

A review of current guidelines and research on the management of sexually transmitted infections in adolescents and young adults

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Abstract: Adolescents and young adults are at high risk for sexually transmitted infections (STIs). Providers have the responsibility to accurately manage these infections to prevent medical complications and the spread of STIs. This article will review the epidemiology, screening recommendations, diagnostic tests, and treatment guidelines for STIs most commonly encountered in this population: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, Herpes simplex virus, and *Trichomonas vaginalis*, as well as the sexually associated infection bacterial vaginosis. This review will discuss ongoing research that explores ways to improve the management of STIs in adolescents and young adults.

Keywords: adolescents, sexually transmitted disease, young adults

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Introduction

More than 1 million sexually transmitted infections (STIs) occur worldwide every day; in 2016 an estimated 376 million new infections with chlamydia, gonorrhea, syphilis, and trichomonas occurred compared with 357 million in 2012.^{1–3} Adolescents and young adults (AYA), defined in this context as persons 15–24 years old, are disproportionately affected: of the 20 million new STIs [including chlamydia, gonorrhea, syphilis, trichomonas, herpes simplex virus (HSV), human papillomavirus (HPV), hepatitis B, and human immunodeficiency virus (HIV)] that occur in the United States (US) each year, half occur among AYA, despite this age group comprising only about one-quarter of the sexually active population.^{4,5}

AYA are at increased risk for acquiring STIs due to behavioral, biological, and cultural factors. Approximately half of sexually experienced 14- to 19-year-olds report having at least three lifetime partners.⁶ Biological factors may contribute to the acquisition of STIs if exposed; cervical ectopy has been shown to increase the risk of acquiring chlamydia and HPV.^{5,7} AYA also experience barriers to accessing care, including lack of transportation and inability to pay.⁵

STIs place individuals at risk for both immediate and longer-term negative health consequences. Undiagnosed infections can lead to pelvic inflammatory disease (PID) in females, which can result in chronic pelvic pain, ectopic pregnancy, and infertility.⁵ Pregnant women may pass on the infection during pregnancy and at time of delivery; chlamydia, gonorrhea, syphilis, and HSV can all lead to potentially serious and life-threatening infections in the infant.⁵ STIs also increase the transmission of HIV.⁸

Given the high risk of STIs in this population, appropriate screening, accurate diagnosis, and timely treatment are necessary to decrease the risk of medical complications and to prevent the spread of infection to sexual partners. This article will review the epidemiology of STIs in AYA, current screening guidelines, and recommendations for the diagnosis and treatment of STIs commonly encountered in AYA, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, HSV, and *Trichomonas vaginalis*. We will also discuss bacterial vaginosis (BV) given its relationship to sexual behavior. A thorough discussion of HIV, *Treponema pallidum* (syphilis), and HPV is beyond the scope of this review.

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Epidemiology

Chlamydia trachomatis

Chlamydia trachomatis (chlamydia) is the most common reportable STI in the US, and, over the last several years, chlamydia cases in the US have continued to increase. The rise in cases is likely due to an increase in incidence as well as changes in screening practices; from 2000 to 2011, the expanded use of nucleic acid amplification tests (NAATs) likely contributed to the increase in cases seen.⁵ AYA accounted for 61.8% of all cases in 2018 and young women were disproportionately affected, with cases rising 12.1% among 15- to 19-year-old females from 2014 to 2018.⁵ Cases among males aged 15–19 years increased 32.8% from 2014 to 2018; the more rapid rise in cases among males may be due to increased transmission or improved case identification among men who have sex with men (MSM).⁵ Data from the European Sexually Transmitted Infections Surveillance Network shows that the overall rate of chlamydia in 26 European countries increased by 3.7% from 2008 to 2017.⁹

Neisseria gonorrhoeae

AYA also account for a disproportionate amount of cases of *Neisseria gonorrhoeae* (gonorrhea), with the highest rate among females 20–24 years old (702.6 cases per 100,000 females).⁵ During 2017–2018, gonorrhea infection rates decreased 1.3% among 15- to 19-year-olds and increased 1.2% among 20- to 24-year-olds.⁵ The rate of gonorrhea has increased in European countries, from 8.2 cases per 100,000 in 2008 to 23 cases per 100,000 in 2017.¹⁰ Of the 23 European countries with gonorrhea surveillance data reported by age, AYA comprised 36% of cases, comparable with that in 25- to 34-year-olds (37% of cases).¹⁰

Herpes simplex virus

HSV is not a reportable STI in the US, but is estimated to be one of the most prevalent. Genital herpes is most commonly caused by HSV-2, with an estimated 50 million people affected in the US.¹¹ Although the overall seroprevalence of HSV-1 and HSV-2 are decreasing in AYA,^{11–13} HSV-1 is becoming a more common cause of genital herpes, particularly in young women and MSM.^{14–16} Among MSM, the proportion of first-episode anogenital herpes cases caused by HSV-1 increased in young adults from 17% in 1992–1994 to 76% in 2004–2006.¹⁴

Trichomonas vaginalis

Trichomonas vaginalis (trichomoniasis) is the most common non-viral STI, with an estimated 3.7 million cases in the US and 156 million cases worldwide.^{2,4} Trichomoniasis is more prevalent among females than males, which is thought to be related to gender differences in susceptibility and host immune response.¹⁷ US national surveillance data from 2013 to 2016 demonstrates an estimated prevalence of 0.7% among females ages 14–19 years old, 2.65% among females 20–29 years old, and 0.48% among males 18–29 years old.^{18,19} Data from Great Britain using the National Survey of Sexual Attitudes and Lifestyles showed a prevalence of 0.6% among women aged 16–24 years; no males screened positive for the infection.²⁰ In a study of three Dutch cohorts, the prevalence was 1.5% in participants screened by general practitioners, 0.7% in a low risk population-based cohort, and 0.6% in those screened at STI clinics.²¹

Bacterial vaginosis

The prevalence of BV in the US is estimated to be 21.2 million among females aged 14–49 years.²² The prevalence of BV varies greatly internationally, but has been shown to be low in Western Europe.²³ A clinical syndrome has not been described in males. Although sexual transmissibility has not been clearly demonstrated, studies reveal that sexual behaviors, including having multiple partners, new sex partners, douching, and lack of condom use play a role in acquisition.^{24,25} In a survey of 103 adult women, participants associated sexual activity, unprotected sex, and sex with a new male partner with BV onset and recurrence.²⁶ Women who have sex with women (WSW) also have a high prevalence of BV.²⁷ BV is associated with increased risk of acquiring STIs, including chlamydia, gonorrhea, trichomoniasis, HSV-2, and HIV.^{28–31}

Special populations

MSM are disproportionately affected by STIs and HIV due to sexual behaviors and the characteristics of the sexual network. Behaviors found to be more common in MSM including longer lifetime periods of new partner acquisition, concurrent partnerships, and greater partner age differences increase the risk of STIs.^{32,33} The incidences of gonorrhea, including antimicrobial resistant gonorrhea, and primary and secondary syphilis are

higher in MSM compared with men who have sex only with women.^{34–37} In 2017, among MSM in the US, the estimated prevalence of urogenital chlamydia was 4.8%, rectal chlamydia was 7.3–9.0%, and pharyngeal chlamydia was 1.4%.^{32,38,39} and the estimated prevalence of urogenital gonorrhea was 8.5%, rectal gonorrhea was 4.5–6.1%, and pharyngeal gonorrhea was 4.6%.^{32,38,39} MSM accounted for 68% of all reported cases of primary or secondary syphilis in 2017; non-white MSM were disproportionately affected.³² In 2018, MSM made up 69% of new HIV diagnoses in adolescents and adults.⁴⁰ Among adolescents aged 13–24 years, 92% of HIV infections were due to male-to-male sexual in 2018.⁴¹

Multiple factors may affect the risk of acquiring STIs among transgender men and women, including sexual behavior, poverty and lack of access to health care, and stigma and discrimination. Among transwomen attending STI clinics (48.4% of study population were less than 30 years), 13.1% were positive for chlamydia, 12.6% were positive for gonorrhea and 14.2% were HIV positive. Among transmen (66.7% of study population were less than 30 years), 7.7% tested positive for chlamydia, 10.5% tested positive for gonorrhea, and 8.3% were HIV positive.⁴² The majority of transwomen and many transmen with extra-genital infections had negative urogenital testing at the same visit, illustrating the importance of extra-genital testing based on sexual practices.⁴²

Screening

Over 39% of high school students report having ever had sexual intercourse.⁴³ Based on US national survey data, at age 14 years 12.5% of females and 13.1% males reported ever having sex, and by age 19 years, 75% reported ever having sex.⁶ Since many STIs are asymptomatic, screening is necessary to detect and prevent the spread of infection. A US national survey of AYA found that among those who were sexually experienced, only 27.0% of females and 9.8% of males had been tested for STIs in the last 12 months.⁴⁴ AYA's perception of being at low risk for infection and concerns regarding confidentiality may prevent them from receiving appropriate screening.⁴⁴ Provider knowledge of, and adherence to, screening guidelines are essential. At an obstetrics and gynecology clinic in Hawaii, among 446 AYA, appropriate screening for chlamydia and

gonorrhea was conducted in 71% of patients, and only 21.6% were tested for HIV.⁴⁵ Ongoing efforts are important to improve rates of screening in those at risk.

Chlamydia

The Centers for Disease Control and Prevention (CDC), United States Preventative Services Task Force (USPSTF), and American Academy of Pediatrics (AAP) recommend routine screening for chlamydia for all sexually active females less than 25 years old (Table 1).^{46,47} According to CDC and AAP recommendations, there is insufficient evidence to recommend routine screening in all sexually active young males, but it should be considered for males at high risk, including in high prevalence settings and in populations with high burden of infection, such as adolescent clinics, sexual health clinics, and correctional facilities.^{46,47}

The 2015 European guidelines on chlamydia recommend screening all sexually active women and men less than 25 years old presenting to STI and sexual health clinics.⁴⁸ However, clinical guidelines vary across European countries; some recommend screening for chlamydia in all sexually active women less than 25 years old and some guidelines extend to men.⁴⁸

Gonorrhea

The CDC, USPSTF, and AAP recommend routine screening for gonorrhea for all sexually active females less than 25 years old; AAP and CDC recommend screening selectively in young men, including those at high risk or in high prevalence settings.^{46,47}

The 2012 European guidelines on gonorrhea management provide less specific guidance on when to screen for gonorrhea, but recommend including gonorrhea testing when screening young adults less than 25 years old for STIs or when screening individuals with new or multiple sex partners.⁴⁹

HSV

HSV serologic screening is not routinely recommended in US or European guidelines,^{46,50} but type-specific testing may be considered for women and men presenting for a STI evaluation.⁴⁶

Table 1. Screening recommendations for STIs.

	US guidelines ⁴⁶	European guidelines
<i>Chlamydia trachomatis</i>	<ul style="list-style-type: none"> • Routine screening for all sexually active females <25 years • Screening in males at high risk or in high prevalence settings 	<ul style="list-style-type: none"> • Screening all males and females <25 years presenting to STI or sexual health clinics⁴⁶
<i>Neisseria gonorrhoeae</i>	<ul style="list-style-type: none"> • Routine screening for all sexually active females <25 years • May consider screening males at high risk 	<ul style="list-style-type: none"> • Screening males and females <25 years when performing other STI screening or in those at high risk⁴⁹
HSV	<ul style="list-style-type: none"> • No routine screening recommended • May consider type-specific serologic testing in males and females presenting for STI testing 	<ul style="list-style-type: none"> • No routine screening recommended⁵⁰
<i>Trichomonas vaginalis</i>	<ul style="list-style-type: none"> • Screen women at high risk or in high prevalence settings • No routine screening for males 	<ul style="list-style-type: none"> • Screen women based on local prevalence⁵¹
BV	<ul style="list-style-type: none"> • No routine screening recommended 	<ul style="list-style-type: none"> • No routine screening recommended⁵¹
HIV	<ul style="list-style-type: none"> • Recommend screening to all adolescents 	<ul style="list-style-type: none"> • All sexually active individuals presenting to STI clinics or at high risk⁵²
<i>Treponema pallidum</i>	<ul style="list-style-type: none"> • No routine screening recommended, but screen based on risk factors 	<ul style="list-style-type: none"> • Routine screening in a high-risk population only⁵³

BV, bacterial vaginosis; HIV, human immunodeficiency virus; HSV, herpes simplex virus; STI, sexually transmitted infection; US, United States

Trichomoniasis

Per CDC guidelines, trichomoniasis screening should be considered for women receiving care in high prevalence settings and at high risk for infection.⁴⁶ AAP recommends against screening for trichomoniasis in asymptomatic women, but to consider screening women at high risk (new or multiple partners, history of STIs, detained or incarcerated, or history of transactional sex).⁴⁷ Trichomoniasis screening is not routinely recommended in males.⁴⁶ According to European/World Health Organization (WHO) guidelines on vaginal discharge, testing asymptomatic women for trichomoniasis should be guided by local prevalence.⁵¹

BV

US and European/WHO guidelines do not recommend routine screening for BV.^{46,51}

Other considerations in screening for STIs in AYA

CDC guidelines recommend HIV screening be offered to all AYA, with the frequency of repeat screening at the discretion of the provider based on individual risk factors.⁴⁶ European guidelines recommend screening all sexually active individuals

presenting to STI clinics and individuals at high risk of being exposed to HIV; screening is recommended every 12 months unless risk factors warrant more frequent testing.⁵²

Routine screening of AYA for other STIs including syphilis, HPV, and hepatitis A and B is not routinely recommended in the US.⁴⁶ Screening for these infections should be based on individual and population risk factors. European guidelines recommend routine screening for syphilis in populations at higher risk: patients with a newly diagnosed STI, HIV positive, hepatitis B and C positive, and patients who engage in high risk sexual behavior (MSM, sex workers, and others at higher risk for acquiring STIs).⁵³ Cervical cancer screening (HPV) in immunocompetent women is recommended starting at age 21 and every 3 years thereafter with cytology.⁴⁶

Special populations

Screening guidelines for MSM reflect the higher prevalence of several STIs in this population. Recommendations in the US include annual testing for HIV and syphilis. Testing for gonorrhea and chlamydia are based on sexual practices: testing for urethral chlamydia and gonorrhea in men

who have had insertive intercourse during the last year, rectal chlamydia and gonorrhea in men who have had receptive anal intercourse during the last year, and pharyngeal gonorrhea in men who have had receptive oral intercourse during the last year (screening for pharyngeal chlamydia is not recommended).⁴⁶ Young MSM with ongoing high risk sexual behaviors should have repeat chlamydia, gonorrhea, and syphilis screening every 3–6 months.⁴⁶ According to European guidelines, MSM should have yearly screening for chlamydia at sexual health clinics,⁴⁸ and be screened for gonorrhea based on sexual practices (including urethral, rectal, and pharyngeal testing as indicated).⁴⁹

Less is known about the transmission of STIs in WSW, and, thus, providers should perform STI and cervical cancer screening according to current guidelines for women.⁴⁶ Among transgender men and women, current recommendations suggest that providers assess STI- and HIV-related risks based on each patient's current anatomy and sexual behaviors.⁴⁶ Further research is needed about risk in these populations.

STI screening recommendations differ for patients with HIV and include: gonorrhea and chlamydia testing at least annually at the site of exposures, syphilis testing annually, and trichomoniasis testing annually.⁴⁶

CDC screening recommendations differ in pregnancy and include: screening all pregnant women for HIV, syphilis, and hepatitis B at the first prenatal visit; women less than 25 years old and those at high risk should be screened for chlamydia and gonorrhea at the first prenatal visit; women at risk for hepatitis C (including history of injection drug use) should be screened at the first prenatal visit.⁴⁶ There is no evidence supporting routine screening for BV, trichomoniasis, or HSV-2 in asymptomatic pregnant women; however, type-specific serologic tests for HSV might be helpful for identifying women at risk for HSV infection and guiding counseling regarding risk for primary HSV infection during pregnancy.⁴⁶

Methods to improve STI screening rates

A 2016 systematic review evaluated interventions to improve screening and re-testing in clinic-based settings and found that incorporating testing into routine clinic flow improved screening

rates among AYAs.⁵⁴ Methods such as offering universal screening regardless of the visit reason and performing universal urine collection at the start of a clinic visit improved STI screening in AYA.^{55–57} In addition, for young adults receiving routine pap smears, placing the collection kit for chlamydia next to the pap smear collection kit also increased screening rates.^{58,59} Other methods, such as offering provider-level education and incentives were less effective at improving screening rates in AYA.⁵⁴

AYA often seek care outside of the primary care office, and utilizing other clinical settings, including school-based health centers (SBHC) and emergency departments (ED), may improve screening rates. Current literature suggests that STI screening programs in SBHCs achieve high rates of diagnosis and treatment of gonorrhea and chlamydia and may improve knowledge and attitudes about STIs, but have not been shown to decrease the prevalence of STIs in the student population.^{60,61} Among patients presenting to the ED, 93% of adolescents and 98% of parents/guardians supported STI screening in the ED, although barriers such as confidentiality, cost, embarrassment, and nondisclosure to parents were noted.⁶² Educating clinicians about STI screening in AYAs may lead to improved detection of chlamydia and gonorrhea in the ED.⁶³

Self-swabs rather than provider-collected swabs are another way to improve STI testing, whether self-collected in clinic or collected through a home self-test. At a large US-based university health center following integration of walk-in self-testing for STIs, there was an increase in chlamydia and gonorrhea testing and diagnosis compared with baseline.⁶⁴ Almost 19% of test-takers opted for self-testing rather than a clinician visit, and among those surveyed, the intervention demonstrated high acceptability and ease of use.⁶⁴ There are potential disadvantages of self-testing without an associated clinic visit: patients do not receive a comprehensive evaluation, which could lead to missed diagnoses and providers do not have the opportunity to offer counseling about safe sex practices and contraception. In addition, home self-testing may make it more challenging to ensure timely patient treatment and appropriate treatment of sexual partners.⁶⁵ It is also important that home self-tests have comparable sensitivities and specificities to laboratory based

tests.⁶⁵ Further research is needed to assess the impact of these unintended consequences of more accessible and private screening options.

Internet-based screening programs may offer another way to improve screening rates. The British Columbia Centre for Disease Control developed an online STI service in which participants complete an online risk assessment and print an order slip for HIV and STI testing to take to a private laboratory.⁶⁶ In the pilot study, 37% of the nearly 900 participants' aged 16–79 years returned testing kits, and, of those, 30% tested more than once.⁶⁷ In follow-up interviews, MSM expressed a preference for this service because of convenience, privacy, and control over specimen collection (self-collected swabs), but the majority of participants anticipated using both the internet service and clinics for future testing.⁶⁶ In another study of an integrated online system for STIs at four North California health departments, 217 women ages 18–30 years enrolled and 67% returned self-collected vaginal swabs for chlamydia, gonorrhea, and trichomonas testing.⁶⁸ A total of 99% of participants reported that they would recommend the service to a friend and 95% preferred it over clinic-based testing.⁶⁸

Internet-based health systems appear to be acceptable among AYA, although participants do express concerns. In the United Kingdom, interviews were conducted with 25 sexually experienced AYA regarding use of a hypothetical smartphone-enabled STI self-testing device; the participants reported that this method would be easier, faster, improve privacy from peers/family, and allow them to avoid embarrassing encounters with providers.⁶⁹ However, participants expressed privacy concerns about the availability of results on their phone, concerns about the self-test's accuracy, and anxiety over not seeing a healthcare professional.⁶⁹

Diagnosis

Table 2 summarizes recommendations for the most appropriate diagnostic methods.

Chlamydia

NAATs are recommended by US and European guidelines for the diagnosis of chlamydia; in females, self-collected or provider-collected vaginal swabs

are preferred over first-catch urine, and in males, first-catch urine should be used.^{46,48,70} Vaginal swabs are preferred for screening purposes; the sensitivity of first-catch urine testing in females is about 10% lower than that of vaginal specimens.^{71–73} NAATs are the preferred test for pharyngeal and rectal specimens^{48,70}; the Aptima Combo2 (Hologic, San Diego, CA, USA) and Xpert CT/NG (Cepheid, Sunnyvale, CA, USA) were FDA-approved in May 2019 for extragenital testing.⁷⁴

Gonorrhoea

NAATs are also recommended by the CDC for diagnosis of gonorrhoea, using vaginal/cervical swabs or first-catch urine in females and first-catch urine in males.⁷⁰ According to the 2012 European guidelines, gonorrhoea can be detected by NAAT, culture or visualization on microscopy for rapid diagnosis, although NAATs are preferred in asymptomatic women.⁴⁹ NAATs are the test of choice for screening for rectal and pharyngeal gonorrhoea, but, given their variable specificity, confirmatory testing is recommended.⁴⁹

HSV

HSV can be diagnosed by DNA polymerase chain reaction (PCR) or culture: PCR has a high sensitivity and specificity, is type-specific and is rapid *versus* culture, which is highly specific, but has lower sensitivity and has a slower turnaround time.⁷⁵ Previously used tests such as Tzanck preparation and direct immunofluorescence are no longer recommended due to low sensitivity and specificity.⁷⁵ Serology testing detects antibodies against HSV and may be useful in certain situations, such as the evaluation of recurrent or atypical genital symptoms with negative HSV PCR or culture, for confirming a prior clinical diagnosis of HSV, or for testing in potentially discordant sexual partners.⁷⁵ Only type-specific assays based on the G1/2 glycoprotein should be used.

According to the 2017 European HSV guidelines, PCR is the gold standard for diagnosis.⁵⁰ Serology is recommended only in particular circumstances: for patients with recurrent or atypical disease when other detection methods have been negative, to differentiate between primary and recurrent infection when this distinction may guide counseling and management, and for testing asymptomatic sexual partners of HSV-infected

Table 2. Preferred diagnostic methods for detection of STIs.

	US guidelines ⁴⁶	European guidelines
<i>Chlamydia trachomatis</i>	<ul style="list-style-type: none"> Females: NAAT by vaginal/cervical swab or first-catch urine Males: NAAT by first-catch urine 	<ul style="list-style-type: none"> Females: NAAT by vulvovaginal swab⁴⁶ Males: NAAT by first-catch urine
<i>Neisseria gonorrhoeae</i>	<ul style="list-style-type: none"> Females: NAAT by vaginal/cervical swab or first-catch urine Males: NAAT by first-catch urine 	<ul style="list-style-type: none"> NAAT, culture or visualization on microscopy⁴⁹ NAATs are preferred in asymptomatic women
HSV	<ul style="list-style-type: none"> DNA PCR or culture Type specific serologic testing in certain circumstances 	<ul style="list-style-type: none"> PCR⁵⁰
<i>Trichomonas vaginalis</i>	<ul style="list-style-type: none"> NAAT 	<ul style="list-style-type: none"> NAAT⁵¹
BV	<ul style="list-style-type: none"> Gram stain using Nugent criteria (preferred) or Amsel criteria 	<ul style="list-style-type: none"> Gram stain using Hay-Ison criteria⁵¹

BV, bacterial vaginosis; HSV, herpes simplex virus; NAAT, nucleic acid amplification test; PCR, polymerase chain reaction; STI, sexually transmitted infection; US, United States

persons, including pregnant women, when there are concerns about transmission.⁵⁰

Trichomoniasis

Per US and European/WHO guidelines, NAAT is preferred for diagnosis of trichomoniasis due to its high sensitivity and specificity (both 95–100%) and the ability to test vaginal, cervical, or urine specimens from women.^{51,75} Xpert TV (Cepheid, Sunnyvale, CA, USA) is FDA-approved for testing in both males and females.⁷⁶ A point of care (POC) test, OSOM *Trichomonas* Rapid Test (Sekisui Diagnostics, Framingham, MA, USA), is available, which offers rapid results with somewhat lower sensitivity of 82–95%.^{77,78} Affirm VP III (Becton Dickinson, Sparks, MD, USA) and culture have low sensitivity, and, therefore, are not preferred diagnostic methods.⁴⁶ Microscopic evaluation of vaginal fluid is the method used most commonly for diagnosis, but has a sensitivity of only 51–65%.⁴⁶

BV

Per CDC recommendations, the gold standard for diagnosis of BV is Gram stain using Nugent criteria, which is a scoring system calculated by assessing for the presence of *Lactobacillus*, *Gardnerella vaginalis*, and *Mobiluncus* species (BV-associated bacteria).^{46,79} However, clinical diagnosis with Amsel criteria may also be used.⁴⁶ Three of four criteria are needed for a diagnosis

by Amsel criteria: increased homogeneous thin vaginal discharge, elevated vaginal pH greater than 4.5, amine odor with the addition of 10% potassium hydroxide to vaginal secretions, and the presence of increased clue cells on microscopic evaluation of a wet preparation.⁸⁰ Amsel criteria has a sensitivity and specificity of 91% when compared with Nugent scoring,⁷⁹ and may be performed by the clinician at the point of care.⁸¹ Per European/WHO guidelines, Gram stain microscopy by Hay-Ison Criteria is the gold standard for the diagnosis of BV.⁵¹ The Hay-Ison Criteria classifies vaginal flora in three different grades: grade I (normal flora with *Lactobacillus* species only), grade II (intermediate flora with reduced amount of *Lactobacillus* and similar amounts of mixed bacterial morphotypes), and grade III (bacterial vaginosis with few or absent *Lactobacillus* morphotype and abundant mixed bacterial morphotypes).

Affirm VP III, a non-amplified DNA probe test that detects *Gardnerella vaginalis*, has acceptable sensitivity compared with Gram stain.⁴⁶ The OSOM BV Blue test (Sekisui Diagnostics, Framingham, MA, USA), a simple, rapid POC test that detects vaginal fluid sialidase activity, has good sensitivity, and does not require a microscope or other specialized equipment to perform.⁸² Studies on the use of PCR for the detection and quantitative analysis of several BV-associated bacteria have demonstrated high sensitivities and specificities when compared with

Amsel or Nugent criteria, but clinical use is not widespread.^{83–85}

Treatment

Treatment recommendations by CDC guide STI management decisions in the US, while European and WHO guidelines provide additional guidance. These guidelines are highlighted below.

Chlamydia

Per US and European guidelines, first-line treatment for uncomplicated urogenital infection with chlamydia is azithromycin 1 g by mouth (PO) once or doxycycline 100 mg PO twice daily for 7 days^{46,48} (Table 3). A meta-analysis of 12 randomized controlled trials demonstrated that azithromycin and doxycycline were equally efficacious.⁸⁶

Per US and European guidelines, azithromycin or doxycycline may be used to treat rectal and pharyngeal chlamydia.^{46,48} European guidelines state that doxycycline is preferred for treatment of rectal chlamydia and a test of cure (TOC) is recommended if azithromycin is used.⁴⁸ A TOC is not recommended by the CDC.⁴⁶ There is growing evidence that doxycycline may be more effective in treatment of rectal chlamydia. A prospective cohort study evaluating women with rectal chlamydia found improved cure rates with doxycycline (95.5%) compared with azithromycin (78.5) ($p < 0.001$).⁸⁷ In a retrospective chart review of 526 men and women with rectal chlamydia, among those who presented for re-testing, the reinfection rate was 5.8% in those treated with doxycycline compared with 19.4% in those treated with azithromycin ($p = 0.01$).⁸⁸ A 2015 systematic review and meta-analysis comparing the efficacy of azithromycin to doxycycline for the treatment of rectal chlamydia found evidence of improved efficacy of doxycycline.⁸⁹ In contrast, a retrospective review of MSM and women attending a STI clinic found no significant differences in patients treated with azithromycin compared with doxycycline for rectal chlamydia, although the number of patients treated with doxycycline was small.⁹⁰ There is a need for further studies to guide treatment of rectal chlamydia.

Treatment of upper genital tract infections, including epididymitis and PID differs from treatment of lower genital tract infections. Treatment for epididymitis that is likely due to chlamydia or

gonorrhoea is ceftriaxone 250 mg intramuscular (IM) once plus doxycycline 100 mg PO twice daily for 10 days.⁴⁶ In MSM who practice insertive anal sex, enteric organisms are also of concern and recommended treatment is ceftriaxone plus levofloxacin or ofloxacin for 10 days.⁴⁶ Outpatient treatment for PID is ceftriaxone 250 mg IM once plus doxycycline 100 mg PO twice daily for 14 days with or without the use of metronidazole.⁴⁶ More complicated infections may require inpatient hospitalization and a more prolonged course of antibiotics.

US and European guidelines recommend re-testing for chlamydia 3 months after treatment.^{46,48} Several studies have evaluated ways to improve rates of re-testing, including the use of phone calls and text message reminders. In an evaluation of three pilot programs in England designed to increase re-testing for chlamydia through phone calls, text messages, and postal kits, among 778 AYAs, 39% were re-tested within 6 months, with females more likely to re-test than males.⁹¹ Two studies from the Netherlands evaluated the role of text messages in AYA. In a study of patients aged 16–23 years, 30.6% of the study participants who received a text message reminder were re-tested compared with 9.2% of historical controls, with a higher re-test rate in women than men.⁹²

Home kits may further increase the rate of re-testing. The REACT trial was an un-blinded randomized controlled trial with 600 women, heterosexual men, and MSM from two Australian health centers randomized to a text message reminder with a postal home collection kit or a text reminder with clinic testing for chlamydia re-testing.⁹³ The trial found that a significantly higher percentage of those in the home collection arm were re-tested compared with the clinic testing arm.⁹³ In a study of 1072 16- to 25-year-olds attending STI clinics, patients received text messages to re-test and were offered a free home test kit and a test for a peer.⁹⁴ Results showed that 34% requested a test and of those 56% re-tested; women were more likely to re-test. One-third of participants also had a peer re-tested.⁹⁴

Gonorrhoea

CDC recommended treatment of gonorrhoea includes ceftriaxone 250 mg IM once plus azithromycin 1 g PO once for treatment of uncomplicated urethral, cervical, and rectal infections.⁴⁶ Dual

Table 3. Recommendations for the treatment of STIs.

	US guidelines ⁴⁶	European guidelines
<i>Chlamydia trachomatis</i>	Azithromycin 1 g PO once or Doxycycline 100 mg PO twice daily for 7 days	Azithromycin 1 g PO once or Doxycycline 100 mg PO twice daily for 7 days ⁴⁶
<i>Neisseria gonorrhoeae</i>	Ceftriaxone 250 mg IM once + Azithromycin 1 g PO once	Ceftriaxone 500 mg IM once + Azithromycin 2 g PO once ⁴⁹
HSV Primary infection	Acyclovir 400 mg PO three times daily for 7–10 days or Acyclovir 200 mg PO five times daily for 7–10 days or Valacyclovir 1 g PO two times daily for 7–10 days or Famciclovir 250 mg PO three times daily for 7–10 days	Acyclovir 400 mg PO three times daily for 5–10 days or Acyclovir 200 mg PO five times daily for 5–10 days or Valacyclovir 500 mg PO two times daily for 5–10 days or Famciclovir 250 mg PO three times daily for 5–10 days ⁵⁰
<i>Trichomonas vaginalis</i>	Metronidazole 2 g PO once or Tinidazole 2 g PO once	Metronidazole 400–500 mg PO twice daily for 5–7 days or Metronidazole 2 g PO once or Tinidazole 2 g PO once ⁵¹
BV	Metronidazole 500 mg PO twice daily for 7 days or Metronidazole gel 0.75%, 5 g intravaginally for 5 days or Clindamycin cream 2% intravaginal gel once daily for 7 days	Metronidazole 400–500 mg PO twice daily for 5–7 days or Metronidazole gel 0.75%, 5 g intravaginally for 5 days or Clindamycin cream 2% intravaginal gel once daily for 7 days ⁵¹

BV, bacterial vaginosis; HSV, herpes simplex virus; IM, intramuscular; PO, by mouth; STI, sexually transmitted infection; US, United States

therapy is recommended due to emerging antimicrobial resistance; using antibiotics with different mechanisms of action may be more effective and make resistant organisms less likely to develop.⁹⁵ Persistent positive tests may be re-treated with the same regimen because the majority are due to reinfection; in cases with a high suspicion of treatment failure, cultures with antimicrobial susceptibility testing should be sent.⁹⁵ Cases of treatment failure may be treated with gemifloxacin PO and azithromycin PO or gentamicin IM plus azithromycin PO.⁹⁵ TOC is recommended only in the case of pharyngeal gonorrhea treated with an alternative regimen (14 days after treatment) or for treatment failure (7–14 days after treatment).^{46,95} Culture or NAAT can be used as a TOC.⁹⁵ Testing for reinfection is recommended 3 months after successful treatment.

European guidelines for treatment of gonorrhea, including urethral, rectal, and pharyngeal infections, is ceftriaxone 500 mg IM once with azithromycin 2 g PO once.⁴⁹ A TOC is recommended in

all cases to identify persistent infection and resistance, and should be performed by NAAT 2 weeks after treatment; repeat positive tests should be cultured with antibiotic susceptibility performed.⁴⁹

Gonorrhea resistance is an increasing concern worldwide. The Gonococcal Isolate Surveillance Project monitors antimicrobial susceptibility in the US. The percentage of isolates with elevated ceftriaxone minimum inhibitory concentrations (MIC) has remained low since 2008 (0.2% in 2017) and the percentage of isolates with elevated cefixime MIC has declined since dual therapy was recommended (from 1.4% in 2011 to 0.4% in 2017).³² During 2014–2017, the number of isolates with elevated azithromycin MIC increased from 2.5% to 4.4%.³² In 2016, The European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) found no isolates with resistance to ceftriaxone (although the proportion of isolates with decreased susceptibility to ceftriaxone increased significantly), 7.5% of isolates resistant to

azithromycin and 2.1% resistant to cefixime across 25 countries.⁹⁶

Appropriate treatment, including avoidance of over-treatment when a patient does not actually have a STI, is an important aspect in preventing antibiotic resistance. In AYAs presenting to the ED, 21.6% were over-treated, with patients presenting with STI exposure or genitourinary symptoms more likely to be over-treated.⁹⁷

As treatment guidelines for gonorrhea change based on patterns of resistance, providers need to be familiar with the most up-to-date treatment recommendations. Among primary care doctors, 64% correctly identified CDC recommended treatment; knowledge of the recommendation for dual therapy decreased with increasing years in practice, as well as with higher socioeconomic status of patients.⁹⁸ In a retrospective review of 542 patients with a mean age of 25 years presenting to a large academic medical center from 2011 to 2013, provider adherence to recommended treatment for gonorrhea was 82%; appropriate follow up occurred in only 31% of cases.⁹⁹ Ongoing provider education is key to appropriately diagnosing and treating STIs in AYA.

HSV

The first clinical outbreak of HSV may be treated with acyclovir, valacyclovir, or famciclovir, which are effective at decreasing the severity and duration of the episode (Table 3).^{46,51} Recurrent genital herpes can be treated episodically (with treatment initiated during the prodrome or within a day of the lesion appearing), often with shorter antiviral regimens. Daily suppressive therapy should be offered to all patients to decrease the frequency and severity of outbreaks, and to decrease the risk of transmission of HSV to uninfected partners.

Trichomoniasis

For treatment of trichomoniasis, US and European guidelines recommend PO metronidazole or tinidazole.^{46,51} Current CDC recommendations are treatment with metronidazole 2g PO in a single dose or tinidazole 2g PO in a single dose, with metronidazole 500mg twice daily for 7 days as alternative treatment.⁴⁶ However, in a multi-center, randomized controlled trial of 623

women with trichomoniasis, 7 day treatment with metronidazole was found to be more effective than single dose treatment,¹⁰⁰ and, thus, may be the preferred treatment option. US guidelines recommend testing for reinfection at 3 months, but in contrast, European guidelines do not recommend follow-up for patients who are asymptomatic.^{46,51} Patients need to be counseled on avoidance of alcohol while taking nitroimidazoles given the risk of a disulfiram-like reaction.

BV

US and European/WHO guidelines agree that BV may be treated with PO metronidazole, topical metronidazole gel or topical clindamycin cream.^{46,51} Because clindamycin cream is oil-based, it may weaken latex condoms for up to 5 days after use. Among pregnant women, oral therapy has not been found to be superior to topical treatment in curing the infection or preventing adverse outcomes and therefore either method may be used.⁴⁶ Routine follow up is not needed unless the patient remains symptomatic.^{46,51} For persistent or recurrent infections, the same or a different recommended treatment regimen can be used.⁴⁶

Alternative therapies may be effective for the treatment of BV. A triple-blind trial on sucrose vaginal gel compared with metronidazole gel found no difference in the reduction of clinical complaints or elimination of Amsel criteria.¹⁰¹ A study of 189 women with BV evaluating a higher dose metronidazole gel (1.3%) for 1, 3, and 4 days compared with standard 5-day treatment with metronidazole gel (0.75%) found that treatment with 1.3% gel demonstrated similar efficacy, safety and tolerability compared with treatment with 0.75% gel.¹⁰²

Recurrence of BV is common, with reported rates of 23% at 1 month, 43% at 3 months and 58% at 12 months.¹⁰³ Women often report frustration and dissatisfaction with current treatment and low levels of satisfaction with clinical management.¹⁰⁴ Evaluation of the use of intravaginal metronidazole for those with frequent recurrences, including twice weekly treatment for 16 weeks,¹⁰⁵ or vaginal suppositories containing metronidazole plus miconazole for five consecutive nights each month for 12 months,¹⁰⁶ have been shown to decrease recurrence. Oral metronidazole, intravaginal

lactate, and probiotics may also decrease the risk of BV recurrence. Current European guidelines recommend use of intravaginal metronidazole for recurrences.⁵¹

Partner management

The testing and treatment of sexual partners is important in preventing the spread of STIs, decreasing the rate of reinfection, and preventing medical complications of asymptomatic infections. Ideally, sexual partners of patients who test positive for a STI should seek testing and treatment from a provider. CDC recommends expedited partner therapy (EPT) for chlamydia and gonorrhea in heterosexual men and women, and the selective use of EPT in women with trichomoniasis, when other partner treatment strategies are impractical or unsuccessful.¹⁰⁷ There is currently no evidence to support the use of EPT in MSM, particularly given the concern for co-infection and need for comprehensive evaluation.¹⁰⁷ Sexual partners of patients with HSV should be evaluated and counseled, with treatment provided to those who are symptomatic.⁴⁶ Type-specific serologic testing may be offered to asymptomatic partners of patients with HSV.⁴⁶ Partner treatment is not recommended for BV.⁴⁶

The 2015 European guidelines on partner management of STIs recommend partner treatment be offered for infections that are curable and/or have serious short- or long-term health implications, including chlamydia, gonorrhea, trichomoniasis, HIV, and syphilis, although the legal status varies across countries.¹⁰⁸ Partner management is not recommended for HSV;¹⁰⁸ however it may be appropriate for providers to offer disease counseling to partners.⁵⁰ The European/WHO guidelines do not recommend treatment of male partners of patients with BV, but in WSW if a patient has BV and has a regular sexual partner, partner testing and treatment may be helpful.⁵¹

Improving time to treatment

The timeliness of treatment can have consequences for the individual and increase the likelihood of infecting others. Time to treatment was evaluated in 450 patients in Australia with positive chlamydia results at six clinics (one urban, three regional and two remote); time to treatment was significantly longer at the remote and regional clinics.¹⁰⁹ SBHCs may also play an important

role: in 540 students with gonorrhea and chlamydia, time to treatment at the SBHC was significantly faster than when treatment was received elsewhere (17 *versus* 28 days).¹¹⁰ This may indicate a role for further utilizing SBHC for testing and treatment in adolescents.

Conclusion

Overall, given the high burden of STIs in AYAs and the risk of medical complications associated with these infections, screening, accurate diagnosis, and timely and appropriate treatment are critical. Familiarity and adherence with STI recommendations and guidelines are important aspects of preventing the spread of STIs. Ongoing research is needed to help guide optimal management of STIs in AYA.

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KGL and CHH contributed to the organization and content of the review article, drafting and editing of the manuscript, and have approved of the final version to be published.

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The authors declare that there is no conflict of interest.


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