Update on Sexually transmitted infections (STI) guidelines

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Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 70 / No. 4
July 23, 2021

Sexually Transmitted Infections Treatment Guidelines, 2021

Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Learning question

Based on the United States Sexually Transmitted Disease Surveillance 2019 data, which group has the highest rates of infection with *Chlamydia trachomatis*?

A. Males 15-24

B. Females 25-34

C. Females 15-24

D. Males 25-34

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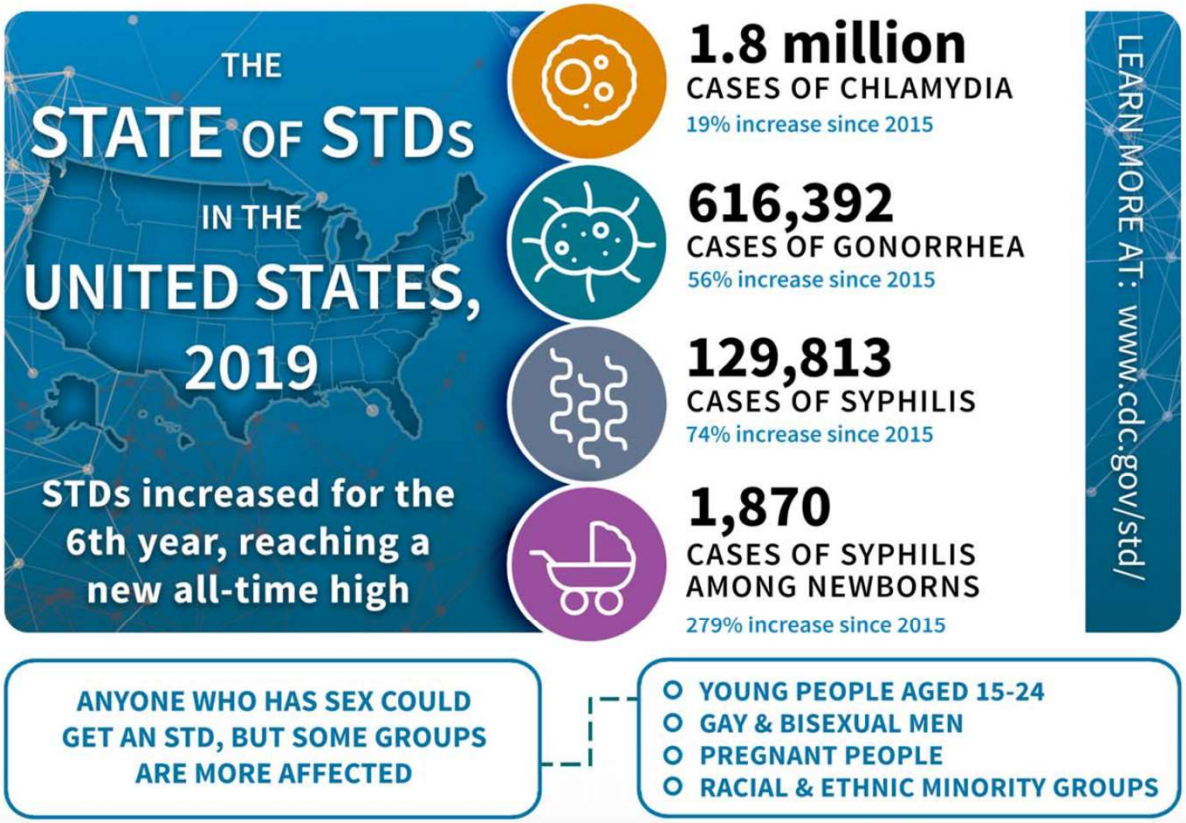

STIs are on the rise

Taking sexual history

BOX 1. The Five P's approach for health care providers obtaining sexual histories: partners, practices, protection from sexually transmitted infections, past history of sexually transmitted infections, and pregnancy intention

1. Partners
- "Are you currently having sex of any kind?"
- "What is the gender(s) of your partner(s)?"

2. Practices
- "To understand any risks for sexually transmitted infections (STIs), I need to ask more specific questions about the kind of sex you have had recently."
- "What kind of sexual contact do you have or have you had?"
  - "Do you have vaginal sex, meaning 'penis in vagina' sex?"
  - "Do you have anal sex, meaning 'penis in rectum/anus' sex?"
  - "Do you have oral sex, meaning 'mouth on penis/vagina'?"

3. Protection from STIs
- "Do you and your partner(s) discuss prevention of STIs and human immunodeficiency virus (HIV)?"
- "Do you and your partner(s) discuss getting tested?"
- For condoms:
  - "What protection methods do you use? In what situations do you use condoms?"

4. Past history of STIs
- "Have you ever been tested for STIs and HIV?"
- "Have you ever been diagnosed with an STI in the past?"
- "Have any of your partners had an STI?"

Additional questions for identifying HIV and viral hepatitis risk:
- "Have you or any of your partner(s) ever injected drugs?"
- "Is there anything about your sexual health that you have questions about?"

5. Pregnancy intention
- "Do you think you would like to have (more) children in the future?"
- "How important is it to you to prevent pregnancy (until then)?"
- "Are you or your partner using contraception or practicing any form of birth control?"
- "Would you like to talk about ways to prevent pregnancy?"

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Summary of Major Changes To The Guidelines

- **Testing**

– Extra-genital gonorrhea/chlamydia testing emphasized

– Consider Mycoplasma genitalium for persistent symptoms

– Syphilis – No Lumbar Puncture for ocular (w/o Cranial Nerve deficits) or otosyphilis

Summary of Major Changes To The Guidelines

- **Treatment**

– Gonorrhea - Ceftriaxone 500mg (weight-based dosing)

– Chlamydia - Doxycycline 100mg Q12 x 7 days preferred

– Trichomonas – Metronidazole for 7 days in women

– Mycoplasma genitalium –sequential treatment (doxy -> moxi)

– Pelvic inflammatory diseases – Add Metronidazole routinely

Summary of Major Changes To The Guidelines

- **Prevention**

– More liberal expedited partner therapy (EPT) supported (MSM)

  - Cefixime for GC EPT

– PEP and PrEP emphasized

  - Inform all sexually active adults and adolescents about PrEP

STI Screening

Women and Heterosexual Men

- Chlamydia, Gonorrhea
  - Women < 25 years or older women (increased risk) annually
    - Self collected vaginal swab
    - No routine extra-genital testing
    - If HIV+ (trichomonas, pap smear)
  - Heterosexual men
    - Consider chlamydia screening (adolescents, corrections, STD clinics)
    - Population based gonorrhea screening not recommended if asymptomatic
    - No extragenital testing
  - Retest 3 months after treatment

Men who Have Sex with Men (MSM)

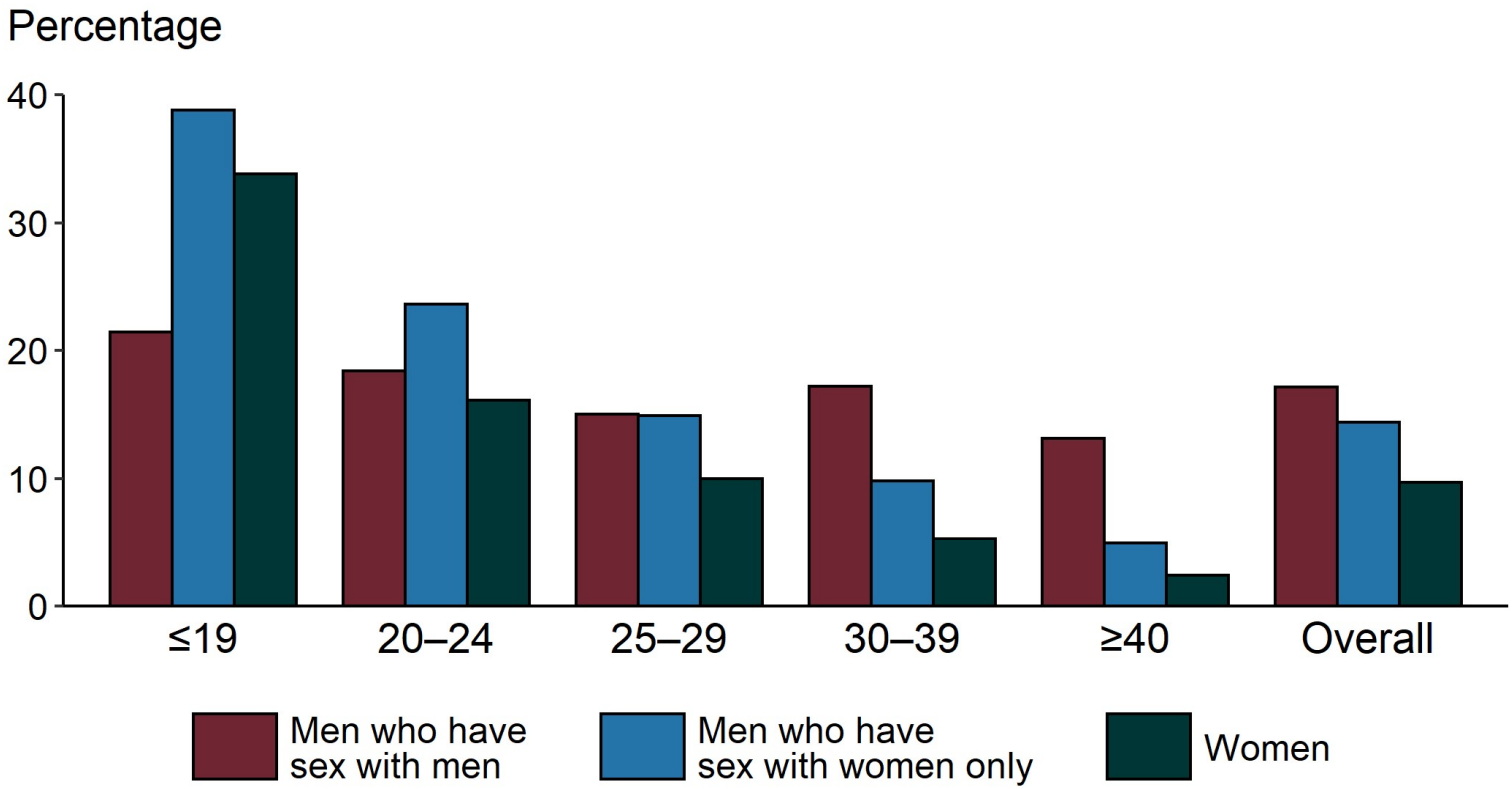
- HIV screening (4th generation)
- Syphilis serology (RPR/treponemal)
- Chlamydia, Gonorrhea
  - Urethral infection (NAAT)
  - Rectal infection (NAAT)
  - Pharyngeal infection gonorrhea (NAAT)
- Hepatitis A, B
- Hepatitis C (MSM/HIV)
  - At least yearly, q3-6 mo based on risk

- All adults and adolescents from 13 to 64 years old should be tested at least once for HIV.

CDC, MMWR, STD Treatment Guidelines 2021

Chlamydia

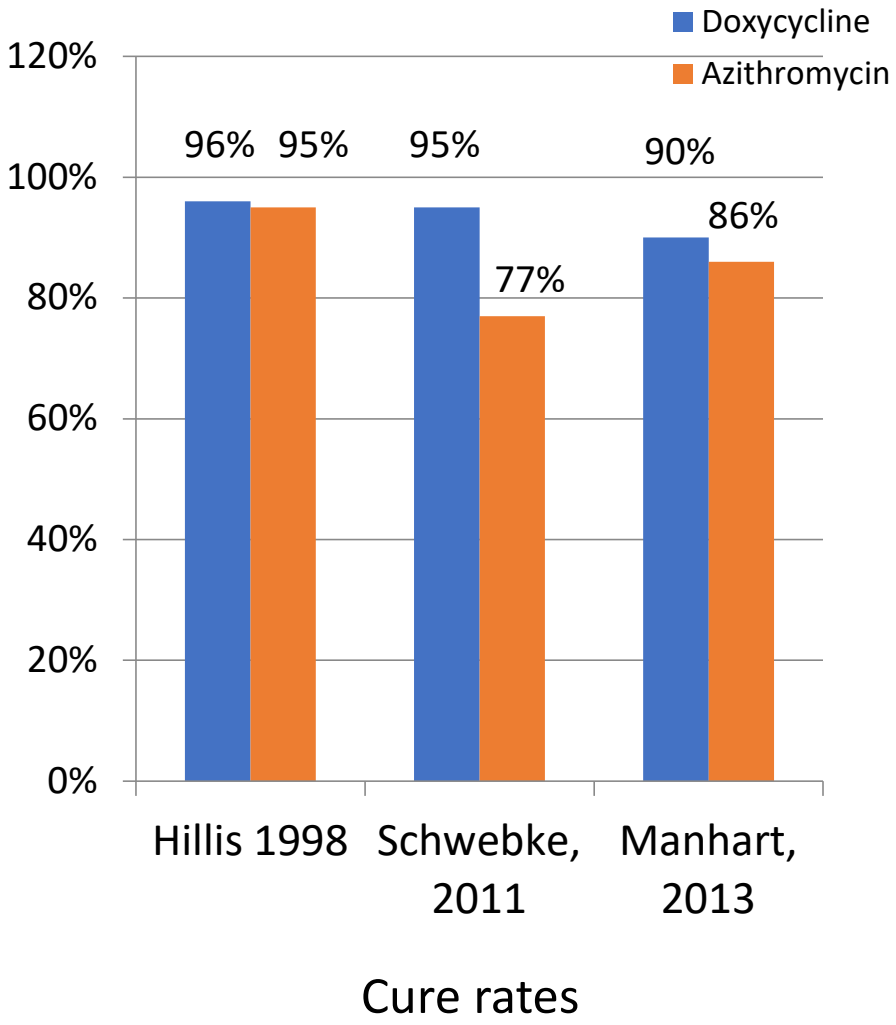
Chlamydia — Proportion of STI Clinic Patients Testing Positive by Age Group and Sex and Sex of Sex Partners, STDI Surveillance Network (SSuN), 2019



NOTE: Results based on unique patients with known sex of sex partners (n=89,448) attending SSuN STD clinics who were tested ≥1 time for chlamydia in 2019.

CDC, 2019 Surveillance Report

Chlamydia Treatment



Cure rates

Azithromycin vs Doxycycline

- RCT data - CT urethritis treatment with Azithromycin has a cure rate of <95% (Schwebke, Manhart, Kissinger, Geisler)
  - Azithro treatment failure 6.2% to 12.8% (WHO's target chlamydia treatment failure rate of < 5%)
- Meta-analysis (Kong 2014)
  - Doxy > Azi 3% (urogenital)
  - Doxy > Azi 7% (sx urethral in men)
- Rectal Infection
  - Several retrospective studies (cure rates doxycycline > azithromycin)
- Retest in 3 months (reinfection)

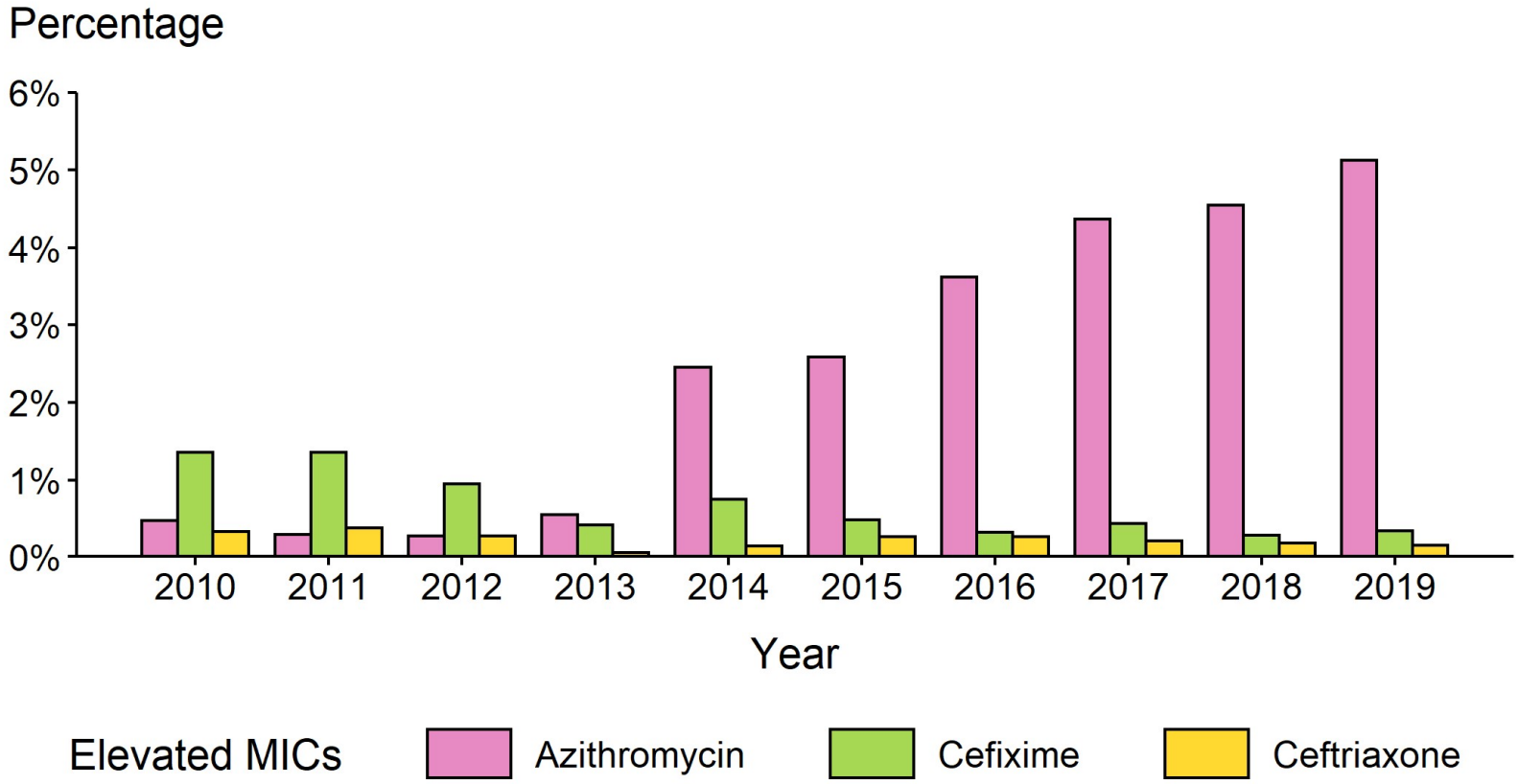
Kissinger, Patricia J., et al. "Azithromycin Treatment Failure for Chlamydia Trachomatis Among Heterosexual Men With Nongonococcal Urethritis." Sexually Transmitted Diseases, vol. 43, no. 10, Lippincott Williams & Wilkins, 2016, pp. 599–602, https://www.jstor.org/stable/48512110.
Kong FY, Tabrizi SN, Law M, et al. Azithromycin versus doxycycline for the treatment of genital chlamydia infection: a meta-analysis of randomized controlled trials. Clin Infect Dis. 2014;59(2):193-205. doi:10.1093/cid/ciu220

Chlamydia Treatment

- Genitourinary infection
  - Microbiologic failure higher among men
- Rectal infection
  - Doxycycline superior to azithromycin (20%-26% difference)
    - highly efficacious - all sites in men and women
  - Rectal infection is not uncommon among women with genitourinary infection (33%-83%) regardless of behavioral risk factors (autoinoculation)
- Azithromycin:
  - efficacious in women and asymptomatic men
  - lower efficacy in urethritis, poor efficacy in rectum, ? pharynx

Gonorrhea

Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2010–2019



NOTE: Elevated MIC = Azithromycin: ≥ 2.0 µg/mL; Cefixime: ≥ 0.25 µg/mL; Ceftriaxone: ≥ 0.125 µg/mL

CDC, 2019 Surveillance Report

Gonorrhea

Preferred Regimen

- **Ceftriaxone 500mg IM x 1**

– For persons weighing ≥150 kg (300 lb), 1 g of IM ceftriaxone should be administered

- If chlamydial infection has not been excluded:

– **Doxycycline 100 mg orally twice daily for 7 days**

Alternative/Cephalosporin Allergy*

- Gentamicin 240mg IM + Azithromycin 2g PO x1
- **Cefixime 800 mg orally as a single dose**
- Ciprofloxacin 500mg PO x 1

***No reliable alternatives for pharyngeal gonorrhea**

- Azithromycin resistance is widespread and increasing
- Wide inter-individual pharmacokinetics
- Resistance prevention concentration unknown, likely higher than dose for cure
- Pharyngeal gonorrhea is common/under-screened (test of cure 7-10 days)

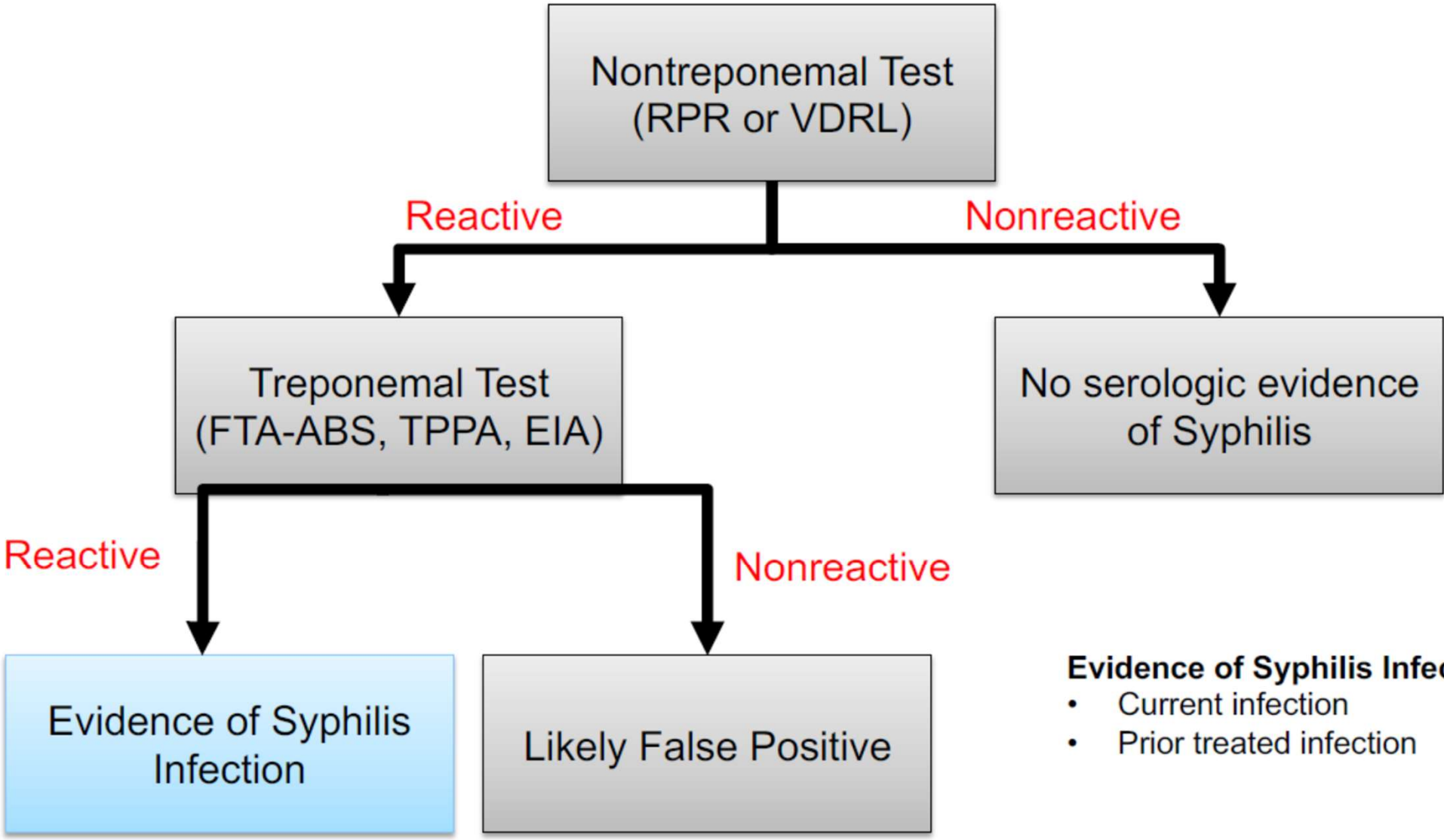
CDC, MMWR, STD Treatment Guidelines 2021

INFECTION	UPDATE: JUNE 2021	2015
GONORRHEA	CEFTRIAXONE 500 MG IM ONCE	CEFTRIAXONE 250 MG IM ONCE PLUS AZITHROMYCIN 1 G ORALLY ONCE
CHLAMYDIA	DOXYCYCLINE 100 MG ORALLY TWICE DAILY FOR 7 DAYS	AZITHROMYCIN 1 G ORALLY ONCE

Comparison of gonorrhea and chlamydia recommended treatment regimen recommendations (2015 vs 2021 CDC guidelines)

CDC, MMWR, STD Treatment Guidelines 2021

Syphilis – Traditional Algorithm

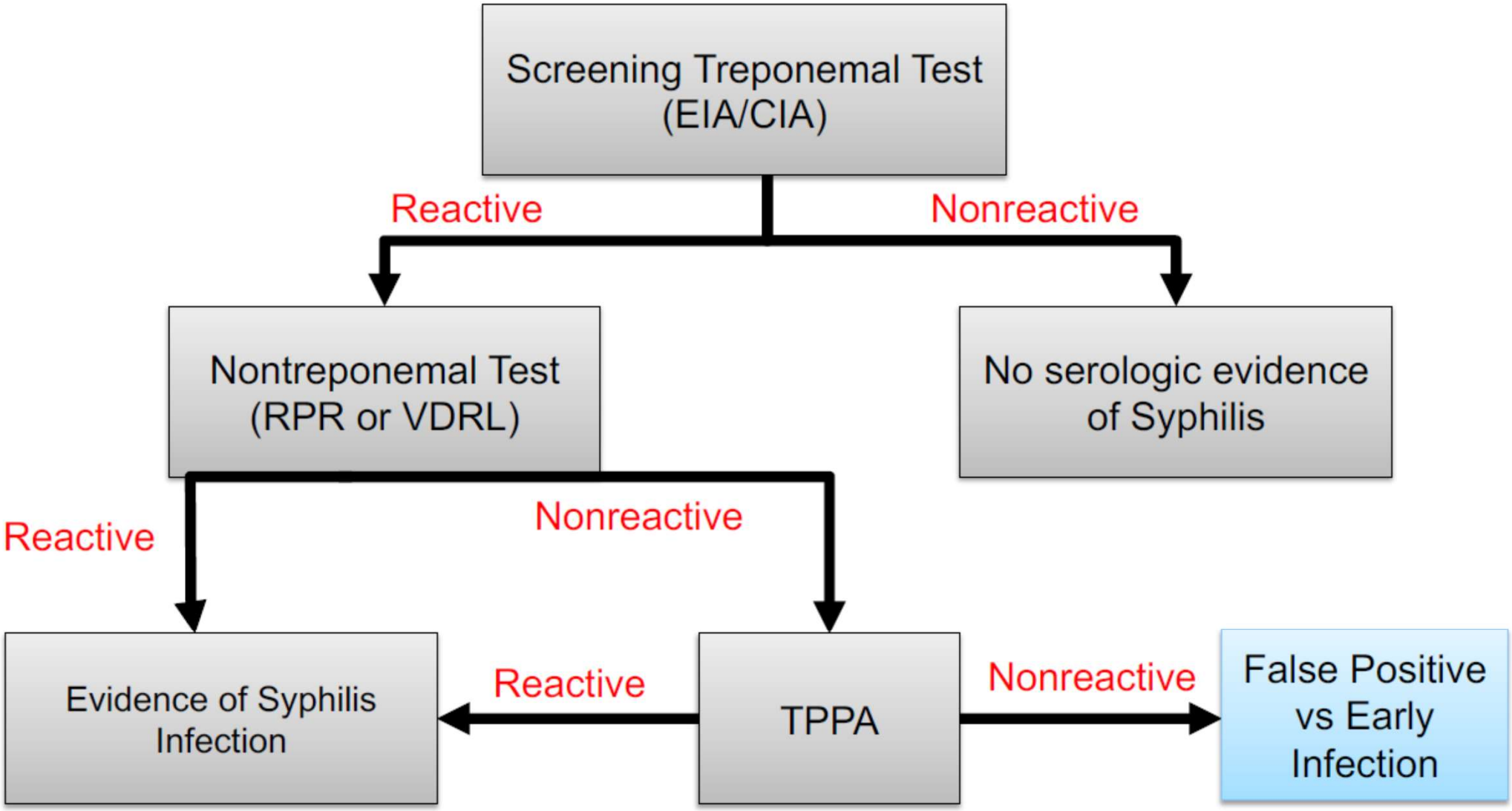


Evidence of Syphilis Infection:

- Current infection
- Prior treated infection

New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. A PDF version is available at www.nycptc.org.

Syphilis – Reverse Algorithm



New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. A PDF version is available at www.nycptc.org.

Syphilis – Treatment

Stage	Treatment	Alternative
Incubation	Benzathine penicillin G 2.4 million units intramuscular injection once	Doxycycline 100mg twice daily for 14 days
Primary		
Secondary		
Early latent		
Late latent	Benzathine penicillin G 2.4 million units intramuscular injection 3 times at one week intervals	Doxycycline 100mg twice daily for 28 days***
Late of unknown duration		
Neurosyphilis, Ocular, or Otic Syphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours, or by continuous infusion, for 10–14 days	Procaine penicillin G 2.4 million units IM once daily *PLUS* Probenecid 500mg 4 times daily for 10–14 days
Tertiary		

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Trichomonas vaginalis

- **Recommended Regimen Among Women**
  - Metronidazole 500 mg orally 2 times/day for 7 days
- **Recommended Regimen Among Men**
  - Metronidazole 2 g orally in a single dose
- **Alternative Regimen for Women and Men**
  - Tinidazole 2 g orally in a single dose

- Because of high rate of reinfection among women treated for trichomoniasis, retesting is recommended for all sexually active women <3 months after initial treatment regardless of whether they believe their sex partners were treated

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Nongonococcal Urethritis (NGU)

Nonspecific diagnosis with various infectious etiologies:

- *C. trachomatis* well established NGU etiology; prevalence varies across populations, accounts for < 50% of overall cases.
- *Mycoplasma genitalium* estimated 10%–25% of cases.
- *Trichomonas vaginalis* 1%–8% of cases depending on population and location.

CDC, MMWR, STD Treatment Guidelines 2021

Mycoplasma genitalium

- Recently described STI.
- It is not a notifiable infection, few data on prevalence.
- 2019 US study: 3300 participants—including both symptomatic and asymptomatic individuals:
  - 1737 female, 1563 male.
  - 61% Black individuals, and 43.2% from southeast US.
  - Prevalence of *M. genitalium* at the urogenital site was 10.3%.
- Among women, M. genitalium has been associated with cervicitis, PID, preterm delivery, spontaneous abortion, and infertility (two-fold increased risk for these outcomes among women infected with M. genitalium

Tuddenham S, Hamill MM, Ghanem KG. Diagnosis and Treatment of Sexually Transmitted Infections: A Review. JAMA. 2022;327(2):161-172. doi:10.1001/jama.2021.23487
Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Mycoplasma genitalium: Clinical presentation

Men

- Dysuria
- Urethral discharge
- Penile irritation and/or urethral discomfort

Women

- Dysuria
- Postcoital bleeding
- Painful intermenstrual bleeding
- Cervicitis
- Pelvic pain

Pinto-Sander N, Soni S. Mycoplasma genitalium infection BMJ 2019; 367 :l5820

Mycoplasma genitalium: Treatment

Recommended Regimens if *M. genitalium* Resistance Testing Is Available
If macrolide sensitive: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally daily for 3 additional days (2.5 g total)
If macrolide resistant: Doxycycline 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days

Recommended Regimen if *M. genitalium* Resistance Testing Is Not Available
If *M. genitalium* is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

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Pelvic inflammatory disease (PID)

- 3 minimum clinical criteria on pelvic examination:
  - cervical motion tenderness
  - uterine tenderness, or
  - adnexal tenderness
- Additional criteria:
  - Oral temperature >38.3°C (>101°F)
  - Abnormal cervical mucopurulent discharge or cervical friability
  - Presence of abundant numbers of WBCs on saline microscopy of vaginal fluid
  - Elevated erythrocyte sedimentation rate (ESR)
  - Elevated C-reactive protein (CRP)
  - Lab documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis*

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Pelvic inflammatory disease (PID)

Decision for hospitalization (based on provider judgment) and whether woman meets any of:

- Surgical emergencies (e.g., appendicitis) cannot be excluded
- Tubo-ovarian abscess
- Pregnancy
- Severe illness, nausea and vomiting, or oral temperature >38.5°C (101°F)
- Unable to follow or tolerate an outpatient PO regimen
- No clinical response to oral antimicrobial therapy

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Pelvic inflammatory disease (PID)

Risk Category	Recommended Regimen	Alternatives
Parenteral treatment	ceftriaxone 1 gm by IV every 24 hours **PLUS** doxycycline 100 mg orally or by IV every 12 hours **PLUS** metronidazole 500 mg orally or by IV every 12 hours	ampicillin-sulbactam 3 gm by IV every 6 hours **PLUS** doxycycline 100 mg orally or by IV every 12 hours
	OR cefotetan 2 gm by IV every 12 hours **PLUS** doxycycline 100 mg orally or by IV every 12 hours	**OR** clindamycin 900 mg by IV every 8 hours **PLUS** gentamicin 2 mg/kg body weight by IV or IM, **FOLLOWED BY** 1.5 mg/kg body weight every 8 hours. Can substitute with 3–5 mg/kg body weight 1x/day
	OR cefoxitin 2 gm by IV every 6 hours **PLUS** doxycycline 100 mg orally or by IV every 12 hours	
Intramuscular/oral treatment	ceftriaxone 500 mg IM in a single dose[6] **PLUS** doxycycline 100 mg orally 2x/day for 14 days **WITH** metronidazole 500 mg orally 2x/day for 14 days	
	OR cefoxitin 2 gm IM in a single dose **AND** probenecid 1 gm orally, administered concurrently in a single dose **PLUS** doxycycline 100 mg orally 2x/day for 14 days **WITH** metronidazole 500 mg orally 2x/day for 14 days	
	OR Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime) **PLUS** doxycycline 100 mg orally 2x/day for 14 days **WITH** metronidazole 500 mg orally 2x/day for 14 days	

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HIV screening recommendations

- All patients aged 13-64 years.
- All patients initiating treatment for Tuberculosis (TB) should be screened for HIV.
- All patients seeking treatment for Sexually transmitted infections (STIs) should be screened for HIV during each visit for a new complaint, regardless of whether the patient is known or suspected to have specific behavior risks for HIV infection.

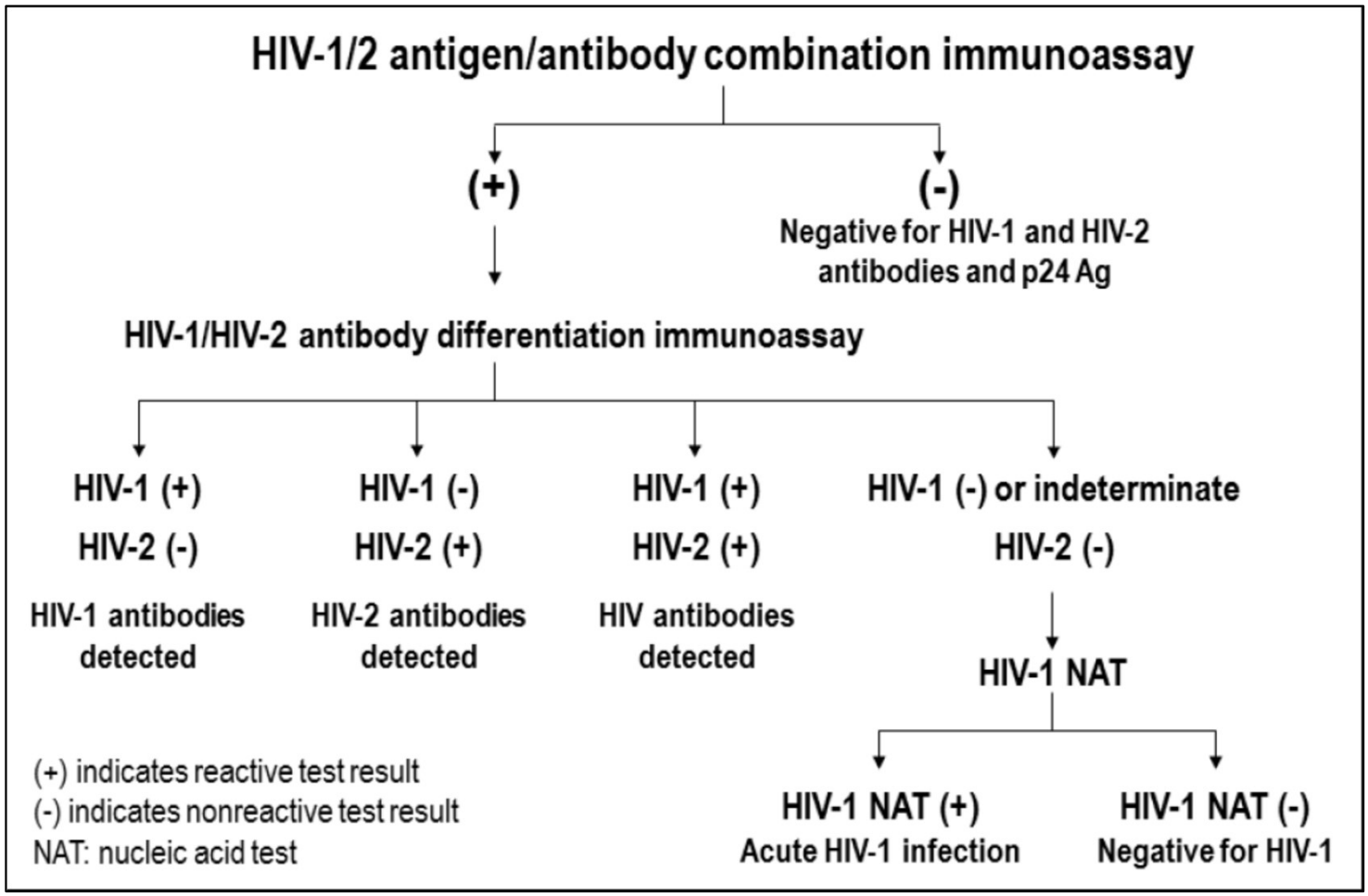
Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep. 2006;55:1-17.

Repeat HIV Screening

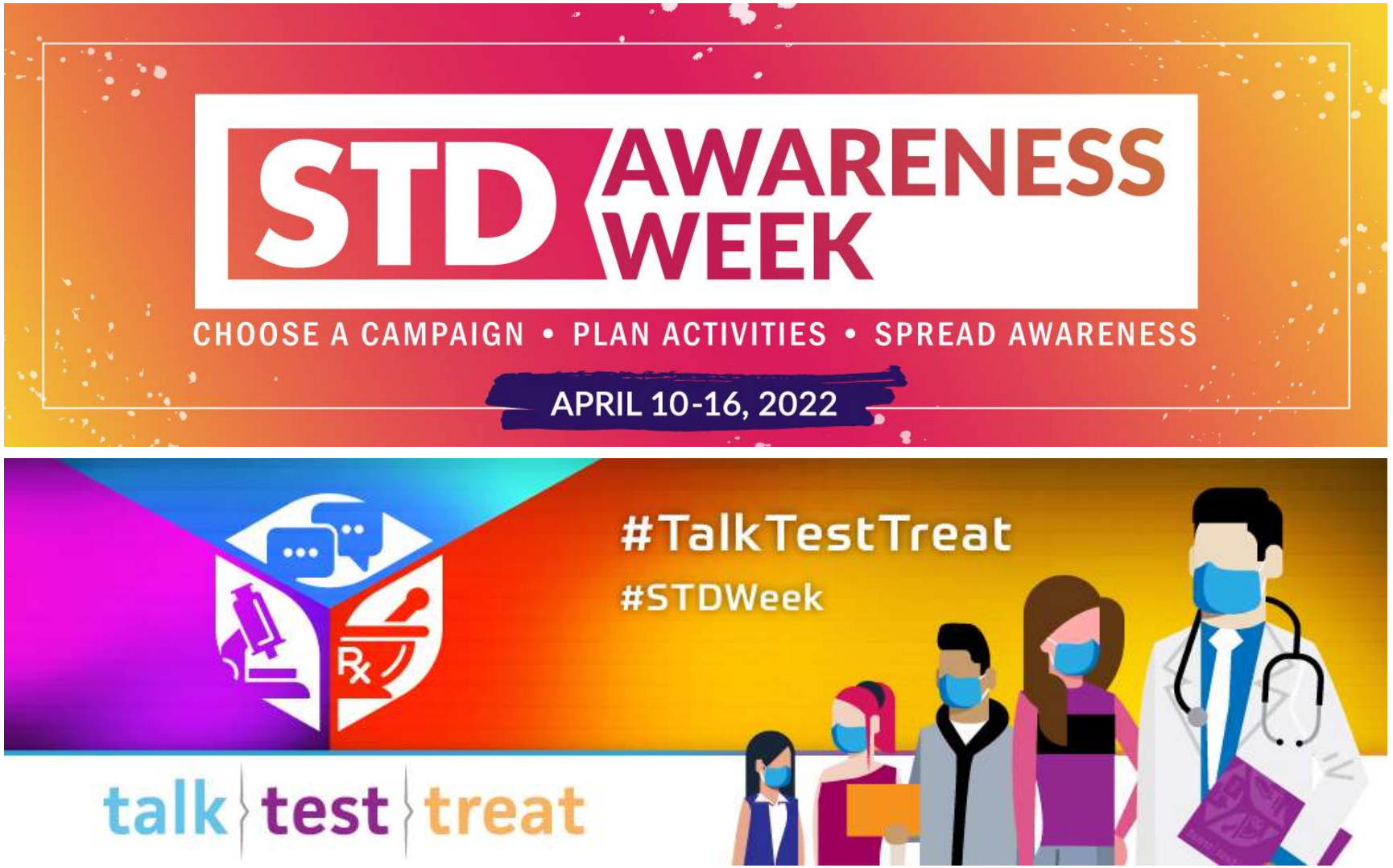
- Health-care providers should subsequently test all persons likely to be at high risk for HIV at least annually:
  - injection-drug users and their sex partners.
  - persons who exchange sex for money or drugs.
  - sex partners of HIV-infected persons.
  - MSM or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test.

Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep. 2006;55:1-17.

Recommended Laboratory HIV Testing Algorithm



Adapted from Interim Guidelines for Laboratories on the Use of a New Diagnostic Testing Algorithm for Human Immunodeficiency Virus (HIV) Infection. New York State Department of Health (http://www.health.ny.gov/diseases/aids/providers/regulations/testing/docs/guidelines_diagnostic_testing.pdf).



Questions? Comments?

https://www.cdc.gov/std/saw/index.htm