not recommended. However, type-specific serologic tests might be useful for identifying pregnant individuals at risk for HSV infection and guiding counseling regarding the risk for acquiring genital herpes during pregnancy.

"* Per USPSTF, sexually active [individuals] 25 years or older are at increased risk for chlamydial and gonococcal infections if they have a new partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI; practice inconsistent condom use when not in a mutually monogamous relationship; have a previous or coexisting STI; have a history of exchanging sex for money or drugs; or have a history of incarceration.

† Type-specific HSV-2 serologic assays for diagnosing HSV-2 are useful in the following scenarios: recurrent or atypical genital symptoms or lesions with a negative HSV PCR or culture result, clinical diagnosis of genital herpes without laboratory confirmation, and a patient's partner has genital herpes. HSV-2 serologic screening among the general population is not recommended. Patients who are at higher risk for infection (e.g., those presenting for an STI evaluation, especially for persons with ≥10 lifetime sex partners, and persons with HIV infection) might need to be assessed for a history of genital herpes symptoms, followed by type-specific HSV serologic assays to diagnose genital herpes for those with genital symptoms."[13]

- "Everyone who is pregnant should be tested for syphilis, HIV, hepatitis B, and hepatitis C starting early in pregnancy. Repeat testing may be needed."[86]
- Pregnant people at risk should also be tested for chlamydia and gonorrhea starting early in pregnancy. Repeat testing may be needed in some cases."[86]
- "[individuals] aged <25 years and those at increased risk for chlamydia (i.e., those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI) should be screened at the first prenatal visit and rescreened during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant."[87]
- "Prenatal screening for some infections (HIV, syphilis, hepatitis B virus, and hepatitis C virus) is recommended for all pregnant [individuals]. Screening for other infections (chlamydia, gonorrhea, and TB) is recommended for some [individuals] at risk for infection."[88]

Preexposure prophylaxis (PrEP)

PrEP is the use of antiretroviral medication to prevent HIV. It is intended for people without HIV who may be exposed to the virus through sex or injection drug use. The CDC recommends "PrEP as part of a comprehensive HIV prevention plan that includes discussing how to take PrEP as prescribed, proper condom use, screening for other sexually transmitted infections (STIs), and other risk-reduction methods."[32] To ensure patients do not acquire HIV while on PrEP, the CDC recommends to "repeat HIV antigen/antibody and HIV-1 RNA tests and assess for signs or symptoms of acute HIV infection to confirm that patients do not have HIV" "at least every 3 months."

Prior to initiating PrEP, the CDC recommends to screen for other STIs (chlamydia, gonorrhea, and syphilis) and recommends serology screening to detect hepatitis B, as individuals with an active HBV infection may require additional monitoring if they begin and then stop PrEP. Additionally, CDC guidance

recommends screening "sexually active people for STIs (vaginal, oral, rectal, urine, as indicated; blood): syphilis and gonorrhea for all PrEP users; chlamydia for MSM and transgender women, even if asymptomatic … at least every 6 months." Heterosexually active people should be screened "for chlamydia (vaginal, urine), even if asymptomatic … at least every 12 months."[32]

International Union Against Sexually Transmitted Infections (IUSTI)

The Management of Anogenital Warts (European): "HPV detection or typing does not influence management and is not recommended. Some practitioners use the acetic acid test to diagnose sub-clinical HPV lesions; its place in diagnosis and management is uncertain."[89]

The Diagnosis and Treatment of Gonorrhea in Adults NAATs, bacterial culture, and microscopy can be used in the diagnosis of uncomplicated gonorrhea. "No test offers 100% sensitivity and specificity." They do state (with a grade C recommendation) that microscopy can be used for testing symptomatic men, but it is not recommended for use in asymptomatic men, rectal infection, or endocervical infection due to low sensitivity. Culture testing is the only method to use for determining antimicrobial susceptibility, but culture testing is not as sensitive as NAAT. For NAAT-based point-of-care tests (POCTs), the guideline says: "several NAAT-based POCTs with high sensitivity and specificity are in late development."[19] The IUSTI includes the following list for "Indications for testing" (grade C recommendation):

- Symptoms or signs of urethral discharge in men;
- Vaginal discharge with risk factor for STI (age <30 years, new sexual partner);
- Mucopurulent cervicitis;
- Persons diagnosed with any other STI;
- Sexual partner of persons with an STI or PID;
- Acute epididymo-orchitis in a male aged <40 years;
- Acute pelvic inflammatory disease;
- When screening young adults (<25 years of age) for sexually transmitted infections;
- When screening individuals with new or multiple recent sexual partners;
- Purulent conjunctivitis in a neonate or adult;
- Mother of a newborn with ophthalmia neonatorum
- Unplanned termination of pregnancy in places or populations of high gonorrhoea prevalence
- When intrauterine interventions are performed in areas of high gonorrhoea prevalence

The Management of Lymphogranuloma Venereum: Lymphogranuloma venereum (LGV) is a condition caused by chlamydia. The clinical features can vary, depending on the site of inoculation (genital versus rectum) and can include hemorrhagic proctitis, lymphadenopathy, papule or pustule formation, and buboes. Reactive inflammatory responses or physical signs of in infection may include "constitutional symptoms such as low-grade fever, chills, malaise, myalgia, [and] arthralgia." Regarding a diagnosis of lymphogranuloma venereum (LGV), "a sample tested *C. trachomatis* positive with a commercial nucleic acid amplification test (NAAT) platform should be confirmed with an LGV discriminatory NAAT." Further, "For sensitive and specific detection of LGV genovar (L1, L2 and L3, including subvariant)-specific *C. trachomatis* DNA, laboratories are currently recommended to use a two-step procedure (1,B):

- "A commercially available NAAT is used to detect *C. trachomatis* DNA/RNA in suspected clinical samples. These tests cannot discriminate between LGV and non-LGV genovars. Although no commercially available *C. trachomatis* NAATs are FDA-cleared for extragenital specimens, for several NAATs sufficient evidence supports the use of these tests for the detection of C.

trachomatis DNA/RNA also in rectal and pharyngeal *C. trachomatis* infections. Some *C. trachomatis* NAAT are CE-labelled for use on rectal and pharyngeal samples in Europe.

- If *C. trachomatis* DNA/RNA is detected, LGV genovar specific *C. trachomatis* DNA should be detected from the same specimen. There are multiplex NAATs for genital ulcerative disease that detect LGV but these have not yet been appropriately evaluated in the context of rectal LGV. Different in-house or laboratory-developed NAATs have been designed and used. The sensitivities of these NAATs are generally lower than the commercially available *C. trachomatis* screening NAAT."[90]

The Management of Syphilis: The three stages (primary, secondary, and tertiary) can be overlapping. Primary syphilis begins with appearance of an ulcer (also known as a chancre), usually in the anogenital region with regional lymphadenopathy. "Any anogenital ulcer should be considered syphilitic unless proven otherwise." The secondary stage is characterized by "multisystem involvement due to bacteriaemia, within the first year but may recur up into the second year after infection" and can include skin rash, generalized lymphadenopathy, arthritis, hepatitis, splenomegaly, and kidney dysfunction. Early neurosyphilis can occur in secondary syphilis and can include "meningitis, cranial nerve palsies, auricular and ophthalmic abnormalities (such as uveitis, retinitis, otitis and papillar oedema)."[23,91] They list the following as conditions of tertiary syphilis:

- "Gummatous syphilis: nodules/plaques or ulcers (skin, mucosae, visceral)"
- "Late neurosyphilis encompasses meningitis, cranial nerve dysfunction, meningovascular syphilis (stroke, myelitis) and parenchymatous neurosyphilis (general paresis, tabes dorsalis)"
- "Cardiovascular syphilis: aortic regurgitation, stenosis of coronary ostia, aortic aneurysm (mainly thoracic)"

The following guidelines were given regarding laboratory testing for *T. pallidum:*

- "Direct detection methods provide definitive diagnosis of syphilis.
- Darkfield examination (DFE) of chancres and erosive cutaneous lesions was the old gold standard method for definitive diagnosis. It gives immediate results. However, the method is labor intensive, subjective, and can result in some false positive and (many) false negative results. Due to the availability of more sensitive and specific tests (specifically the PCR), it is not recommended for routine diagnosis anymore.
- Polymerase chain reaction (PCR) testing is the preferred method particularly but not exclusively for oral and other lesions where contamination with commensal treponemes is likely. It can be performed using tissues, cerebrospinal fluid (CSF) or blood (although insensitive in the latter). There is no internationally approved PCR assay for *T. pallidum* and accordingly, it is crucial to select a strictly validated and quality-assured method and always use it with appropriate quality controls.
- Immunohistochemistry using a polyclonal antibody against *T. pallidum* can be efficient to identify treponemes in skin, mucosal and tissue lesions, but it is not suitable for routine diagnosis.
- Hybridization in tissues is not used for routine diagnosis.
- Warthin-Starry (argentic) staining on tissues is very difficult to perform and of limited value in most cases.
- (Direct fluorescent antibody test is obsolete)
- For molecular epidemiological typing, PCR, PCR-restriction fragment length polymorphism (RFLP) and/or DNA-sequencing (e.g. multilocus sequence typing (MLST) or whole genome sequencing)

can be performed on clinical specimens. However, due to the highly conserved genome of *T. pallidum* the discriminatory ability of typing methods is in general low."[91]

Primary Screening Test(s)

- "TT [TPHA, MHA-TP, TPPA or EIA/ELISA/CLIA] – a TT-based screening algorithm, using by preference an automatized EIA/ELISA/CLIA, is used in many large, well-resourced European laboratories and is particularly suitable for automated high-throughput screening of asymptomatic populations including blood/plasma donors. The algorithm identifies persons with previous successful treatment of syphilis as well as those with untreated syphilis. It is usually more sensitive in detecting very early syphilis compared to the use of a screening NTT. However, it can also result in a high number of false positive tests (i.e. very low positive predictive value) in low-prevalence populations.
- NTT [RPR or VDRL] – a NTT-based screening algorithm; preferably quantitative (i.e. to detect prozone phenomenon in infectious syphilis), is still recommended in some countries. In this algorithm, only active syphilis is detected, however, it has a lower sensitivity compared to using a TT as primary screening test, and in particular very early syphilis can be missed.
- TT combined with a NTT - this algorithm is particularly useful in cases where the suspicion of very early syphilis is high (recent chancre, contacts of syphilis cases etc.), because in some patients NTT may become reactive before TT."[91]

Confirmatory test(s) if any screening test is positive

- "In the case a TT being used alone as a primary screening test, if positive, a confirmatory TT of a different type is of limited value in informing treatment, but a reflex quantitative NTT (reaching at least 1:8 to 1:16 dilution) should be performed in all cases on the same serum (1, B). Although a confirmatory TT may be important for counselling, notification and may have a psychological impact, it has limited impact on treatment.69 In patients with a positive TT, a negative NTT and no suspicion of very early syphilis (no chancre), both tests should be repeated after 1 month (1, D). However, CLIA and EIA used in many European settings have suboptimal specificity, resulting in a low positive predictive value in low prevalence population. If such tests are used, additionally a reflex confirmatory test by TPHA or TPPA should be performed (1, C).
- In the case a NTT alone is used as a primary screening test, a positive test must be followed by a reflex TT on the same serum. If quantitative NTT was not initially done, the NTT should be repeated quantitatively (1, B).
- In the case both a TT and a NTT are used as primary screening tests such as (EIA/ELISA/CLIA/TPHA/TPPA plus VDRL/RPR), the NTT must be performed quantitatively (if not initially done) in case of positive or discrepant screening tests (1, B).
- The IgG-immunoblot for Treponema pallidum has no added major value to other TT. It is expensive and interpretation of undetermined immunoblot is elusive (1 to 4 bands).

The Management of Chlamydia Trachomatis Infections: With a Grade 1 recommendation, they recommend using NAATs that identify specific nucleic acid, either DNA or RNA) *of C. trachomatis* "due to their superior sensitivity, specificity, and speed."[92]

The following list contains the indications for laboratory testing (Level of evidence: high certainty; Grade 1 recommendation)

- Symptoms or signs of urethritis

- Cervical or vaginal discharge with risk factors for STI
- Acute epididymo-orchitis in a male aged <40 years or with risk factors for STI
- Acute pelvic pain and/or symptoms or signs of PID
- Proctitis/proctocolitis with risk factors for STI
- Purulent or follicular conjunctivitis in a neonate or adult
- Atypical neonatal pneumonia

The following list contains the indications for laboratory testing (Level of evidence: low certainty; Grade 2 recommendation)

The available evidence regarding asymptomatic screening to prevent longer-term adverse outcomes and reduce population spread is weak or absent

- Risk factor(s) for C. trachomatis infection and/or other STI (age <25 years, new sexual contact in the last year, more than one partner in the last year)
- Diagnosis of other STIs, including human papillomavirus or bacterial vaginosis (BV)
- Termination of pregnancy
- Prior to any transcervical procedure e.g. intrauterine interventions or manipulations
- Sexual contact of persons with a C. trachomatis infection or other STI or PID

The Management of Genital Herpes: The principle changes to the IUSTI guidelines in this recent version is that "HSV DNA detection is now considered the gold standard for diagnosis." With a grade D recommendation, "serological testing is not routinely recommended in asymptomatic patients." They note that there are specific groups where it may be useful, including symptomatic pregnant women (B), sexual partners of HSV-positive people (A), those with a history of recurrent or atypical genital disease (C), and those with first-episode genital herpes whose differentiation may aid in counseling and management (C) (because seroconversion happens typically at 90 days post-infection).[93]

Male Training Center for Family Planning & Reproductive Health (MTC), Office of Population Affairs, Department of Health and Human Services

In general, the MTC recommends at least annual testing for chlamydia, gonorrhea, syphilis, HIV/AIDS, and Hepatitis C for anyone in an at-risk population, including MSM. For syphilis, certain populations require testing at 3-6 month intervals, including those who exchange sex for drugs, commercial sex workers, and young MSM.

The MTC does not recommend screening for pharyngeal chlamydia infections. They do recommend follow-up test three months after initial positive chlamydia test. They recommend using a urine-based NAAT for chlamydia for at-risk male populations under the age of 25, which include MSM, patients at STI clinics, and military personnel (under the age of 30), and inmates entering jails or detention centers (under the age of 30). Men who have had receptive anal intercourse in the preceding year should have a NAAT performed on a rectal swab to check for rectal chlamydial infection.

The MTC recommends using NAAT for gonorrhea testing of at-risk male adolescents and adults, including MSM. "Males with gonorrhea infection should be re-screened for reinfection at 3 months." Annual exams for MSM include screening for urethral infections, pharyngeal infections using NAAT for those "who have had receptive oral intercourse" during the preceding year, and rectal infections using NAAT of rectal swabs for those "who have had receptive anal intercourse" during the preceding year.

"More frequent STD screening (i.e., at 3 – 6 month intervals) is indicated for MSM who have multiple or anonymous partners."[63]

Public Health Agency of Canada (PHAC)

The Public Health Agency of Canada (PHAC) provides public health guidance for the prevention and management of sexually transmitted and blood-borne infections (STBBI). PHAC's STBBI guides outline recommendations for a variety of STBBIs as follows:
Anogenital warts (AGW)

- "AGW are usually diagnosed by visual inspection. Confirmation of diagnosis with biopsy should be considered for atypical or recalcitrant AGW. HPV testing is not recommended for people with AGW, as results would not alter clinical management or treatment."[94]

Chlamydia trachomatis infections including lymphogranuloma venereum (LGV)

- "Nucleic acid amplification tests (NAAT) are the most sensitive tests for detecting *C. trachomatis*.
- Screen females using NAAT on vaginal or cervical swabs, or first-void urine. Screen males using NAAT on first-void urine. As appropriate, obtain specimens from exposed extra-genital sites (pharyngeal or rectal swabs).
- Definitive diagnosis of LGV requires genotyping. Request genotyping for *C. trachomatis*-positive specimens in people who have symptoms consistent with LGV and in sexual partners of people diagnosed with LGV."[95]

Genital herpes

- "In symptomatic people, herpes is commonly diagnosed with viral identification techniques such as the Nucleic Acid Amplification Test (NAAT) or viral culture.
- If testing is not possible or testing of a symptomatic person yields negative results, HSV type-specific serology (TSS) may be useful for diagnosis. TSS testing can identify the need for preventive measures by demonstrating whether partners are serodifferent (both partners have HSV, but different types), serodiscordant (only one partner has HSV) or concordant (both partners have the same HSV type)."[96]

Gonorrhea

- "Nucleic acid amplification tests (NAAT) are the most sensitive tests for detecting *N. gonorrhoeae*. NAAT can be done on first-void urine samples or vaginal, cervical and urethral swabs. For extra-genital specimens, check with local laboratory about the availability of NAAT.
- Although culture is less sensitive than NAAT, it provides antimicrobial susceptibility information, which is important for optimizing treatment and public health monitoring of antimicrobial resistance trends."[97]

Mycoplasma genitalium

- "Nucleic acid amplification tests (NAAT) for *M. genitalium* may be done on urine, cervical, vaginal, urethral or meatal swabs and endometrial biopsies."[98]

Syphilis

- "Syphilis is usually diagnosed through serology regardless of suspected stage of infection. Interpretation of serology results can be complex, and different testing algorithms may be useby provinces and territories. Consult with your local laboratory regarding testing protocols."[99]

American Academy of Pediatrics (AAP)

Chlamydia: The AAP recommends annual screening for sexually active females 25 years old or younger. They also recommend annual urethral and rectal chlamydia screenings for sexually active MSM, but more frequent screening (every 3-6 months) for those who are in a higher risk category, such as multiple partners, sex-for-drugs, and so on. Anyone who has been exposed to chlamydia in the past 60 days should also be tested. "Consider screening sexually active males annually in settings with high prevalence rates, such as jails or juvenile corrections facilities, national job training programs, STD clinics, high school clinics, and adolescent clinics for patients who have a history of multiple partners." Anyone who has tested positive for chlamydia should be retested three months after receiving treatment.

Gonorrhea: Similar to chlamydia, the AAP recommends annual screening for sexually active females under the age of 25. "Routinely screen sexually active adolescent and young adults MSM for pharyngeal, rectal, and urethral gonorrhea infection annually if engaging in receptive oral or anal intercourse or insertive intercourse, respectively." Again, like chlamydial infections, those participating in higher risk activities should be tested every three to six months. Anyone who has been exposed to gonorrhea in the past 60 days should also be tested. Finally, the screening recommendations for other males are similar to the recommendations concerning chlamydial infections. Anyone who has tested positive for gonorrhea should be retested three months after receiving treatment.

Syphilis: "The routine screening of nonpregnant, heterosexual adolescents is not recommended. However, screening is recommended for all sexually active adolescent and young adults MSM annually or every 3 to 6 months if high risk and can be considered for youth whose behaviors put them at higher risk."[100]

National Institute for Health and Care Excellence (NICE)

The NICE released their guidelines concerning cancer of the upper aerodigestive tract in 2016 (with updates in 2018 online). Recommendation 1.6.1: "Test all squamous cell carcinomas of the oropharynx using p16 immunohistochemistry. Regard the p16 test result as positive only if there is strong nuclear and cytoplasmic staining in more than 70% of tumour cells." In Recommendation 1.6.2: "Consider high-risk HPV DNA or RNA in-situ hybridisation in all p16-positive cancers of the oropharynx to confirm HPV status." In explaining their recommendations, NICE states, "HPV testing is currently recommended in cancer of the oropharynx because it has significant prognostic implication."[101]

In 2022, NICE released a guideline on reducing sexually transmitted infections geared towards preventive interventions for STIs n people 16 years and older. The guideline includes ways to help increase the uptake of STI testing and raise awareness of pre-exposure prophylaxis for HIV. Regarding improvements in the frequency of STI testing the NICE recommends increasing self sampling. "Offer a range of STI testing options based on local need, including remote self-sampling, in-person attendance at specialist clinics or in community pharmacies, primary care, and outreach services. Offer people without symptoms remote self-sampling as an alternative option to clinic attendance. Self-sampling should test for the same infections as those tested for at the clinic."[102]

There is also a strong recommendation that clinics "promote HPV, hepatitis A and hepatitis B vaccination with gay, bisexual and other men who have sex with men who are eligible for the vaccines." There is an increasing need to raise awareness of pre-exposure prophylaxis (PrEP) for HIV and NICE recommends healthcare professionals "Support people who are taking PrEP, for example in decisions around the use of barrier methods and attending follow-up appointments. Continue to offer them all other relevant sexual health services, such as information, behavioral support and condom provision and Support people who are taking PrEP to get regular HIV testing and STI screening (every 3 months)."[102]

Canadian Paediatric Society (CPS)

The 2024 update to the CPS practice point titled "Diagnosis and management of congenital syphilis – Avoiding missed opportunities" included the following:

> "The potential for asymptomatic syphilis infection and its nonspecific or subtle maternal disease manifestations make serology the cornerstone of diagnosis. At a minimum, syphilis serology is recommended at the time of the first prenatal visit, with recommendations for repeat testing at 28 to 32 weeks and at delivery in areas with outbreaks or for individuals with ongoing risk of infection. Repeat testing should also be performed in the context of clinical suspicion of maternal reinfection, a new maternal STI at any point during pregnancy (e.g., gonorrhea, chlamydia), in case of a stillbirth after 20 weeks gestation, or in accordance with provincial/territorial guidelines. Newborn infants ideally should not be discharged from hospital until results of maternal syphilis testing are known and appropriate steps for management are arranged."[103]

The CPS published "Comprehensive sexual health assessments for adolescents", which includes the following screening recommendations:[104]

Table 2. Recommended STI screening for asymptomatic immunocompetent youth

Specimens	Testing	Population to test
First catch urine* (*refers to first part of urinary stream) OR Urethral or cervical swab OR Vaginal swab (may be self-collected)	NAAT for: Chalmydia trachomatis AND Neisseria Gonorrhoeae (NG)	All sexually active youth<25 years
Pharyngeal swab	Culture for Chlamydia and NG (and/or NAAT if available in local lab)	Those who have performed oral sex
Anal swab Insert swab 2 to 3 cm into the anal canal, press laterally to sample epithelium. If visible fecal contamination, discard the swab and obtain another	Culture for Chlamydia and NG (and/or NAAT if available in local lab)	Those who report anal receptive intercourse (including MSM)

British Association for Sexual Health and HIV

UK National Guideline for the Management of Lymphogranuloma Venereum: "Commercial molecular diagnostic techniques to detect *C. trachomatis* remain the primary test of choice, with referral of *C.*

trachomatis-positive specimens for molecular tests to confirm the presence of LGV-associated DNA." Testing should be performed on anyone exhibiting symptoms of an LGV infection, including hemorrhagic proctitis, primary lesions, suspected LGV-associated pharyngitis, secondary lesions, buboes, lymphadenitis, and/or lymphadenopathy. Main diagnostic techniques include using either NAATs, "culture on cycloheximide-treated McCoy cells of material from suspected LGV lesions," or serology testing. "Serology cannot necessarily distinguish past from current LGV infection, which might prove restrictive given the high number of recurrent LGV infections now seen in MSM."[105]

UK National Guideline for the Management of Anogenital Herpe : The clinical signs and symptoms of an HSV infection can include "painful ulceration, dysuria, vaginal or urethral discharge" as well as systemic symptoms of fever and myalgia. Other signs can include bilateral lymphadenitis—although, alternating sides can occur in subsequent episodes—and proctitis. With a Grade 1A recommendation, "The confirmation and typing of the infection and its type, by direct detection of HSV in genital lesions, are essential for diagnosis, prognosis, counselling, and management." BASHH gives a "1B" recommendation of directly testing swabs from either the base of the anogenital lesions or the rectal mucosa in suspected proctitis. They recommend with a "1B" rating that virus typing be performed to differentiate HSV-1 from HSV-2 in newly diagnosed cases of genital herpes. NAATs are the preferred testing method (grade "1A" recommendation) since HSV culture tests can miss around 30% of PCR-positive samples.[106]

UK National Guideline for the Management of Infection with Chlamydia Trachomatis (updated 2018): "Testing for genital and extra-genital chlamydia should be performed using NAATs (Grade B)." MSM who test positive for both HIV and chlamydia should be tested for LGV even if asymptomatic for the latter (Grade B). They give a Grade B recommendation for LGV testing in patients presenting with proctitis and a Grade C recommendation for treating both sexes presenting with proctitis the same.[107]

The guidelines were updated in 2018, but NAAT testing is still considered the current standard of care for all chlamydia cases by the BASHH; "Although no test is 100% sensitive or specific, NAATs are known to be more sensitive and specific than EIAs."[108]

UK National Guidelines on the Management of Syphilis (updated 2024): They recommend (2A) "where appropriate expertise and equipment are available, dark ground microscopy should be performed on possible chancres" and (1A) that "molecular testing for *T. pallidum* is appropriate on lesions where the organism may be expected to be located." Within the section on serology, they recommend (1B) that "An EIA/CLIA detecting both IgM and IgG is the screening test of choice"; "positive screening tests should be confirmed with a different treponemal test (not the FTA-abs) and a second specimen for confirmatory testing obtained" (1B); "a quantitative RPR should be performed when screening tests are positive" (1A); and (1B) negative serological tests for syphilis should be repeated at two weeks after observation of possible chancres that are dark ground microscopy and/or PCR negative.[109]

Infectious Diseases Working Party of the German Society for Hematology and Medical Oncology (AGIHO/DGHO) and the German Working Group for Blood and Marrow Transplantation (DAG-KBT)

In 2016, the AGIHO/DGHO and the DAG-KBT released the "Infectious diseases in allogeneic haematopoietic stem cell transplantation: prevention and prophylaxis strategy guidelines 2016." In this guideline, they note that "comprehensive pre-transplant assessment of the allogeneic haematopoietic stem cell transplantation (allo-HCT) recipient for infectious complications is a valuable tool to identify patients at increased risk for distinct infectious diseases. All candidates for allo-HCT should undergo a test for IgG antibodies specific for syphilis infection. Serologic testing for syphilis is recommended. Frequently TPHA/TPPA or VDRL are utilized. Important are the combinations of nontreponemal (e.g.

VDRL) and treponemal tests. If a nontreponemal test is positive, confirmation of infection with treponemal test (e.g. TPPA or TP-EIA) should be performed."[110]

Cumulative Guideline Table

Year & Society	Condition	Microorganism	Recommendation
2026 NCCN	Anal Carcinoma	HPV	HPV linked to anal cancers and HPV positivity linked to positive OS
2026 NCCN	Cervical Cancer	HPV	Overwhelming evidence of link between HPV and cervical cancer; chronic HPV infection status used in aiding treatment/surgical options
2026 NCCN	Head and Neck Cancers/ Oropharyngeal Cancer	HPV	Requires HPV p16 testing by IHC; HPV status is imperative in determining therapy
2026 NCCN	Occult Primary Cancers (Squamous Cell Carcinoma)	HPV	If clinical presentation in the head and neck nodes is noted, check p16 IHC and ISH results
2026 NCCN	Penile Cancer	HPV	HPV linked to penile cancer; HPV status of lesions important for determining therapy
2026 NCCN	Vulvar Cancer (Squamous Cell Carcinoma)	HPV	HPV linked to vulvar cancer, especially HSIL; recommends HPV testing for "appropriate patients"
2021 USPSTF	NA	Chlamydia, Gonorrhea	Testing in sexually active women age 24 or younger and older women of at-risk populations; insufficient evidence concerning routinely screening in general population of males
2014 USPSTF	Oropharyngeal Cancer	HPV	Insufficient evidence to assess testing for HPV in cases of asymptomatic oropharyngeal cancer
2016 USPSTF	Asymptomatic Genital Herpes	HSV-2	Do not recommend testing asymptomatic patients for HSV-2
2016 USPSTF	NA	Syphilis	Grade A recommendation for screening asymptomatic patients of HIGH RISK categories but they do NOT recommend screening in asymptomatic patients not in high risk categories; recommend screening HIV-positive men and MSM every three months
2021 CDC	Genital, Anal, or Perianal Ulcers	Syphilis, HSV	Recommends syphilis serology, darkfield exam, or PCR testing if possible; culture or PCR for genital herpes; serologic testing for type-specific HSV antibody

Year & Society	Condition	Microorganism	Recommendation
2021 CDC	NA	Syphilis	Darkfield examination of exudate can be used for early diagnosis; presumptive diagnosis requires use of two tests—both a treponemal test and a non-treponemal test; any signs of CNS infection require additional testing
2021 CDC	NA	Chlamydia	Testing of women under age of 25 as well as older women and men if they fall in a high-risk category; do NOT recommend testing of asymptomatic men and older women
2021 CDC	NA	Gonorrhea	Testing of women under age of 25 as well as older women and men if they fall in a high-risk category; do NOT recommend testing of asymptomatic men and older women; men showing signs of urethral gonococcal infection should be tested
2021 CDC	NA	HPV	Recommends against using oncogenic HPV testing for asymptomatic men, women aged 25 and over, or for general STI testing. There is no approved test for HPV in men, and routine testing is not recommended for anal, penile, or throat cancers in men.
2021 CDC	Anogenital Warts	HPV	"HPV testing is not recommended for anogenital wart diagnosis, because test results are not confirmatory and do not guide genital wart management."
2021 CDC	Cervical Screening	HPV	For women aged 30 or older, HPV testing can be part of cervical screening. For women ages 30-65, if co-testing Pap test and HR-HPV, then frequency is every 5 years…if only doing a Pap test, the frequency is every 3 years HPV tests to screen for cervical cancer are recommended for women 30 years and older. They are not recommended to screen, men, adolescents, or women under the age of 30.
2019 IUSTI	Anogenital Warts	HPV	Do not recommend HPV testing for symptomatic anogenital warts since it adds no information for clinical use.

Year & Society	Condition	Microorganism	Recommendation
2020 IUSTI	NA	Gonorrhea	Culture testing is only method to determine antimicrobial susceptibility, but NAAT testing is more sensitive. Includes list of symptoms for testing.
2019 IUSTI	Lymphogranuloma venereum	Chlamydia	To diagnose LGV, a sample tested *C. trachomatis* positive with a commercial nucleic acid amplification test (NAAT) platform should be confirmed with an LGV discriminatory NAAT. For sensitive and specific LGV detection, laboratories are recommended to use a two-step procedure.
2014, 2020 IUSTI	NA	Syphilis	Like the CDC, they recommend a two-test method for diagnosing syphilis (one non-Treponema test and one Treponema test) if any initial screening test is positive
2015 IUSTI (published in 2016)	NA	Chlamydia	Recommends using an NAAT for chlamydia testing and lists signs/symptoms that require testing
2017 IUSTI	Genital herpes	HSV	Typically, does not recommend testing in asymptomatic patients; HSV DNA detection now replaces culture as gold standard
2014 MTC	NA	Chlamydia	Do not recommend pharyngeal screenings. Do recommend NAAT of at-risk groups with a 3-month follow-up test for patients who tested positive
2014 MTC	NA	Gonorrhea	Do recommend annual NAAT of at-risk groups with a 3-month follow-up test for patients who tested positive; more frequent testing in certain MSM populations
2014 MTC	NA	Syphilis	Do recommend annual testing of at-risk groups with 3-6 month testing of certain populations (commercial sex workers, inmates of correctional facilities, persons who exchange sex for drugs, and so on)
2017 Canadian Guidelines on STIs	NA	Chlamydia, Syphilis, Gonorrhea, HSV, and HPV	NAATs are more specific and sensitive than culture testing when available. For gonorrheal infections, only culture can test for antimicrobial susceptibility in gonorrhea.

Year & Society	Condition	Microorganism	Recommendation
2014 AAP	Adolescents & young adults	Chlamydia, Gonorrhea	All sexually active young women (under the age of 25) and MSM should have annual screenings. For those at higher risk, they should be screened every 3-6 months. Anyone who tests positive should be retested 3 months after receiving treatment.
2014 AAP	Adolescents & young adults	Syphilis	Do NOT recommend routine screening except for sexually active young MSM.
2016 NICE	Oropharyngeal Cancers	HPV	Test all carcinomas of the oropharynx using p16 IHC; consider using high-risk HPV DNA/RNA in situ hybridization in all p16-positive cancers
2018 CPS	Pregnant women	Syphilis	Testing at first prenatal visit as well as 28-32 weeks; if not tested during pregnancy, child does not leave the hospital without being tested
2020 CPS	Adolescents/young adults	Chlamydia, Syphilis, Gonorrhea	See detailed testing and frequency in table within the guidelines above
2015 BASHH (published in 2016)	NA	Syphilis	Dark-field microscopy or PCR tests can be performed. For serology, EIA/CLIA is the screening test of choice (preferably where both IgM and IgG are detected). Positive tests must be followed by a quantitative RPR or VDRL.
2013 BASHH	Suspected LGV	Chlamydia	Testing should use either NAAT, culture testing, or serology; however, the latter cannot distinguish current from past infections.
2014 BASHH (published in 2015)	Anogenital herpes	HSV	NAAT is preferred over other forms of testing (“A” grade). Differentiation of virus type should be determined on new cases of genital herpes (“B” grade).
2015, 2018 BASHH	NA	Chlamydia	Test for chlamydia using NAATs. Both sexes presenting with proctitis should be treated the same with respect to LGV testing. HIV-positive men with chlamydia should also be tested for LGV, even if asymptomatic.

Abbreviations: CLIA = chemiluminescent assay; EIA = enzyme immunoassay; GC = gonococcal; HPV = human papillomavirus; HR-HPV = high risk or oncogenic HPV testing; HSIL = high-grade squamous intraepithelial lesions; HSV = herpes simplex virus; IHC = immunohistochemistry; LGV = lymphogranuloma venereum; MSM = men having sex with men; NA = not applicable; NAAT = nucleic acid amplification testing; OS = overall survival; RPR = rapid plasma reagin test; VDRL = Venereal Diseases Research Laboratory carbon antigen test

VI. Applicable State and Federal Regulations

Food and Drug Administration (FDA)

The FDA has approved many tests for HSV, chlamydia, gonorrhea, and syphilis. Some of these tests are discussed in the "Proprietary Testing" section of this policy. In addition to these tests, many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

VII. Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment.

CPT	Code Description
86592	Syphilis test, non-treponemal antibody; qualitative (eg, VDRL, RPR, ART)
86593	Syphilis test, non-treponemal antibody; quantitative
86631	Antibody; Chlamydia
86632	Antibody; Chlamydia, IGM
86694	Antibody; herpes simplex, non-specific type test
86695	Antibody; herpes simplex, type 1
86696	Antibody; herpes simplex, type 2
86780	Antibody; Treponema pallidum
87081	Culture, presumptive, pathogenic organisms, screening only
87110	Culture, Chlamydia, any source
87140	Culture, typing; immunofluorescent method, each antiserum
87181	Susceptibility studies, antimicrobial agent; agar dilution method, per agent (eg, antibiotic gradient strip)
87270	Infectious agent antigen detection by immunofluorescent technique; Chlamydia trachomatis
87285	Infectious agent antigen detection by immunofluorescent technique; Treponema pallidum
87320	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Chlamydia trachomatis
87490	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, direct probe technique
87491	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, amplified probe technique
87492	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, quantification
87494	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis and Neisseria gonorrhoeae, multiplex amplified probe technique

CPT	Code Description
87528	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, direct probe technique
87529	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, amplified probe technique
87530	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, quantification
87563	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma genitalium, amplified probe technique
87590	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, direct probe technique
87591	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, amplified probe technique
87592	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, quantification
87623	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), low-risk types (eg, 6, 11, 42, 43, 44)
87624	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), high-risk types (eg, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68), pooled result
87625	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), types 16 and 18 only, includes type 45, if performed
87626	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), separately reported high-risk types (eg, 16, 18, 31, 45, 51, 52) and high-risk pooled result(s)
87660	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, direct probe technique
87661	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, amplified probe technique
87797	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; direct probe technique, each organism
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87799	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; quantification, each organism
87800	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; direct probe(s) technique
87808	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Trichomonas vaginalis
87810	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; Chlamydia trachomatis
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (list separately in addition to code for primary procedure)
88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure

CPT	Code Description
88344	Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure
0064U	Antibody, Treponema pallidum, total and rapid plasma reagin (RPR), immunoassay, qualitative Proprietary test: BioPlex 2200 Syphilis Total & RPR Assay Lab/Manufacturer: Bio-Rad Laboratories
0065U	Syphilis test, non-treponemal antibody, immunoassay, qualitative (RPR) Proprietary test: BioPlex 2200 RPR Assay Lab/Manufacturer: Bio-Rad Laboratories
0096U	Human papillomavirus (HPV), high-risk types (ie, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68), male urine Proprietary test: HPV, High-Risk, Male Urine Lab/Manufacturer: Molecular Testing Labs/Roche Cobas
0210U	Syphilis test, non-treponemal antibody, immunoassay, quantitative (RPR) Proprietary test: BioPlex 2200 RPR Assay - Quantitative Lab/Manufacturer: Bio-Rad Laboratories
0402U	Infectious agent (sexually transmitted infection), Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, Mycoplasma genitalium, multiplex amplified probe technique, vaginal, endocervical, or male urine, each pathogen reported as detected or not detected Proprietary test: Abbott Alinity™ m STI Assay Lab/Manufacturer: Abbott Molecular, Inc
0455U	Infectious agents (sexually transmitted infection), Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis, multiplex amplified probe technique, vaginal, endocervical, gynecological specimens, oropharyngeal swabs, rectal swabs, female or male urine, each pathogen reported as detected or not detected Proprietary test: Abbott AlinityTM m STI Assay Lab/Manufacturer: Abbott Molecular, Inc
0463U	Oncology (cervix), mRNA gene expression profiling of 14 biomarkers (E6 and E7 of the highest-risk human papillomavirus [HPV] types 16, 18, 31, 33, 45, 52, 58), by real-time nucleic acid sequence-based amplification (NASBA), exo- or endocervical epithelial cells, algorithm reported as positive or negative for increased risk of cervical dysplasia or cancer for each biomarker Proprietary test: Proofer '7 HPV mRNA E6 and E7 Biomarker Test Lab/Manufacturer: Global Diagnostics Labs, LLC, PreTect AS, a Mel-Mont Medical, Inc
0483U	Infectious disease (Neisseria gonorrhoeae), sensitivity, ciprofloxacin resistance (gyrA S91F point mutation), oral, rectal, or vaginal swab, algorithm reported as probability of fluoroquinolone resistance Proprietary test: Ciprofloxacin Susceptibility of Neisseria gonorrhoeae Lab/Manufacturer: MedArbor Diagnostics, SpeeDx, Inc
0484U	Infectious disease (Mycoplasma genitalium), macrolide sensitivity (23S rRNA point mutation), oral, rectal, or vaginal swab, algorithm reported as probability of macrolide resistance Proprietary test: Macrolide Resistance of Mycoplasma genitalium Lab/Manufacturer: MedArbor Diagnostics, SpeeDx, Inc

Current Procedural Terminology© American Medical Association. All Rights reserved.

VIII. Evidence-based Scientific References

1. Ghanem KG, Tuddenham S. Screening for sexually transmitted infections. Updated December 16, 2025. https://www.uptodate.com/contents/screening-for-sexually-transmitted-infections
2. Palefsky JM. Human papillomavirus infections: Epidemiology and disease associations. Updated February 25, 2025. https://www.uptodate.com/contents/human-papillomavirus-infections-epidemiology-and-disease-associations
3. Albrecht MA. Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus infection. Updated October 28, 2024. https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-genital-herpes-simplex-virus-infection
4. CDC. Sexually Transmitted Infections Treatment Guidelines, 2021 - Adolescents. Updated July 22, 2021. https://www.cdc.gov/std/treatment-guidelines/adolescents.htm
5. CDC. About Syphilis. Updated January 30, 2025. https://www.cdc.gov/syphilis/about/index.html
6. Cantor AG, Pappas M, Daeges M, Nelson HD. Screening for syphilis: Updated evidence report and systematic review for the us preventive services task force. *JAMA*. 2016;315(21):2328-2337. doi:10.1001/jama.2016.4114
7. CDC. Syphilis (Treponema pallidum): 2018 Case Definition. Updated August 16, 2021. https://ndc.services.cdc.gov/case-definitions/syphilis-2018/
8. CDC. About Chlamydia. Updated January 31, 2025. https://www.cdc.gov/chlamydia/about/index.html
9. LeFevre ML. Screening for Chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Annals of internal medicine*. Dec 16 2014;161(12):902-10. doi:10.7326/m14-1981
10. CDC. About Gonorrhea. Updated January 31, 2025. https://www.cdc.gov/gonorrhea/about/index.html
11. CDC. Sexually Transmitted Infections Treatment Guidelines, 2021. Updated July 23, 2021. https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf
12. CDC. About Trichomoniasis. Updated January 31, 2025. https://www.cdc.gov/trichomoniasis/about/index.html
13. CDC. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. Updated March 22, 2024. https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm
14. CDC. Mycoplasma genitalium. Updated July 22, 2021. https://www.cdc.gov/std/treatment-guidelines/mycoplasmagenitalium.htm
15. Hsu K. Clinical manifestations and diagnosis of Chlamydia trachomatis infections in adults and adolescents. Updated May 1, 2024. https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-chlamydia-trachomatis-infections-in-adults-and-adolescents
16. CDC. Sexually Transmitted Infections Surveillance, 2024 (Provisional). Updated Sept. 24 2025. https://www.cdc.gov/sti-statistics/annual/index.html
17. Goldstein E, Martinez-García L, Obermeier M, et al. Simultaneous identification of Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium, and Trichomonas vaginalis–multicenter evaluation of the Alinity m STI assay. *Journal of Laboratory Medicine*. 2021;45(4-5):213-223. doi:10.1515/labmed-2020-0136
18. Ghanem KG. Clinical manifestations and diagnosis of Neisseria gonorrhoeae infection in adults and adolescents. Updated March 6, 2026. https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-neisseria-gonorrhoeae-infection-in-adults-and-adolescents

19. Unemo M, Ross J, Serwin AB, Gomberg M, Cusini M, Jensen JS. 2020 European guideline for the diagnosis and treatment of gonorrhoea in adults. *Int J STD AIDS*. Oct 29 2020:956462420949126. doi:10.1177/0956462420949126
20. WHO. Syphilis. Updated May 29, 2025. https://www.who.int/news-room/fact-sheets/detail/syphilis
21. Hicks CB, Clement M. Syphilis: Epidemiology, pathophysiology, and clinical manifestations in patients without HIV. Updated December 20, 2023. https://www.uptodate.com/contents/syphilis-epidemiology-pathophysiology-and-clinical-manifestations-in-patients-without-hiv
22. Hicks CB, Clement M. Syphilis: Screening and diagnostic testing. Updated August 21, 2024. https://www.uptodate.com/contents/syphilis-screening-and-diagnostic-testing
23. Janier M, Hegyi V, Dupin N, et al. 2014 European guideline on the management of syphilis. *Journal of the European Academy of Dermatology and Venereology : JEADV*. Dec 2014;28(12):1581-93. doi:10.1111/jdv.12734
24. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports*. Jun 5 2015;64(Rr-03):1-137.
25. CDC. About Genital Herpes. Updated February 20, 2024. https://www.cdc.gov/herpes/about/index.html
26. Riley LE, Wald A. Genital herpes simplex virus infection and pregnancy. Updated October 17, 2024. https://www.uptodate.com/contents/genital-herpes-simplex-virus-infection-and-pregnancy
27. CDC. About Genital HPV Infection. Updated January 31, 2025. https://www.cdc.gov/sti/about/about-genital-hpv-infection.html
28. Feldman S, Crum CP. Cervical cancer screening tests: Techniques for cervical cytology and human papillomavirus testing. Updated November 20, 2025. https://www.uptodate.com/contents/cervical-cancer-screening-tests-techniques-for-cervical-cytology-and-human-papillomavirus-testing
29. USPSTF. Genital Herpes Infection: Serologic Screening. Updated February 14, 2023. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/genital-herpes-serologic-screening
30. USPSTF. Prevention of Acquisition of HIV: Preexposure Prophylaxis. Updated August 22, 2023. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis#citation47
31. WHO. Global HIV & AIDS statistics — Fact sheet. https://www.unaids.org/en/resources/fact-sheet
32. CDC. Clinical Guidance for PrEP. Updated February 10, 2025. https://www.cdc.gov/hivnexus/hcp/prep/index.html
33. BD. BD receives FDA Approval for HPV Test with Extended Genotyping Capabilities. https://www.bd.com/en-us/company/news-and-media/press-releases/july-22-2020-bd-receives-fda-approval-for-hpv-test-with-extended-genotyping-capabilities
34. FDA. BD ONCLARITY HPV ASSAY. https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pma&id=391601
35. FDA. 501(k) Premarket Notification Xpert CT/NG. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K121710
36. FDA. 501(k) Premarket Notification Xpert CT/NG, GeneXpert Dx System, GeneXpert Infinity-48s and GeneXpert Infinity-80 Systems, GeneXpert Infinity-48 System, Xpert Vaginal/Endocervical Specimen Collection, Xpert Urine Specimen Collection Kit, Xpert Swab Specimen Collection Kit. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K190441
37. FDA. 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY K121710. https://www.accessdata.fda.gov/cdrh_docs/reviews/K121710.pdf
38. FDA. 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY K190441. https://www.accessdata.fda.gov/cdrh_docs/reviews/K190441.pdf

39. Cepheid. Xpert® CT/NG. https://www.cepheid.com/Package%20Insert%20Files/Xpert-CTNG-US-ENGLISH-Package-Insert-301-0234--Rev-K.pdf
40. Abbott. Alinity m STI AMP Kit. https://www.molecularcatalog.abbott/int/en/alinity-m-sti-assay
41. Cook RL, Hutchison SL, Ostergaard L, Braithwaite RS, Ness RB. Systematic review: noninvasive testing for Chlamydia trachomatis and Neisseria gonorrhoeae. *Annals of internal medicine*. Jun 7 2005;142(11):914-25. doi:10.7326/0003-4819-142-11-200506070-00010
42. Golden M, O'Donnell M, Lukehart S, et al. Treponema pallidum Nucleic Acid Amplification Testing To Augment Syphilis Screening among Men Who Have Sex with Men. *J Clin Microbiol*. Aug 2019;57(8)doi:10.1128/jcm.00572-19
43. Wong EH, Klausner JD, Caguin-Grygiel G, et al. Evaluation of an IgM/IgG sensitive enzyme immunoassay and the utility of index values for the screening of syphilis infection in a high-risk population. *Sexually transmitted diseases*. Jun 2011;38(6):528-32. doi:10.1097/OLQ.0b013e318205491a
44. Tsang RS, Martin IE, Lau A, Sawatzky P. Serological diagnosis of syphilis: comparison of the Trep-Chek IgG enzyme immunoassay with other screening and confirmatory tests. *FEMS immunology and medical microbiology*. Oct 2007;51(1):118-24. doi:10.1111/j.1574-695X.2007.00289.x
45. Juarez-Figueroa L, Uribe-Salas F, Garcia-Cisneros S, Olamendi-Portugal M, Conde-Glez CJ. Evaluation of a rapid strip and a particle agglutination tests for syphilis diagnosis. *Diagnostic microbiology and infectious disease*. Oct 2007;59(2):123-6. doi:10.1016/j.diagmicrobio.2007.04.008
46. Feltner C, Grodensky C, Ebel C, et al. Serologic Screening for Genital Herpes: An Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. Dec 20 2016;316(23):2531-2543. doi:10.1001/jama.2016.17138
47. Glass N, Nelson, Heidi D. Screening for Genital Herpes Simplex: A Brief Update for the U.S. Preventive Services Task Force. Updated December 20, 2023. https://www.uspreventiveservicestaskforce.org/Home/GetFile/1/733/herpesup/pdf
48. Castle PE, Stoler MH, Wright TC, Jr., Sharma A, Wright TL, Behrens CM. Performance of carcinogenic human papillomavirus (HPV) testing and HPV16 or HPV18 genotyping for cervical cancer screening of women aged 25 years and older: a subanalysis of the ATHENA study. *The Lancet Oncology*. Sep 2011;12(9):880-90. doi:10.1016/s1470-2045(11)70188-7
49. Guenat D, Launay S, Riethmuller D, Mougin C, Pretet JL. Validation of Novaprep((R)) HQ+ liquid-based cytology medium for high-risk human papillomavirus detection by hc2. *Infectious agents and cancer*. 2016;11:41. doi:10.1186/s13027-016-0092-7
50. Tshomo U, Franceschi S, Tshokey T, et al. Evaluation of the performance of Human Papillomavirus testing in paired urine and clinician-collected cervical samples among women aged over 30 years in Bhutan. *Virology journal*. Apr 8 2017;14(1):74. doi:10.1186/s12985-017-0744-2
51. Pham MD, Wise A, Garcia ML, et al. Improving the coverage and accuracy of syphilis testing: The development of a novel rapid, point-of-care test for confirmatory testing of active syphilis infection and its early evaluation in China and South Africa. *EClinicalMedicine*. Jul 2020;24:100440. doi:10.1016/j.eclinm.2020.100440
52. Bristow CC, Morris SR, Little SJ, Mehta SR, Klausner JD. Meta-analysis of the Cepheid Xpert(®) CT/NG assay for extragenital detection of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) infections. *Sex Health*. Aug 2019;16(4):314-319. doi:10.1071/sh18079
53. Cosentino LA, Danby CS, Rabe LK, et al. Use of Nucleic Acid Amplification Testing for Diagnosis of Extragenital Sexually Transmitted Infections. *J Clin Microbiol*. Sep 2017;55(9):2801-2807. doi:10.1128/jcm.00616-17
54. Kelly H, Coltart CEM, Pant Pai N, et al. Systematic reviews of point-of-care tests for the diagnosis of urogenital Chlamydia trachomatis infections. *Sexually transmitted infections*. Dec 2017;93(S4):S22-s30. doi:10.1136/sextrans-2016-053067

55. Guy RJ, Causer LM, Klausner JD, et al. Performance and operational characteristics of point-of-care tests for the diagnosis of urogenital gonococcal infections. *Sexually transmitted infections*. Dec 2017;93(S4):S16-s21. doi:10.1136/sextrans-2017-053192
56. Brischetto A, Gassiep I, Whiley D, Norton R. Retrospective Review of Treponema pallidum PCR and Serology Results: Are Both Tests Necessary? *J Clin Microbiol*. May 2018;56(5)doi:10.1128/jcm.01782-17
57. Zhiyan L, Meiling W, Ping L, Jinhua D, Zhenlin Y, Zhenru F. Consistency Between Treponema pallidum Particle Agglutination Assay and Architect Chemiluminescent Microparticle Immunoassay and Characterization of Inconsistent Samples. *Journal of clinical laboratory analysis*. Jul 2015;29(4):281-4. doi:10.1002/jcla.21765
58. Liu TY, Xie R, Luo L, et al. Diagnostic validity of human papillomavirus E6/E7 mRNA test in cervical cytological samples. *Journal of virological methods*. Feb 2014;196:120-5. doi:10.1016/j.jviromet.2013.10.032
59. Yao YL, Tian QF, Cheng B, Cheng YF, Ye J, Lu WG. Human papillomavirus (HPV) E6/E7 mRNA detection in cervical exfoliated cells: a potential triage for HPV-positive women. *Journal of Zhejiang University Science B*. Mar. 2017;18(3):256-262. doi:10.1631/jzus.B1600288
60. Arbyn M, Roelens J, Simoens C, et al. Human papillomavirus testing versus repeat cytology for triage of minor cytological cervical lesions. *The Cochrane database of systematic reviews*. Mar 28 2013;(3):Cd008054. doi:10.1002/14651858.CD008054.pub2
61. Gaydos CA, Ako MC, Lewis M, Hsieh YH, Rothman RE, Dugas AF. Use of a Rapid Diagnostic for Chlamydia trachomatis and Neisseria gonorrhoeae for Women in the Emergency Department Can Improve Clinical Management: Report of a Randomized Clinical Trial. *Ann Emerg Med*. Jul 2019;74(1):36-44. doi:10.1016/j.annemergmed.2018.09.012
62. NCCN. NCCN Clinical Practice Guidelines in Oncology Anal Carcinoma. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf
63. Marcell AV, Health MTCfFPaR. Preventive Male Sexual and Reproductive Health Care: Recommendations for Clinical Practice. https://californiaptc.com/wp-content/uploads/2019/12/Preventative-Male-Sexual-and-Reproductive-Health-Care.pdf
64. NCCN. NCCN Clinical Practice Guidelines in Oncology Cervical Cancer. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf
65. NCCN. NCCN Clinical Practice Guidelines in Oncology Head and Neck Cancers https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
66. NCCN. NCCN Clinical Practice Guidelines Occult Primary (Cancer of Unknown Primary [CUP]). https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf
67. NCCN. NCCN Clinical Practice Guidelines in Oncology Penile Cancer https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf
68. NCCN. NCCN Clinical Practice Guidelines in Oncology Vulvar Cancer (Squamous Cell Carcinoma). https://www.nccn.org/professionals/physician_gls/pdf/vulvar.pdf
69. USPSTF. Screening for Chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. Updated September 14, 2021. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/chlamydia-and-gonorrhea-screening
70. USPSTF. Chlamydia and Gonorrhea: Screening. Updated September 14, 2021. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/chlamydia-and-gonorrhea-screening
71. Moyer VA. Screening for oral cancer: U.S. preventive services task force recommendation statement. *Annals of internal medicine*. 2014;160(1):55-60. doi:10.7326/M13-2568

72. Force UPST. Screening for Syphilis Infection in Nonpregnant Adolescents and Adults: US Preventive Services Task Force Reaffirmation Recommendation Statement. *JAMA*. 2022;328(12):1243-1249. doi:10.1001/jama.2022.15322
73. Force UPST. Screening for Syphilis Infection During Pregnancy: US Preventive Services Task Force Reaffirmation Recommendation Statement. *JAMA*. 2025;333(22):2006-2012. doi:10.1001/jama.2025.5009
74. CDC. Clinical Guidance for STIs. Updated July 18, 2025. https://www.cdc.gov/sti/hcp/clinical-guidance/index.html
75. CDC. Genital Herpes. Updated September 21, 2022. https://www.cdc.gov/std/treatment-guidelines/herpes.htm
76. Papp JR PI, Fakile Y, Pereira L, Pillay A, Bolan GA. CDC Laboratory Recommendations for Syphilis Testing. *CDC MMWR Recomm Rep 2024*. 2024;73(No. RR-1):1–32doi:10.15585/mmwr.rr7301a1
77. CDC. Neurosyphilis, Ocular Syphilis, and Otosyphilis. Updated March 7, 2024. https://www.cdc.gov/syphilis/hcp/neurosyphilis-ocular-syphilis-otosyphilis/
78. Dykewicz CA, Jaffe HW, Kaplan JE. Guidelines for Preventing Opportunistic Infections Among Hematopoietic Stem Cell Transplant Recipients. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr4910a1.htm
79. CDC. Laboratory Testing for Chlamydia pneumoniae. Updated September 17, 2025. https://www.cdc.gov/cpneumoniae/php/laboratories/index.html
80. CDC. Drug-Resistant Gonorrhea. Updated February 15, 2024. https://www.cdc.gov/gonorrhea/hcp/drug-resistant/index.html
81. CDC. Gonococcal Isolate Surveillance Project (GISP) Profiles. Updated April 15, 2025. https://www.cdc.gov/sti-statistics/gisp-profiles/index.html
82. Papp JR, Schachter J, Gaydos CA, Van Der Pol B. Recommendations for the laboratory-based detection of Chlamydia trachomatis and Neisseria gonorrhoeae--2014. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports*. Mar 14 2014;63(Rr-02):1-19.
83. CDC. HPV & Men Fact Sheet. Updated April 18, 2022. https://www.ihs.gov/sites/nptc/themes/responsive2017/display_objects/documents/sti_community/CDC-%20STD%20Facts%20-%20HPV%20and%20Men.pdf
84. CDC. Trichomoniasis. Updated September 21, 2022. https://www.cdc.gov/std/treatment-guidelines/trichomoniasis.htm
85. CDC. Sexual Assault and Abuse and STIs – Adolescents and Adults. Updated July 22, 2021. https://www.cdc.gov/std/treatment-guidelines/sexual-assault-adults.htm
86. CDC. Getting Tested for STIs. Updated January 31, 2025. https://www.cdc.gov/sti/testing/index.html
87. CDC. STI Treatment Guidelines, 2021- Chlamydial Infection. Updated July 22, 2021. https://www.cdc.gov/std/treatment-guidelines/chlamydia.htm
88. CDC. HIV, Viral Hepatitis, STD & Tuberculosis Prevention in Pregnancy. Updated January 25, 2024. https://www.cdc.gov/pregnancy-hiv-std-tb-hepatitis/about/index.html
89. Gilson R, Nugent D, Werner RN, Ballesteros J, Ross J. 2019 IUSTI-Europe guideline for the management of anogenital warts. *Journal of the European Academy of Dermatology and Venereology : JEADV*. Aug 2020;34(8):1644-1653. doi:10.1111/jdv.16522
90. de Vries HJC, de Barbeyrac B, de Vrieze NHN, et al. 2019 European guideline on the management of lymphogranuloma venereum. *Journal of the European Academy of Dermatology and Venereology : JEADV*. Oct 2019;33(10):1821-1828. doi:10.1111/jdv.15729
91. Janier M, Unemo M, Dupin N, Tiplica GS, Potocnik M, Patel R. 2020 European guideline on the management of syphilis. *Acta Clin Belg*. Jun 6 2020;doi:10.1080/17843286.2020.1773112

92. John A White NHD-M, Christian JPA, Hoebe CRK, Jonathan DC Ross and Magnus, Unemo. 2025 European guideline on the management of Chlamydia trachomatis infections. *Int J STD AIDS*. 2025;doi:10.1177/09564624251323678
93. Patel R, Moran B, Clarke E, et al. 2024 European guidelines for the management of genital herpes. *Int J STD AIDS*. 2024;doi:10.1111/jdv.20450
94. Public Health Agency of Canada. Anogenital warts guide: Key information and resourcess. Public Health Agency of Canada. Updated Febuary 20, 2025. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/anogenital-warts.html
95. Public Health Agency of Canada. Chlamydia and LGV guide: Key information and resources. Updated Febuary 20, 2025. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/chlamydia-lgv.html
96. Public Health Agency of Canada. Genital herpes guide: Key information and resources. Updated December 12, 2021. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/herpes-simplex-virus.html
97. Public Health Agency of Canada. Gonorrhea guide: Key information and resources. Updated December 23, 2024. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/gonorrhea.html
98. Public Health Agency of Canada. Mycoplasma Genitalium guide: Key information and resources. Updated December 22, 2021. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/mycoplasma-genitalium.html
99. Public Health Agency of Canada. Syphilis guide: Key information and resources. Updated April 15, 2025. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html
100. Murray P, Braverman P, Adelman W, et al. Screening for nonviral sexually transmitted infections in adolescents and young adults. *Pediatrics*. Jul 2014;134(1):e302-11. doi:10.1542/peds.2014-1024
101. NICE. National Institute for Health and Care Excellence: Clinical Guidelines. *Cancer of the Upper Aerodigestive Tract: Assessment and Management in People Aged 16 and Over*. National Institute for Health and Care Excellence (UK) Copyright (c) National Collaborating Centre for Cancer.; 2018.
102. NICE. Reducing sexually transmitted infections. Updated June 15, 2022. https://www.nice.org.uk/guidance/ng221
103. Society CP. Diagnosis and management of congenital syphilis – Avoiding missed opportunities. Updated March 28, 2024. https://www.cps.ca/en/documents/position/congenital-syphilis
104. Canadian Paediatric Society. Comprehensive sexual health assessments for adolescents. Updated December 7, 2020. https://cps.ca/en/documents/position/comprehensive-sexual-health-assessments-for-adolescents
105. White J, O'Farrell N, Daniels D. 2013 UK National Guideline for the management of lymphogranuloma venereum: Clinical Effectiveness Group of the British Association for Sexual Health and HIV (CEG/BASHH) Guideline development group. *Int J STD AIDS*. Aug 2013;24(8):593-601. doi:10.1177/0956462413482811
106. Patel R, Green J, Moran B, et al. British Association of Sexual Health and HIV UK national guideline for the management of anogenital herpes, 2024. *Int J STD AIDS*. 2024;0(0):1-16. doi:10.1177/09564624241282396
107. Nwokolo NC, Dragovic B, Patel S, Tong CY, Barker G, Radcliffe K. 2015 UK national guideline for the management of infection with Chlamydia trachomatis. *Int J STD AIDS*. Mar 2016;27(4):251-67. doi:10.1177/0956462415615443

108. BASHH. Update on the treatment of Chlamydia trachomatis (CT) infection. Updated September 2018. https://www.bashh.org/_userfiles/pages/files/resources/updateonthetreatmentofchlamydiatrachomatisinfectionfinal16918.pdf
109. Kingston M, Apea V, Evans C, et al. BASHH UK guidelines for the management of syphilis 2024. *Int J STD AIDS*. 2024;0(0):1-19. doi:10.1177/09564624241280406
110. Ullmann AJ, Schmidt-Hieber M, Bertz H, et al. Infectious diseases in allogeneic haematopoietic stem cell transplantation: prevention and prophylaxis strategy guidelines 2016. *Ann Hematol*. Sep 2016;95(9):1435-55. doi:10.1007/s00277-016-2711-1

IX. Revision History

Revision Date	Summary of Changes
01/01/2022	Initial Effective Date
05/20/2022	Updated background, guidelines, and evidence-based scientific references. Literature review did not necessitate any modifications to the coverage criteria. Removal of CPT codes 82565 and 82575. Added codes 86701- 86706, 86780, 86803, 86804, 87340, 0167u, G0432, G0433 G0435, G0472. G0499, and S3645.
04/04/2023	Updated background, guidelines, and evidence-based scientific references. Literature review necessitated the following changes in coverage criteria: References to specific STI testing in pregnant individuals was removed, as this is covered under G2035. Note added to the end of the "Policy Description" to reflect this: "For STI screening in pregnant individuals, please see Avalon Policy AHS-G2035Prenatal Screening (Nongenetic)." New CC10: "When an individual meets the conditions described above for both chlamydia and gonorrhea, multitarget PCR testing (targets limited to C. trachomatis and N. gonorrhoeae) MEETS COVERAGE CRITERIA." CC16 and CC17 were removed, as coverage for T. vaginalis is addressed in M2057-Diagnosis of Vaginitis including Multi-target PCR Testing. Note added to "Policy Description" to reflect this change. The following edits were made for clarity: CC2, 5, and 9, language changed from "DNMCC except for the following" to "MCC only for the following situations" to match the overall formatting of the rest of our CC. All CC edited for clarity and consistency of sentence structure Added CPT codes 0353U, 0354U. Removed CPT codes 87660, 87661, 87808 Committee Approved: 04/04/2023
06/28/2023	Off-Cycle Review: Updates to the G2042-Pediatric Preventive Screening resulted in changes to this policy. No further updates outside of the CC. Due to concerns with the specificity of the vaginitis policy being specific to vaginitis and not the broader implications of T. vaginalis in all individuals, coverage for T. vaginalis outside of vaginitis has been restored to this policy. Policy description changed to note that while the policy covers T. vaginalis "T. vaginalis (for guidance on T. vaginalis in vaginitis, see AHS M2057-Diagnosis of Vaginitis Including Multi-Target PCR Testing)" **Addition of CC17 and 18: "17) NAATs or PCR-based testing for T. vaginalis MEETS COVERAGE CRITERIA in the following situations: a) Symptomatic individuals (see Note 7).

	b) Asymptomatic individuals belonging to a high-risk group: i) Concurrent STI or history of STIs. ii) Individuals in high prevalence settings, such as STI clinics. iii) Individuals who exchange sex for payment. **18) Rapid identification of Trichomonas by enzyme immunoassay DOES NOT MEET COVERAGE CRITERIA." CC2, CC5, and CC9, which address screening for syphilis, chlamydia, and gonorrhea, respectively, in asymptomatic individuals without high-risk factors, new subcriteria: "c) For sexually active individuals less than 18 years of age (annually)." was added. HPV testing as a cervical cancer screen is addressed in G2002. Thus, it has been removed as a subcriteria, making the CC a single approved HPV test under this policy: "15) In the diagnosis and/or assessment of cancer or cancer therapy (immunohistochemistry testing for p16 or NAAT testing for high-risk human papillomavirus [HR-HPV]), testing for HR-HPV MEETS COVERAGE CRITERIA." Addition of new Note 1: "Note 1: For sexually active children and adolescents under the age of 18, risk factors for chlamydia, gonorrhea, and/or syphilis infection as defined by the CDC include: initiating sex early in adolescence; living in detention facilities; receiving services at STD clinics; being involved in commercial sex exploitation or exchanging sex for drugs, money, food, or housing; having multiple sex partners, having sequential sex partnerships of limited duration or concurrent partnerships; failing to use barrier protection consistently and correctly; having lower socioeconomic status, and facing numerous obstacles to accessing healthcare. At-risk individuals also include: males who have sex with males (YMSM); transgender youths; youths with disabilities, substance abuse, or mental health disorders (CDC, 2022b)." This resulted in a change to other note numbers, which were adjusted accordingly within CC. HSV-1 and HSV-2: replaced written out name for consistency of CC structure in CC12, CC13, and CC14. Added CPT codes 87660, 87661, 87808 Committee Approved: 06/28/2023
12/07/2023	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review necessitated the following changes to coverage criteria: Addition of CC 1d: "d) Treponemal Ig testing and nontreponemal testing (once prior to transplant) as a part of a pre-transplant assessment in both donors and recipients of an allogeneic hematopoietic stem cell transplantation (allo-HCT)." Addition of bullet points to Note 3, signs and symptoms of neuro, ocular, and otosyphilis and late/tertiary syphilis: "• Signs and symptoms of neurosyphilis can include severe headache, trouble with muscle movements, muscle weakness or paralysis (not being able to move certain parts of the body), numbness, and changes in mental status (trouble focusing, confusion, personality change) and/or dementia (problems with memory, thinking, and/or making decisions). • Signs and symptoms of ocular syphilis can include eye pain or redness, floating spots in the field of vision ("floaters"), sensitivity to light, and changes in vision (blurry vision or even blindness).

	• Signs and symptoms of otosyphilis may include hearing loss, ringing, buzzing, roaring, or hissing in the ears ("tinnitus"), balance difficulties, and dizziness or vertigo. • Signs and symptoms of late/tertiary syphilis include inflammatory lesions of the cardiovascular system (e.g., aortitis, coronary vessel disease), skin (e.g., gummatous lesions), and bone (e.g., osteitis)." Moved Trichomonas CC from being CC17/18 to being CC10/11. Addition of new CC12 and CC13: "12) For symptomatic individuals (see Note 8), testing for Mycoplasma genitalium using NAAT MEETS COVERAGE CRITERIA. 13) For asymptomatic individuals (see Note 8), screening for M. genitalium using NAAT DOES NOT MEET COVERAGE CRITERIA." Former CC10, now CC14, edited to expand panel coverage from chlamydia and gonorrhea to those plus trichomonas and M.genitalium. CC now reads: "14) When an individual meets any of the conditions described above, multitarget PCR testing (targets limited to C. trachomatis, N. gonorrhoeae, T. vaginalis, and M.genitalium) MEETS COVERAGE CRITERIA." Added CPT code 87563, 0402U Committee Approved: 12/07/2023
10/21/2024	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review necessitated the following changes to coverage criteria: New CC23: "23) Nucleic acid testing to determine antimicrobial susceptibility in N. gonorrhoeae or macrolide resistance in M. genitalium DOES NOT MEET COVERAGE CRITERIA." Added CPT code 0483U, 0484U, 0455U, 0463U Removed CPT code 0167U, 0354U, 0353U Committee Approved: 10/21/2024
02/11/2026	CAB Review Q4 2025: Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review necessitated the following changes to coverage criteria: For clarity, added "qualitative" to "qualitative NAAT" in CC4, CC7, CC10, CC12, CC15 CC5, CC20.c., and Note 2 edited for clarity Individual organism amplified probe testing for T. vaginalis now solely addressed in this policy, with multi-organism vaginitis panels that also test for T. vaginalis remaining in M2057. Results in expansion of CC10 and new Note 8. CC10 now reads: "10) Qualitative NAAT for T. vaginalis MEETS COVERAGE CRITERIA in the following situations: a) For symptomatic individuals (see Note 7). b) Follow up testing a minimum of three months after initial trichomoniasis diagnosis. c) Annual screening for asymptomatic individuals belonging to a high-risk group (see Note 8). d) Annual screening for asymptomatic individuals who have an HIV infection. e) As a part of follow-up in a victim of sexual assault." CC21 and CC22 updated to focus on the recommended STI screens for individuals being considered for or actively receiving PrEP. Removed references to screens outside of STIs other than HIV (e.g., measurement of creatine, pregnancy

	testing); HIV screening recommendations for this population now fully addressed in M2116. CC24 updated to include direct probe detection. Now reads: “24) Direct probe detection and/or quantitative NAAT for the following microorganisms DOES NOT MEET COVERAGE CRITERIA:” Note 4 and Note 7 updated to align with CDC. New Note 8: “Note 8: High-risk for Trichomoniasis: • Receiving care in high-prevalence settings (e.g., STI clinics, correctional facilities) • Having multiple sexual partners • Exchanging sex for money or drugs • Having a previous or concurrent STI • Drug misuse • History of incarceration • Sexually active individuals with an HIV-positive status” Added CPT code 87800, 87626 Removed CPT code 82565, 82575, 84702, 84703, 86701, 86702, 86703, 86705, 86803, 86804, 87660, G0432, G0433, G0435, G0472, G0475, S3645, 0500T Revised code description for CPT code 87624 Committee Approved: 02/11/2026
06/17/2026	CAB Review Q2 2026: Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review necessitated the following changes to coverage criteria: Moving prenatal STI screening from the Prenatal Screening policy into this policy. Results in the addition of CC2.a., 5.e., 6.a., and 10.a.; change to 5.d. 2.a.: “a) For pregnant individuals as part of the first prenatal visit.” 5.d.: added “for non-pregnant individuals” 5.e.: “e) At least four weeks after initial chlamydial diagnosis as a TOC for pregnant individuals.” 6.a.: “a) For pregnant individuals 24 years of age or younger as part of the first prenatal visit.” 10.a.: “a) For pregnant individuals 24 years of age or younger as part of the first prenatal visit.” New CC3: “3) For individuals who are currently diagnosed with a syphilis infection or who have a past history of a syphilis infection, treponemal Ig testing DOES NOT MEET COVERAGE CRITERIA.” Former CC3, now CC4: Addition of antigen testing, now reads: “4) Polymerase chain reaction (PCR) testing, nucleic acid amplification testing (NAAT), and antigen testing for syphilis DO NOT MEET COVERAGE CRITERIA.” Former CC6, now CC7: Addition of culture testing, changing “serology” to “antibody and antigen testing”, now reads: “7) Culture testing, antibody testing, and antigen testing for chlamydia or LGV DO NOT MEET COVERAGE CRITERIA.” Former CC7.c., now CC8.c., replaced “As a TOC for treatment” with “c) At least three months after initial gonorrhea diagnosis as a TOC.” Former CC12, now CC13, fixed reference to note with M. genitalium symptoms (typo indicated Note 8, fixed to reference Note 9). Former CC13, now CC14, removed reference to note, as symptoms are addressed in

	CC13 and don't need addressed here in CC14 Reordered former CC16 and CC17 so HSV criteria that MCC are first, followed by the HSV CC that DNMCC. CC17 changed "serologic" to "antibody" for clarity Former CC16, now CC18, replaced "immunoassay" with "antibody and antigen" for clarity on HSV-1 testing and added "antigen testing for HSV-2", now reads: "18) Antibody and antigen testing for HSV-1 and and/or herpes simplex (non-specific type test) and antigen testing for HSV-2 DO NOT MEET COVERAGE CRITERIA." Removed former CC21, as Hepatitis B testing for those being considered for PrEP is now addressed in the Hepatitis policy. CC24, removed HPV, as ordering of HPV testing is no longer defined by direct/amplified/quantitative and instead just by HPV type. Changes to the vaginitis policy result in all targeted Trich testing being managed by the STI policy, results in addition of CC24.f: "f) Trichomonas vaginalis" Added CPT code 87140, 87270, 87285, 87320, 87660, and 87810 Removed CPT code 86704, 86706, 87340, and G0499 Off-cycle coding modification: Added CPT code 87494 Committee Approved: 06/17/2026