CARE TRANSFORMATION COLLABORATIVE RHODE ISLAND

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ADVANCING INTEGRATED HEALTHCARE

Best Practices in Team-Based Care

Best Practices in STI Screening for RI Primary Care Practices

August 15, 2023

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Dr. Erica Hardy, MD, MMSc

Care Transformation Collaborative of RI

Agenda

Topic *Presenter*	Time
Welcome *Susanne Campbell, Senior Program Administrator, CTC-RI*	8:00-8:05
Presentations and Questions • *Dr Philip A. Chan, M.D., M.S.* • *Dr. Erica Hardy, MD, MMSc-- A Focus on Congenital Syphilis & Pregnancy* • *Questions*	8:05-8:55
Closing *Susanne Campbell, Senior Program Administrator, CTC-RI*	8:55-9:00

CTC-RI Conflict of Interest Statement

Session presenter has no financial relationships with a commercial entity producing healthcare-related products used on or by patients.

All relevant financial relationships of those on the session planning committee have been disclosed and, if necessary, mitigated.

Objectives

1. Review epidemiology of common STIs in Rhode Island
2. Discuss screening for common STIs in primary care settings
3. Provide updated recommendations on STI care and management in primary care settings

Best Practices in STI Screening for Rhode Island Primary Care Practices

BROWN UNIVERSITY

Providence, Rhode Island
August 15th, 2023

Philip A. Chan, MD, MS
Associate Professor, Brown University
Medical Director, Rhode Island Department of Health
Chief Medical Officer, Open Door Health

Disclosures

- Funding from the NIH, CDC, and SAMHSA.
- Medical Director, Rhode Island Department of Health.
- Chief Medical Officer, Open Door Health.
- No commercial conflicts of interest.

Sexually Transmitted Infections
Federal Implementation Plan
for the United States | 2021–2025

STI National Strategic Plan

Treatment

Vision: The United States will be a place where sexually transmitted infections are prevented and where every person has high-quality STI prevention, care, and treatment while living free from stigma and discrimination.

The STI Plan has five high-level goals:

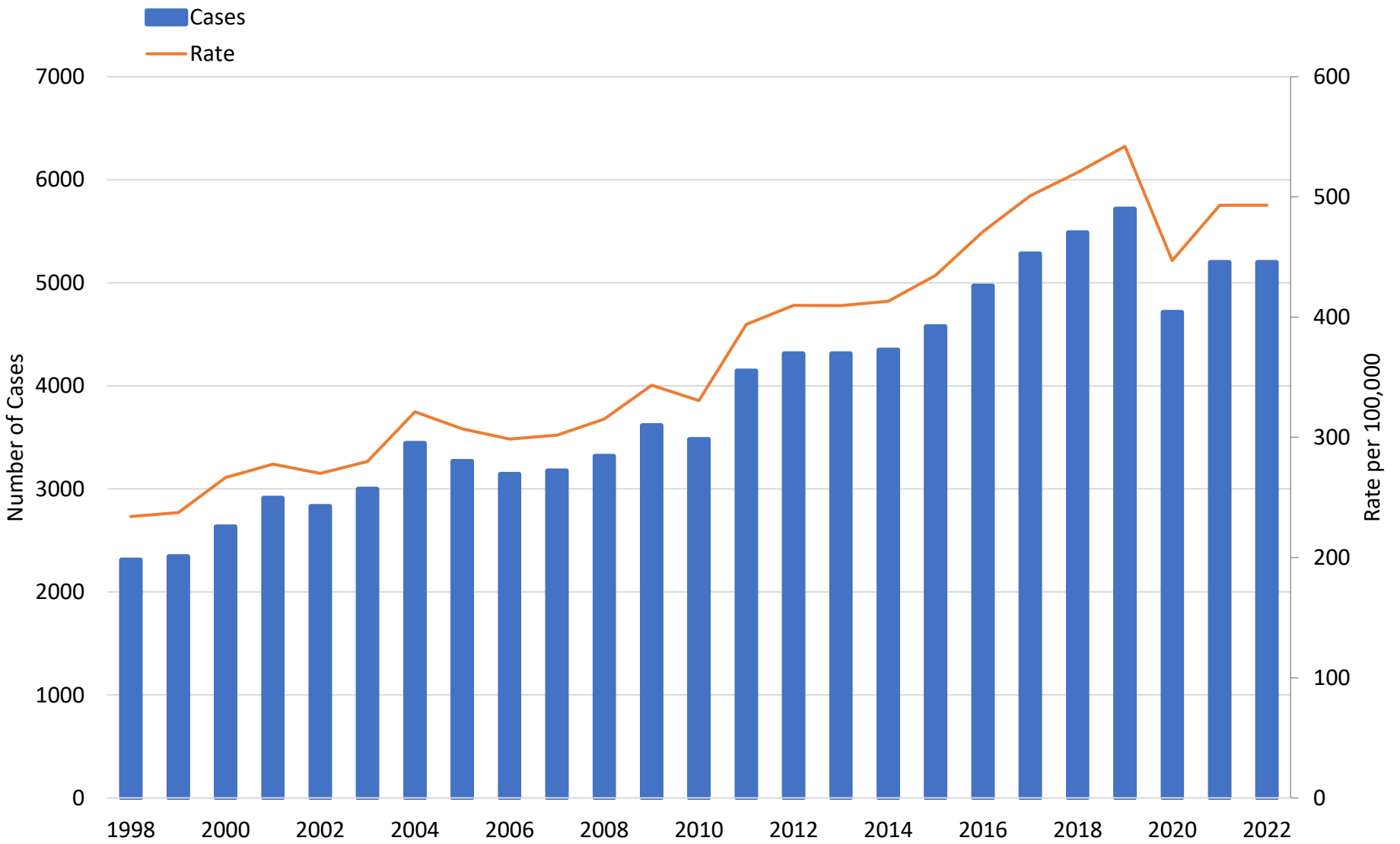
- **Prevent** new STIs.
- Improve the health of people by **reducing adverse (harmful) outcomes** of STIs.
- Accelerate progress in STI **research**, technology, and innovation.
- Reduce STI-related health **disparities** and health inequities.
- Achieve **integrated, coordinated efforts** that address the STI epidemic.

Priority Populations:

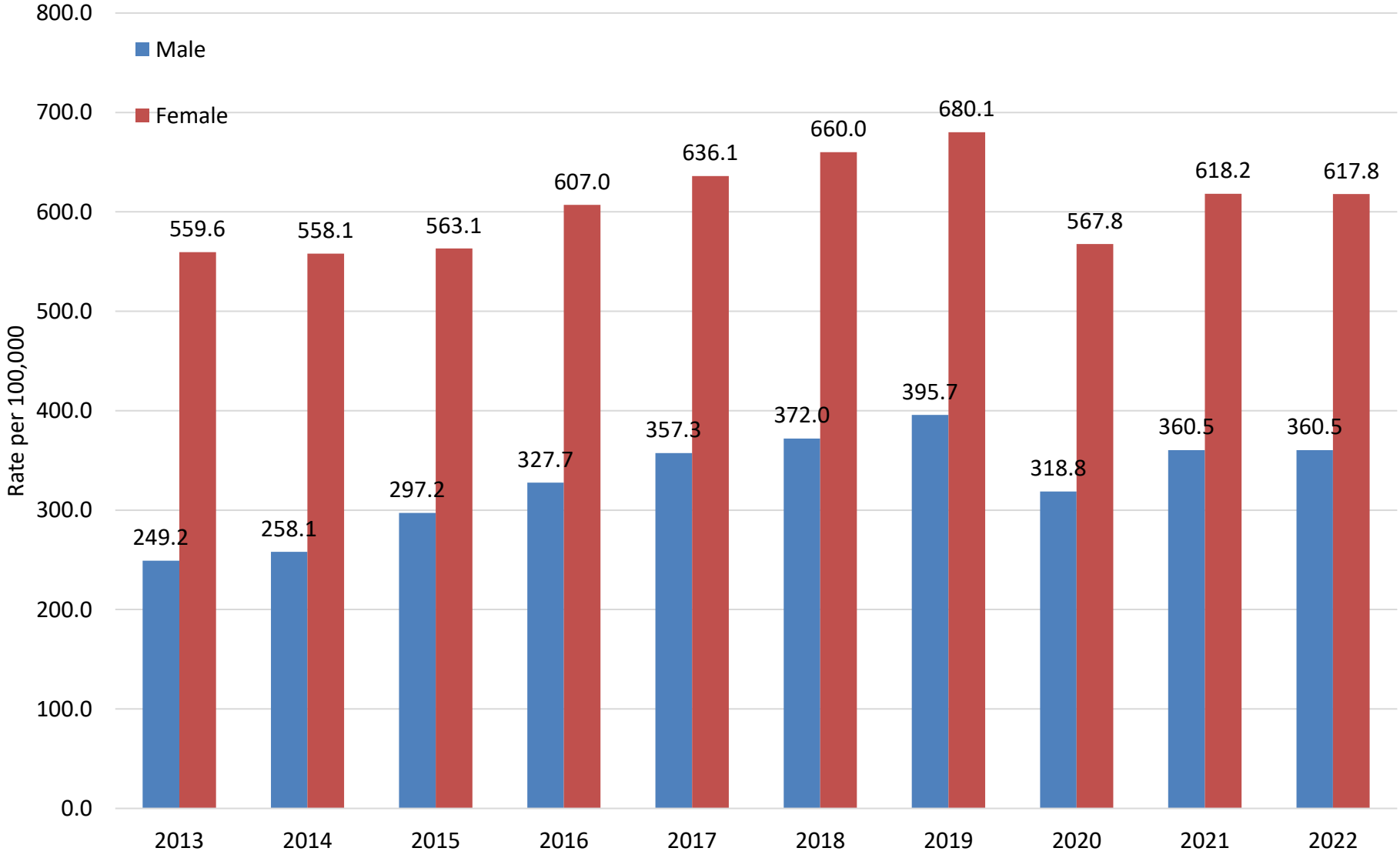
- Adolescents and young adults
- Men who have sex with men (MSM)
- Pregnant women
- Black, American Indian/Alaska Native, and Hispanic Communities
- Geographic regions

www.hhs.gov/programs/topic-sites/sexually-transmitted-infections/plan-overview/index.html

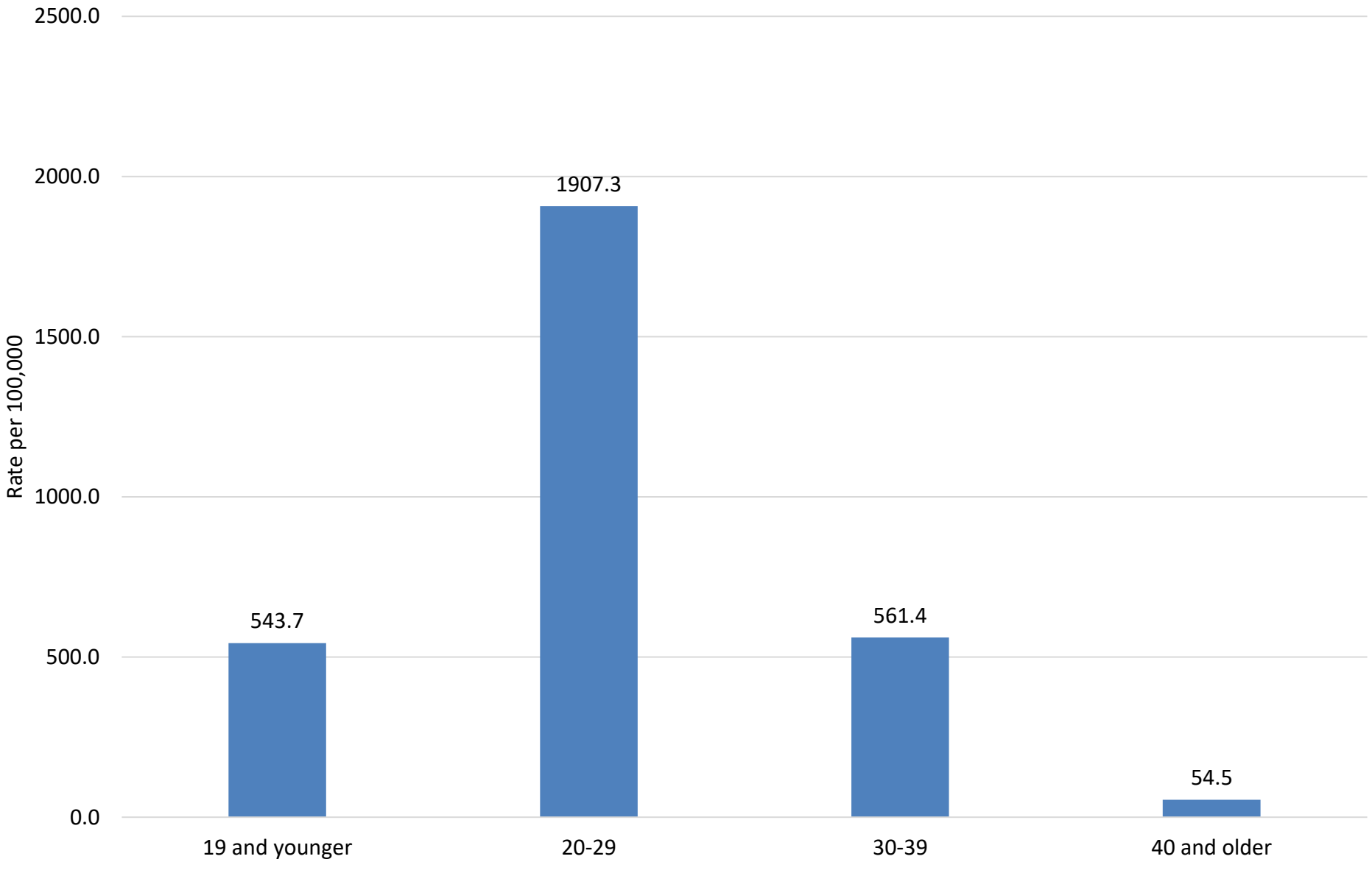
Chlamydia, 1998-2022



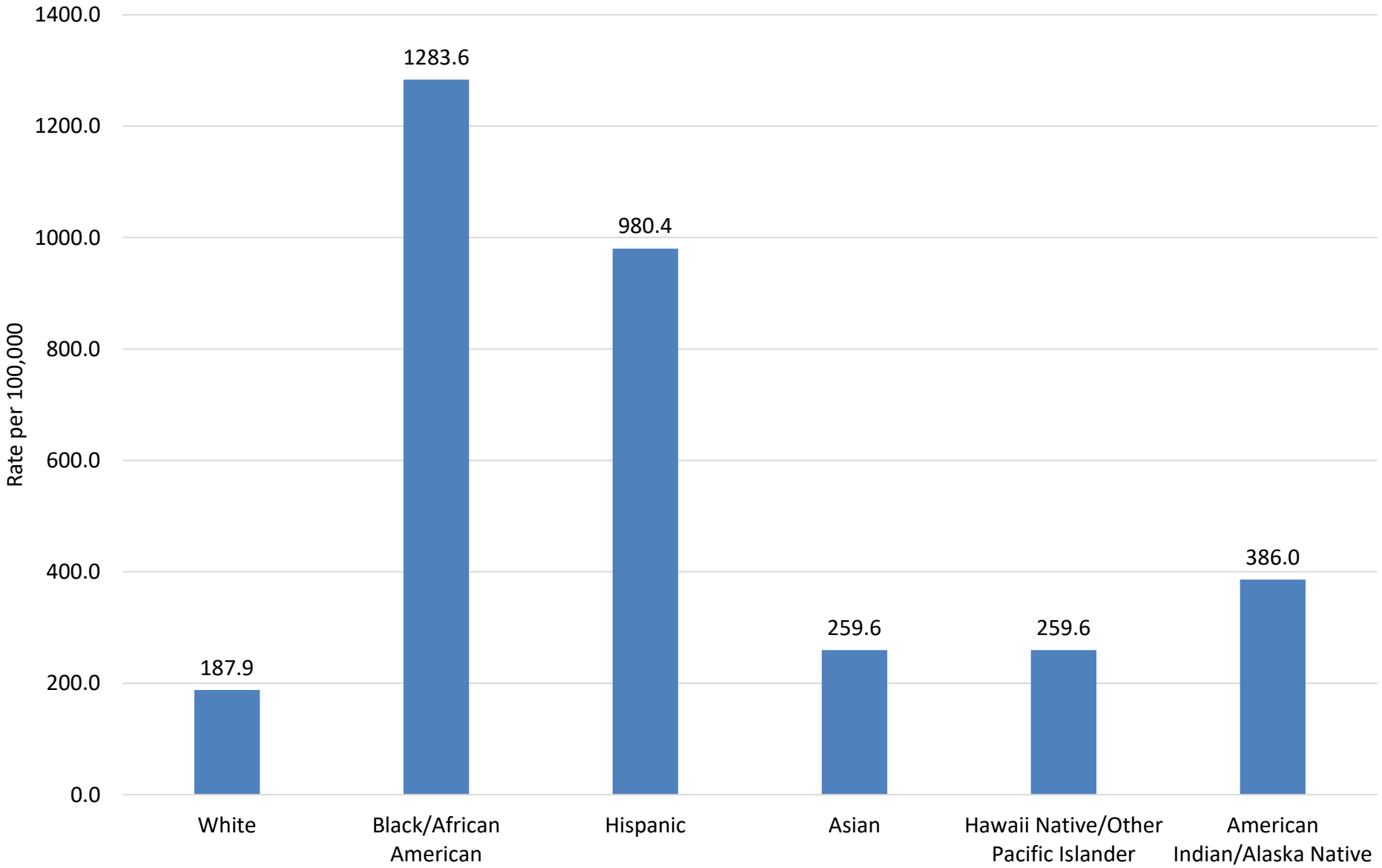
Chlamydia Rates by Sex, 2013-2022



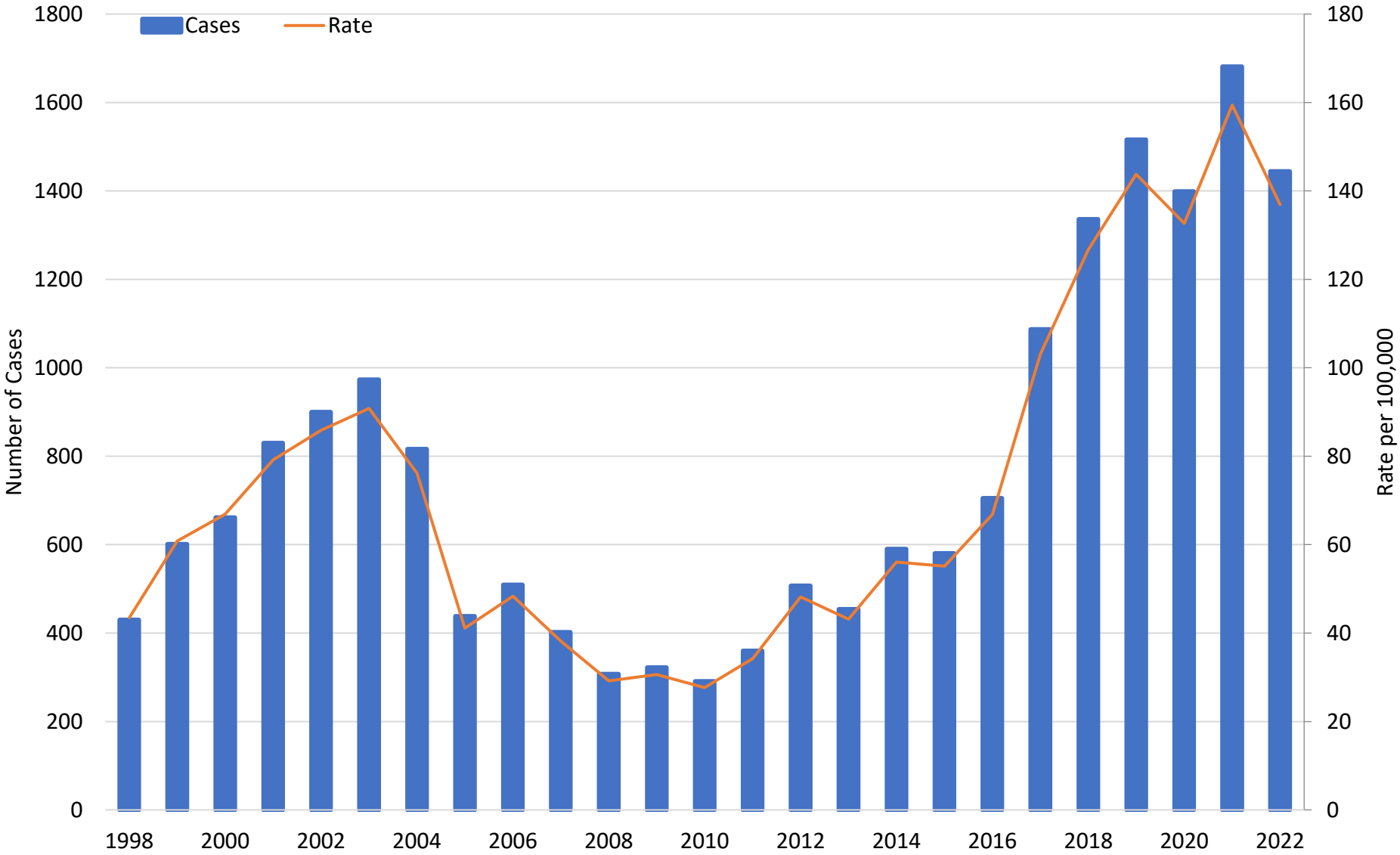
5-Year Average Rate of Chlamydia by Age Group, 2018-2022



5-Year Average Rate of Chlamydia by Race & Ethnicity, 2018-2022



Gonorrhea, 1998-2022



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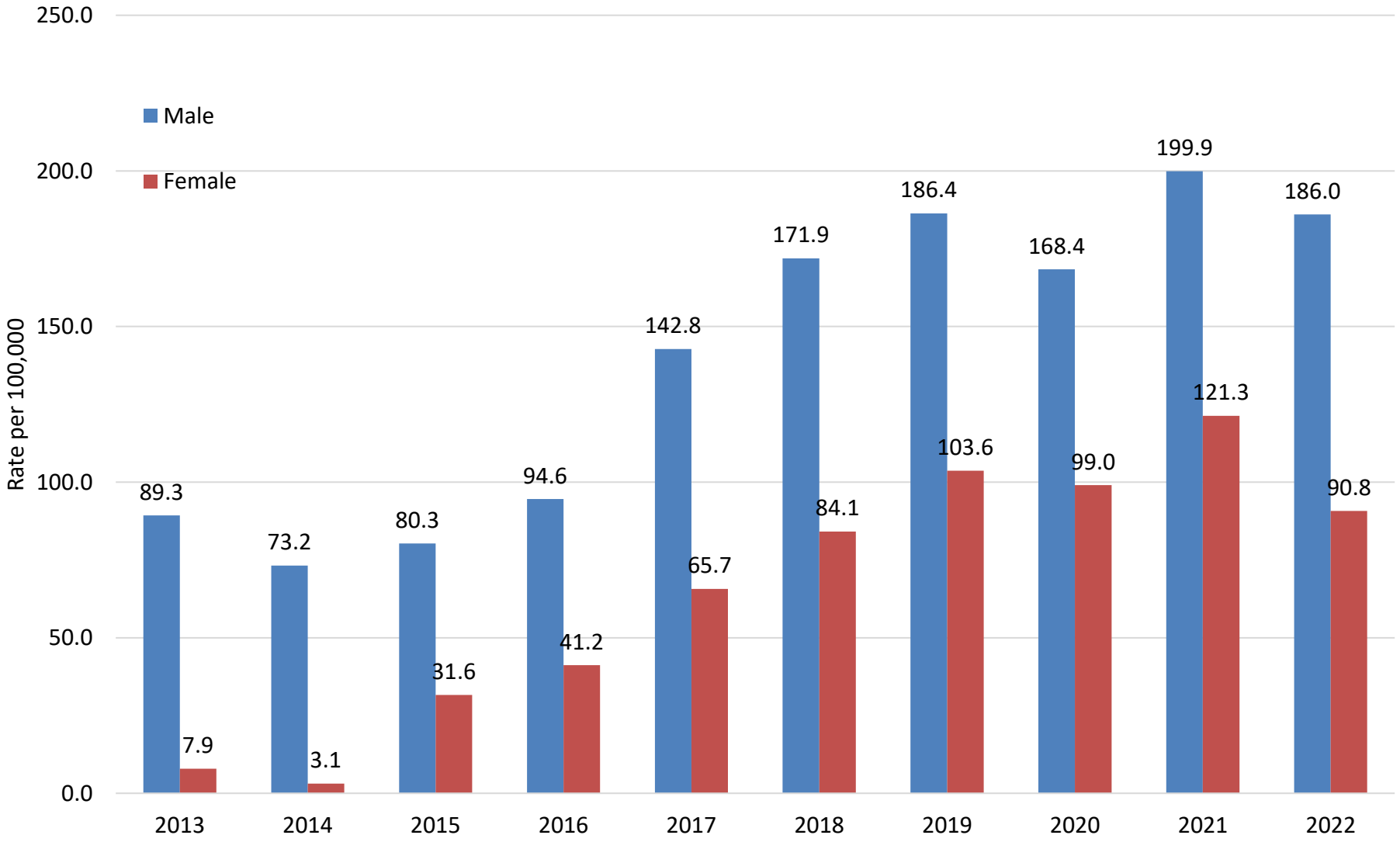

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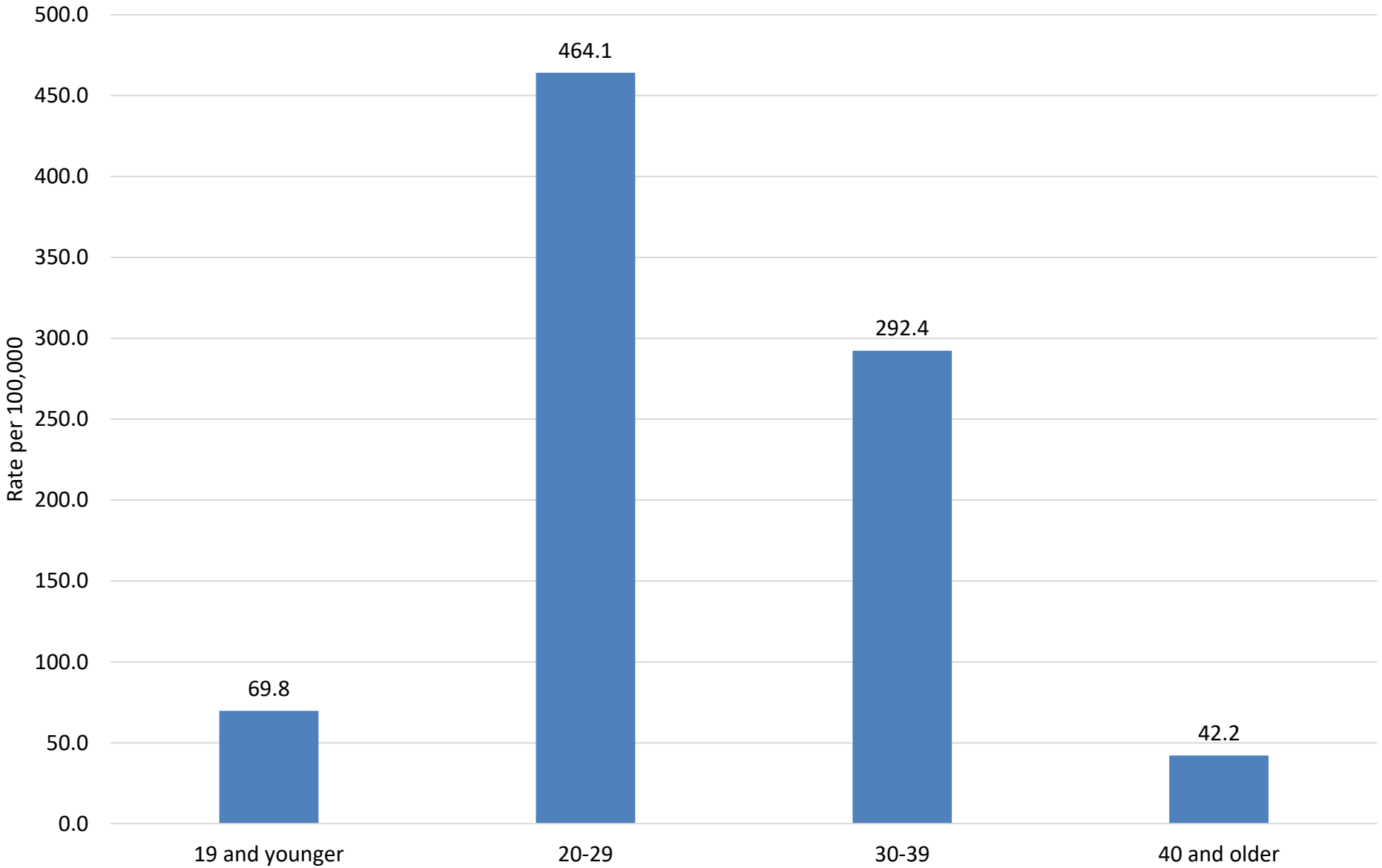

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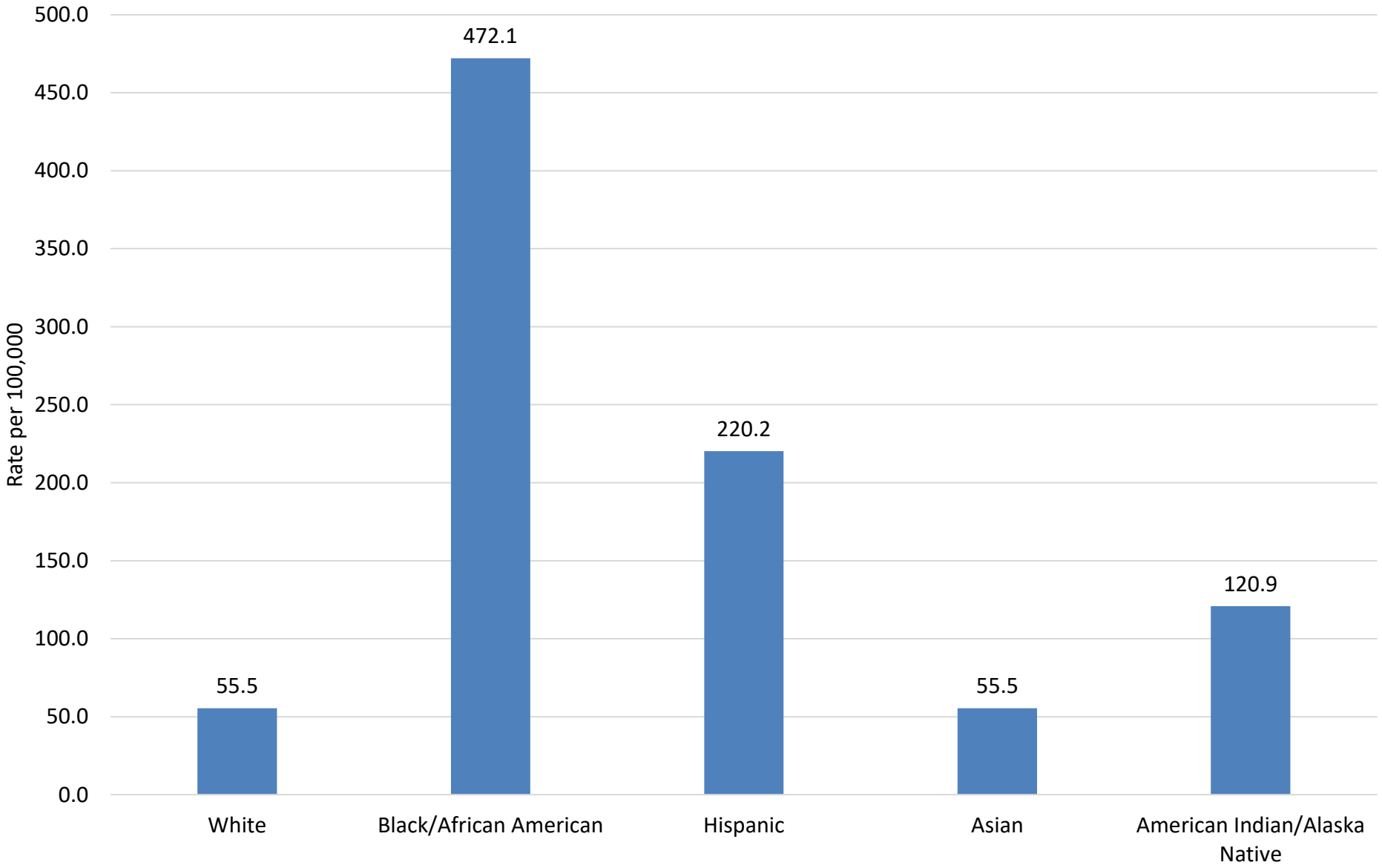
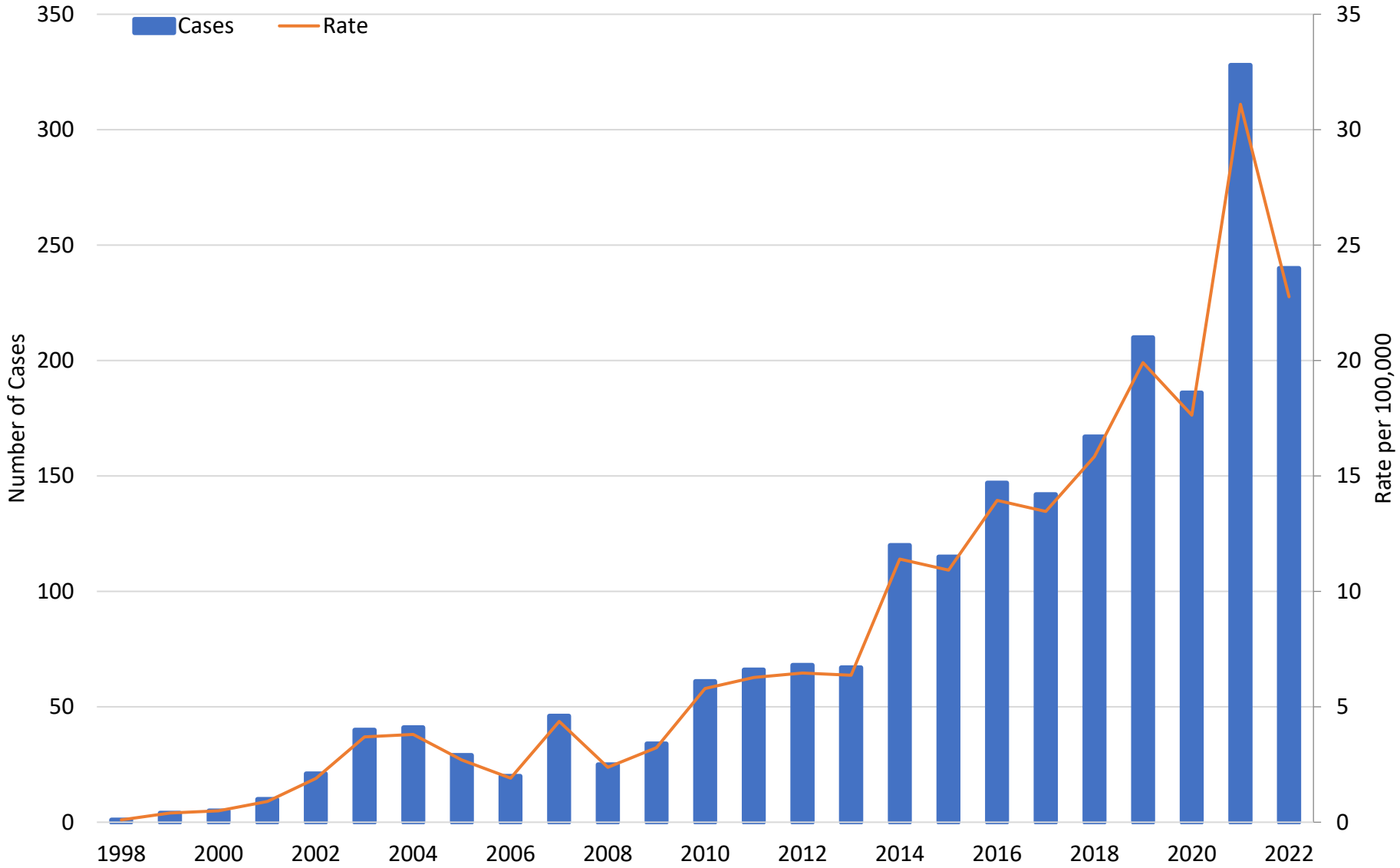
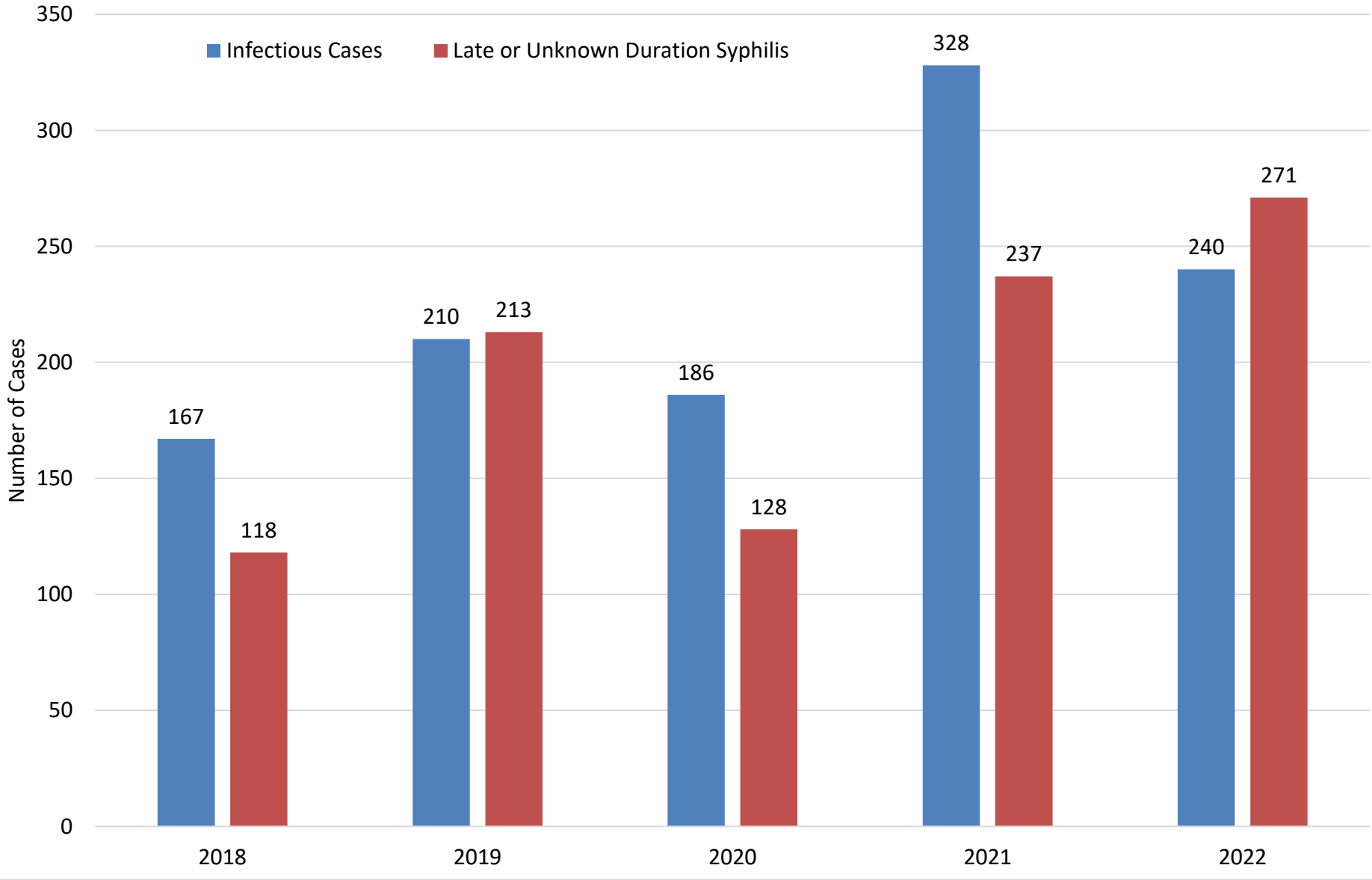


Infectious Syphilis, 1998-2022



Syphilis by Infectious Stage, 2018-2022



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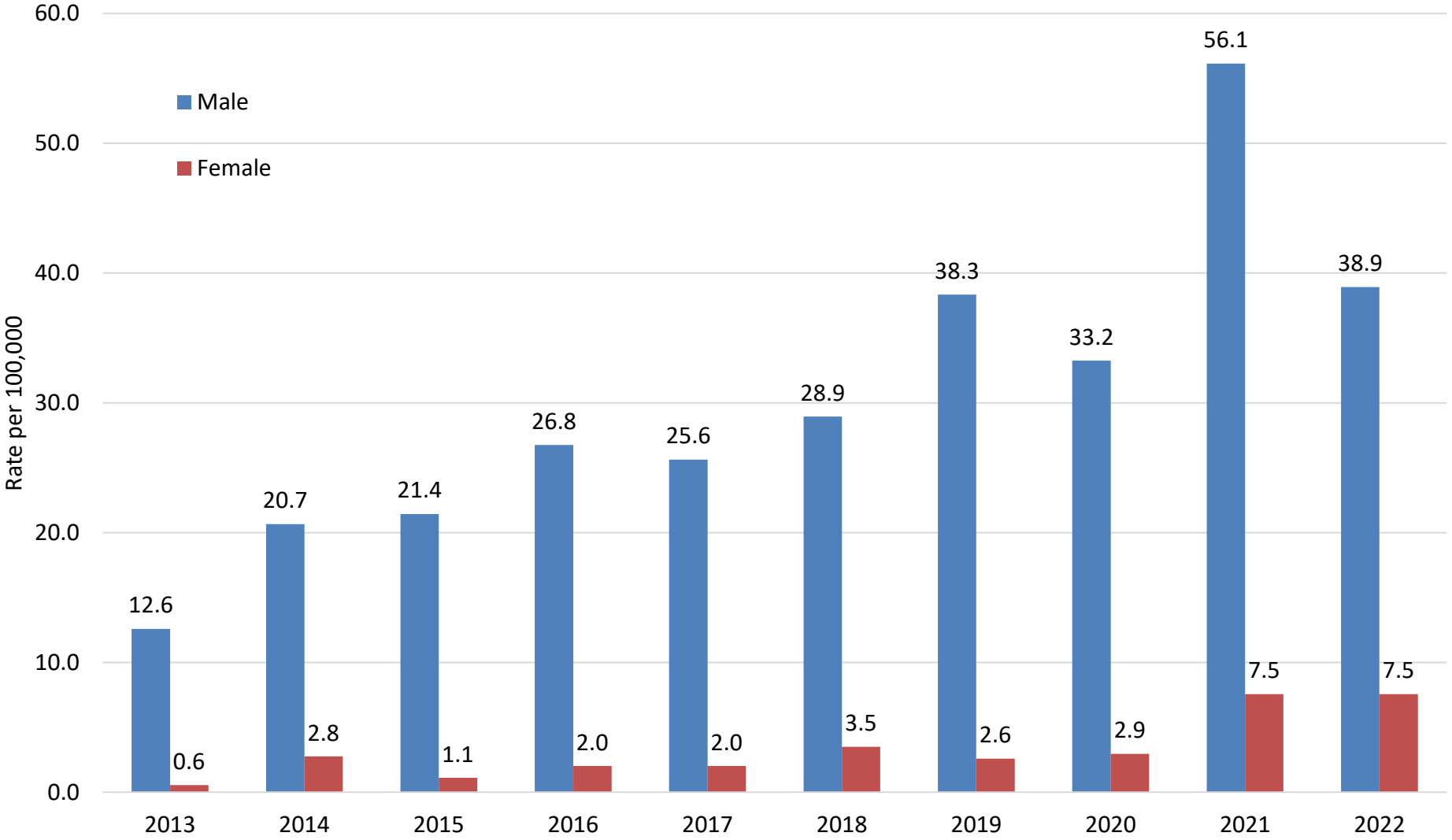
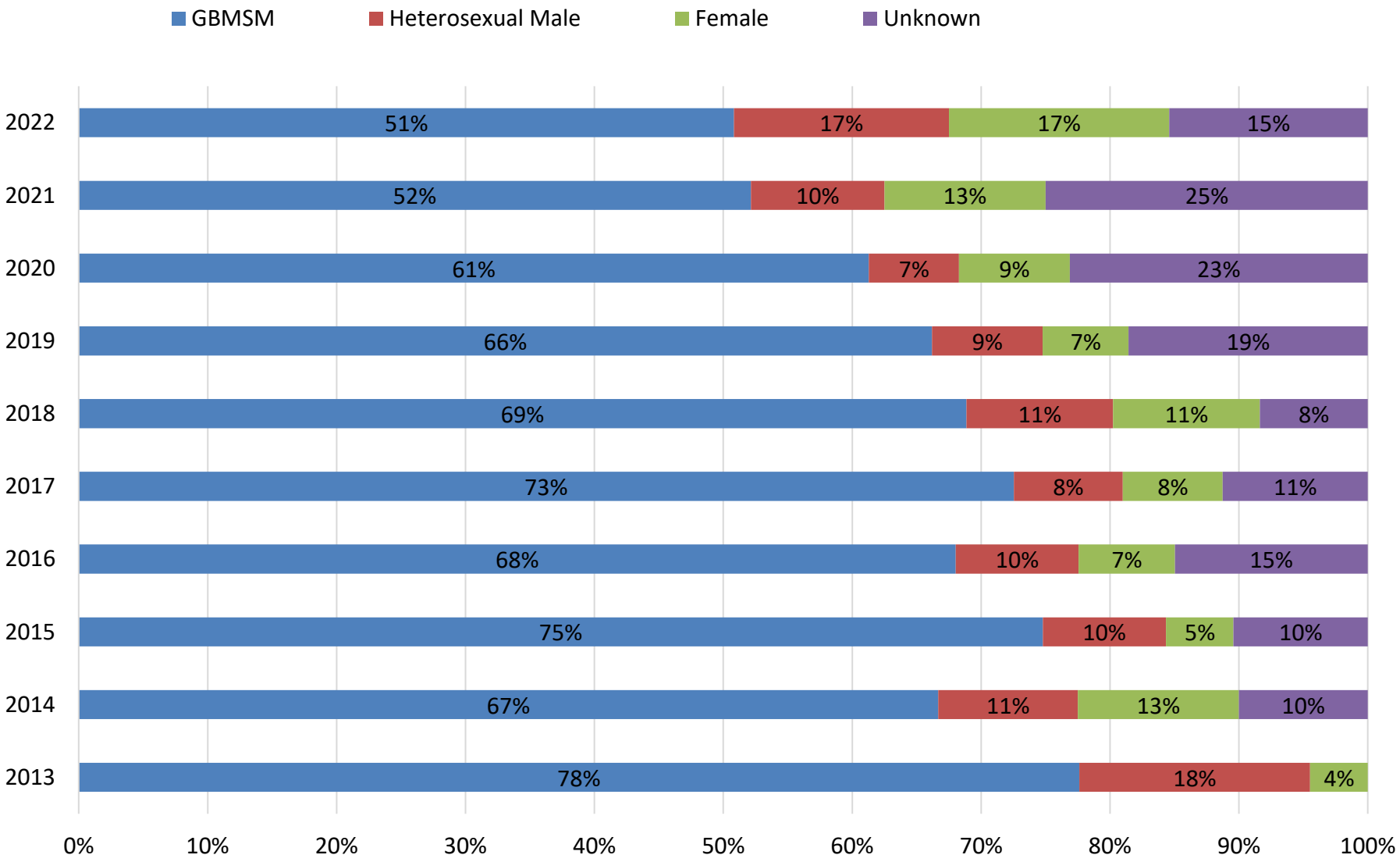


Infectious Syphilis by Known Sexual Orientation, 2013-2022



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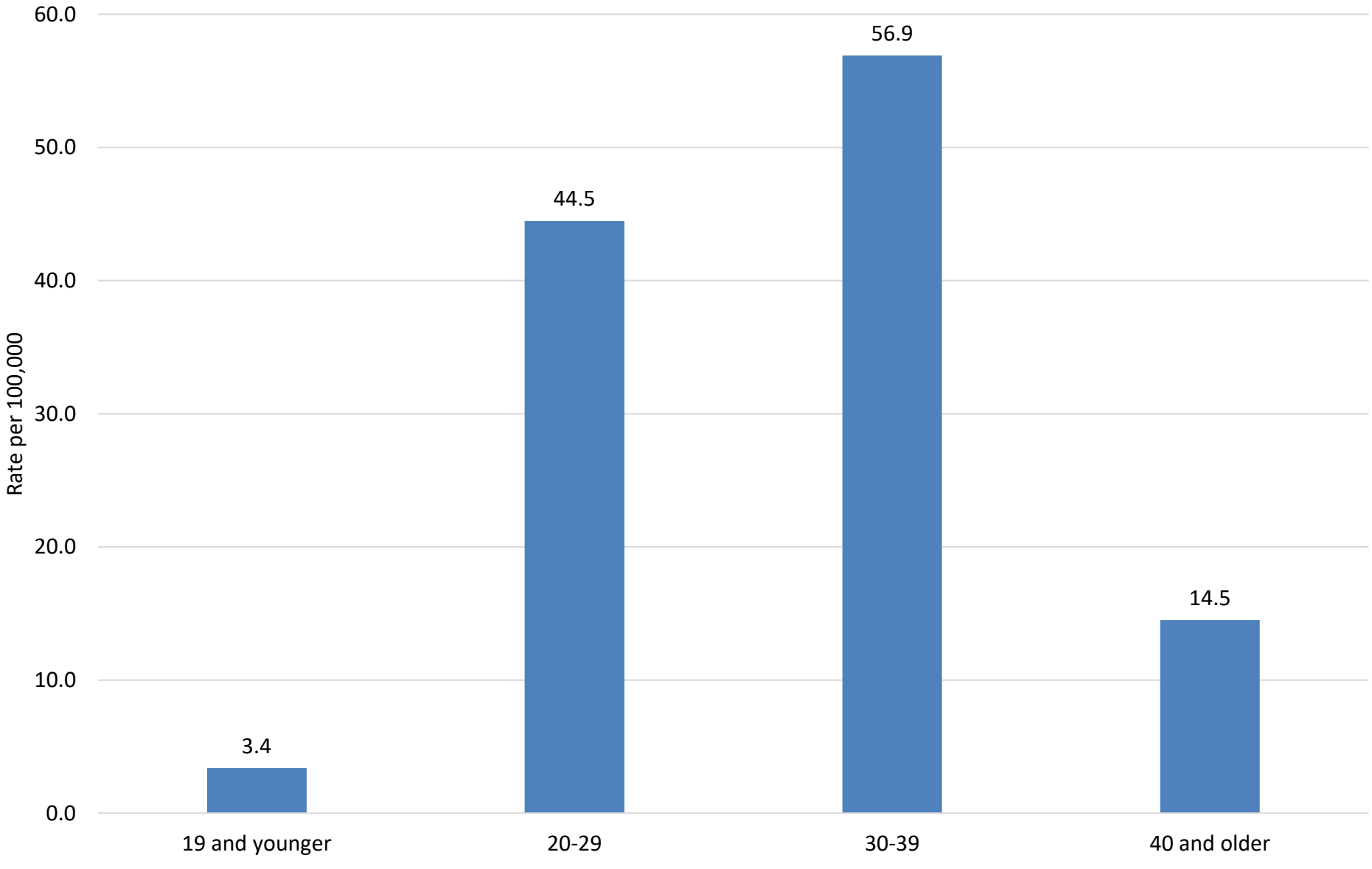

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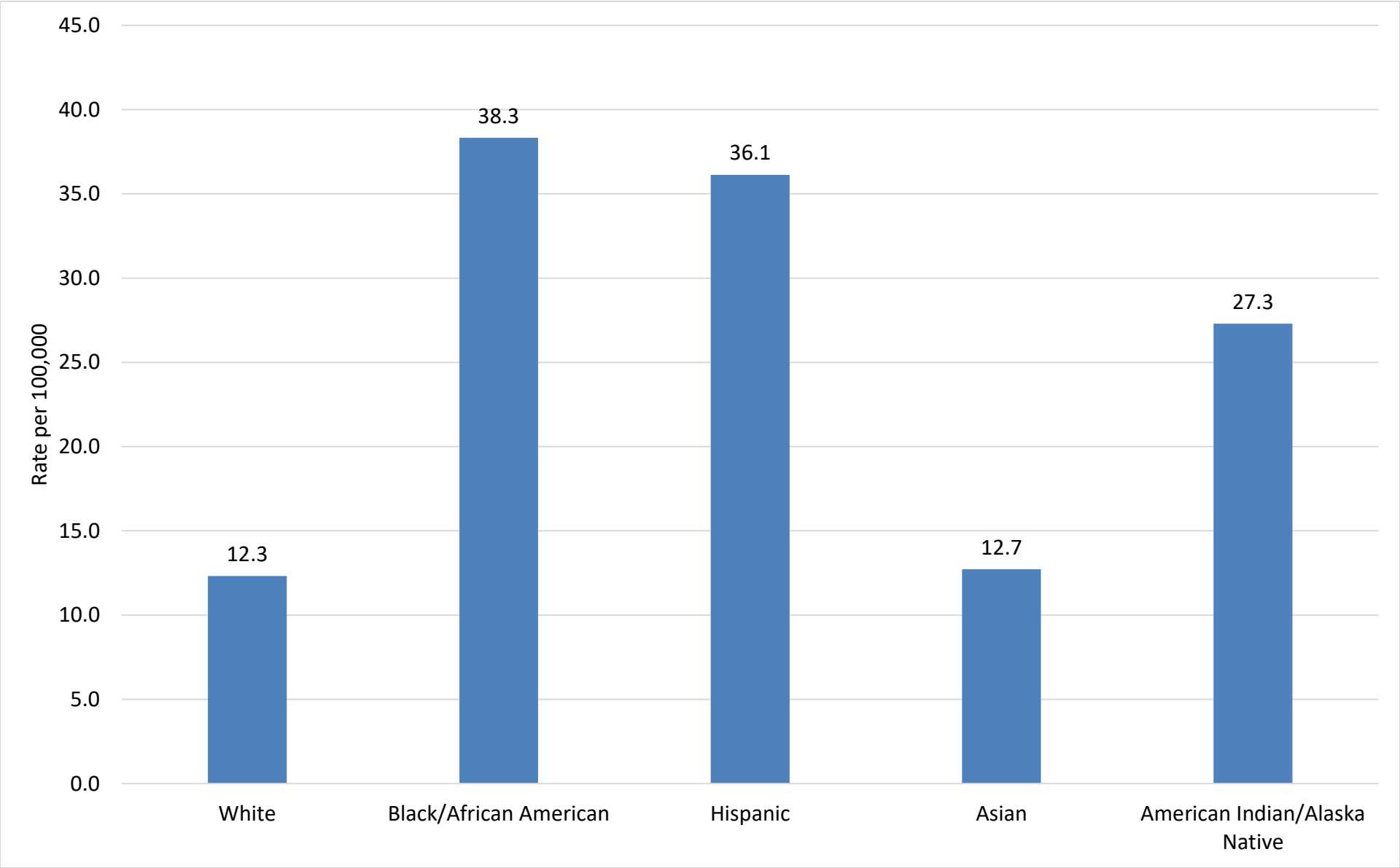
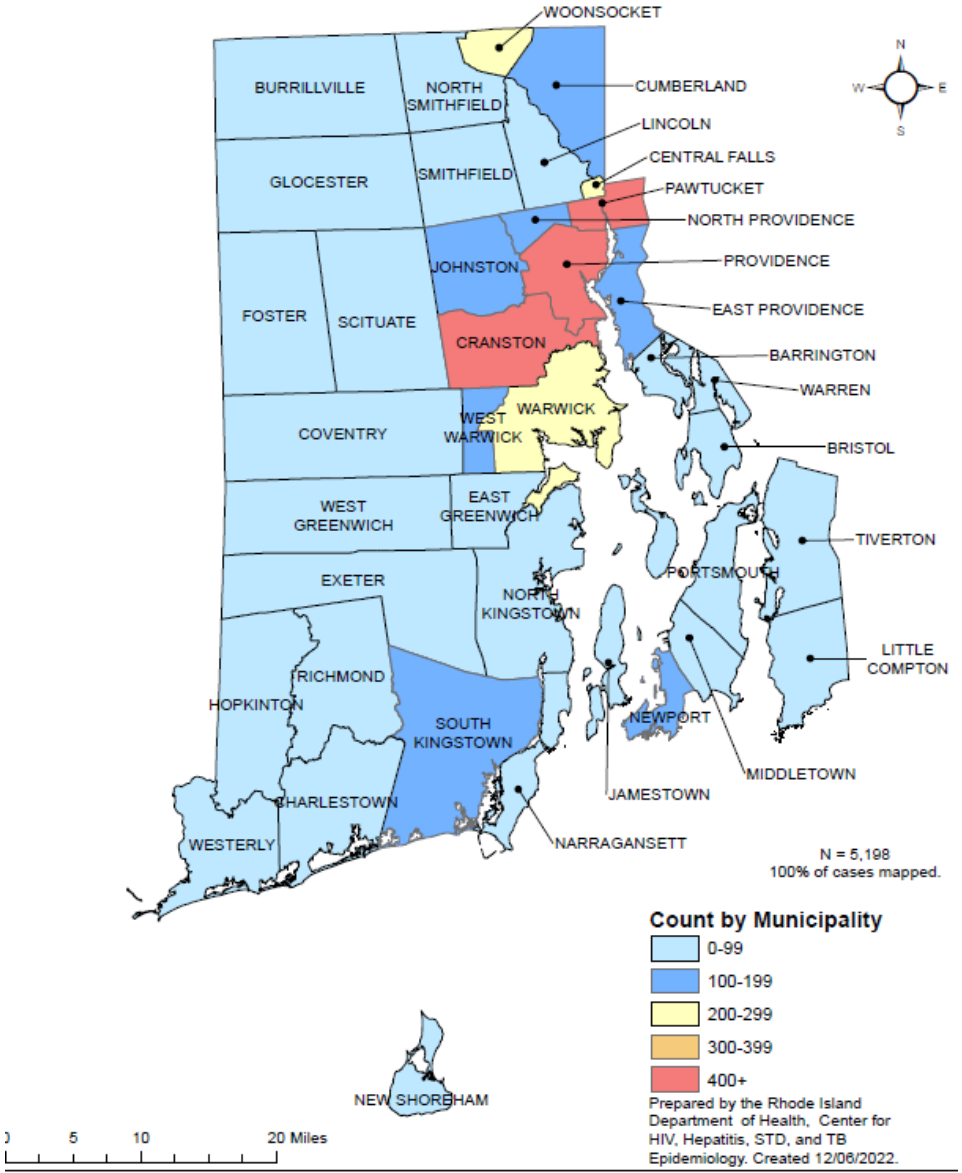


Chlamydia in Rhode Island, 2021



- 79% residents of Providence County
- 65% female | 35% male
- 59% aged 15-24 years
- 78% under 30 years old
- 30% non-Hispanic white
- 30% Hispanic
- 17% non-Hispanic black

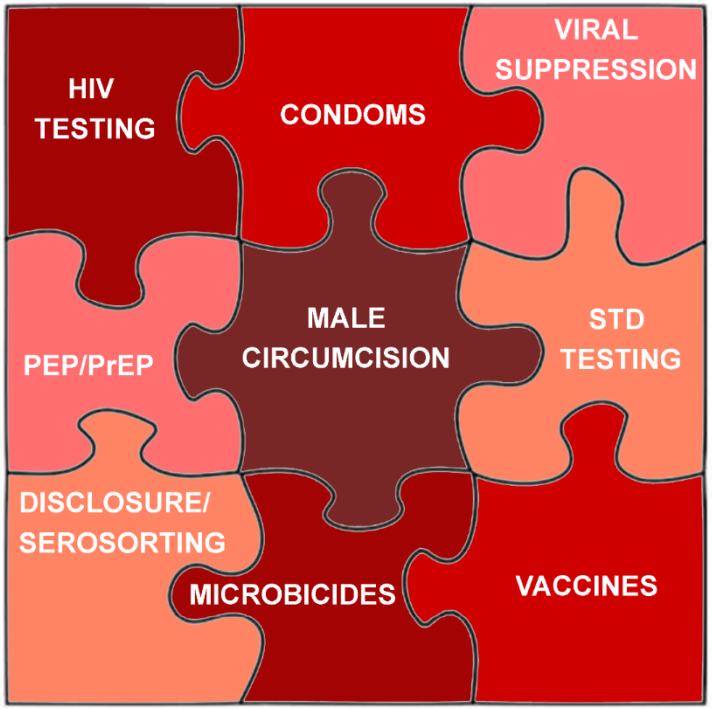
STI Screening and Prevention

STI Screening

Who should I test?

General Population (CDC/USPSTF)

- HIV at least once (CDC: 13-64 years old)
- HCV at least once (18+ years old; unless HCV prevalence <0.1%)



Cis-gender women (CDC/USPSTF)

- Chlamydia/gonorrhea annual opt-out testing (24 years and younger;
- Chlamydia/gonorrhea testing if at-risk* (25+ years)

*Previous/current STI; new or >1 sex partner; sex partner with multiple partners, sex partner with an STI; condomless sex not in a monogamous relationship; history of incarceration; history exchanging sex for money/drugs.

**Chlamydia rectal testing and gonorrhea rectal and pharyngeal testing can be considered for females based on sexual behaviors

Men who have sex with men (CDC/USPSTF)

- At least annual testing for HIV, syphilis, gonorrhea (urogenital, rectal, and pharyngeal) and chlamydia* (urogenital, rectal). Every 3-6 months if multiple risk factors.

*Pharyngeal screening for chlamydia is not technically recommended because the clinical significance is unclear given most people are symptomatic and the prevalence is low. However, most clinics test for both.

Transgender and Gender Diverse (CDC)

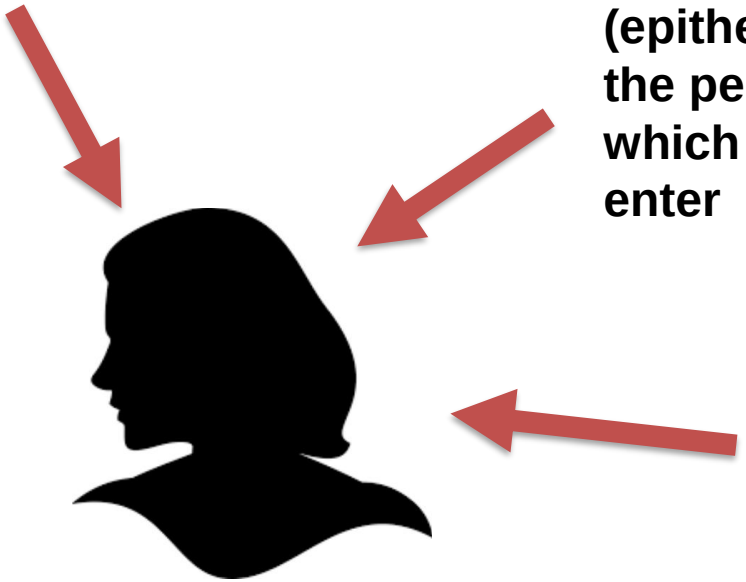
- Based on anatomy;
- Extragenital testing.

www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm

STIs and Risk of HIV Infection

STIs increase the risk of acquiring HIV (3-5x increased susceptibility)

STIs in the HIV+ partner can increase viral shedding



STIs cause breaks in the skin (epithelial lining) surrounding the penis, vagina and anus which allows HIV to more easily enter

STIs increase the concentration of CD4 cells in the genital tract, a target of HIV

Ward et al., *Curr Opin HIV AIDS*, 2010

STIs and Risk of HIV Infection

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10% of new HIV infections may be due to gonorrhea and chlamydia!

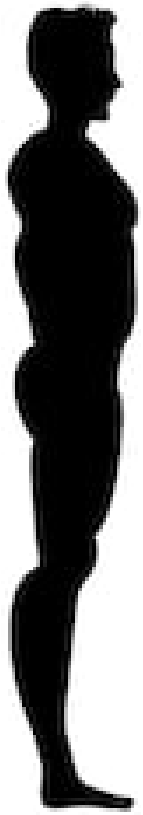
STIs increase the concentration of CD4 cells in the genital tract, a target of HIV

Jones at al., *STDs*, 2019

The Importance of Extragenital STD Testing

Over 70% of gonorrhea (GC) and chlamydia (CT) infections among MSM are missed by urogenital screening only

Receptive anal sex can lead to rectal GC/CT infection that would be missed with urogenital screening only



Performing oral sex can lead to pharyngeal GC/CT infection that would be missed with urogenital screening only

"Don't forget the triple dip!"

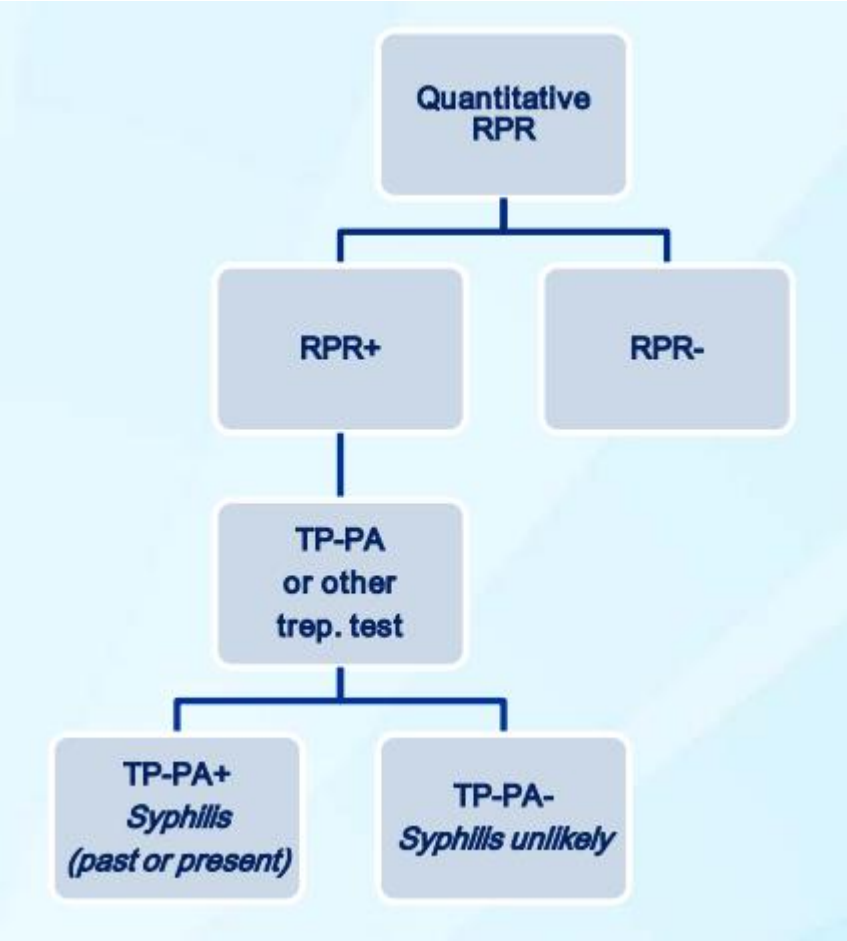
*Self-collected swabs are OKAY

Urogenital screening tests for the presence of GC/CT in the urethra

Patton at al., CID, 2014

Syphilis

Traditional Testing Algorithm



Non-treponemal tests (e.g., RPR, VDRL)

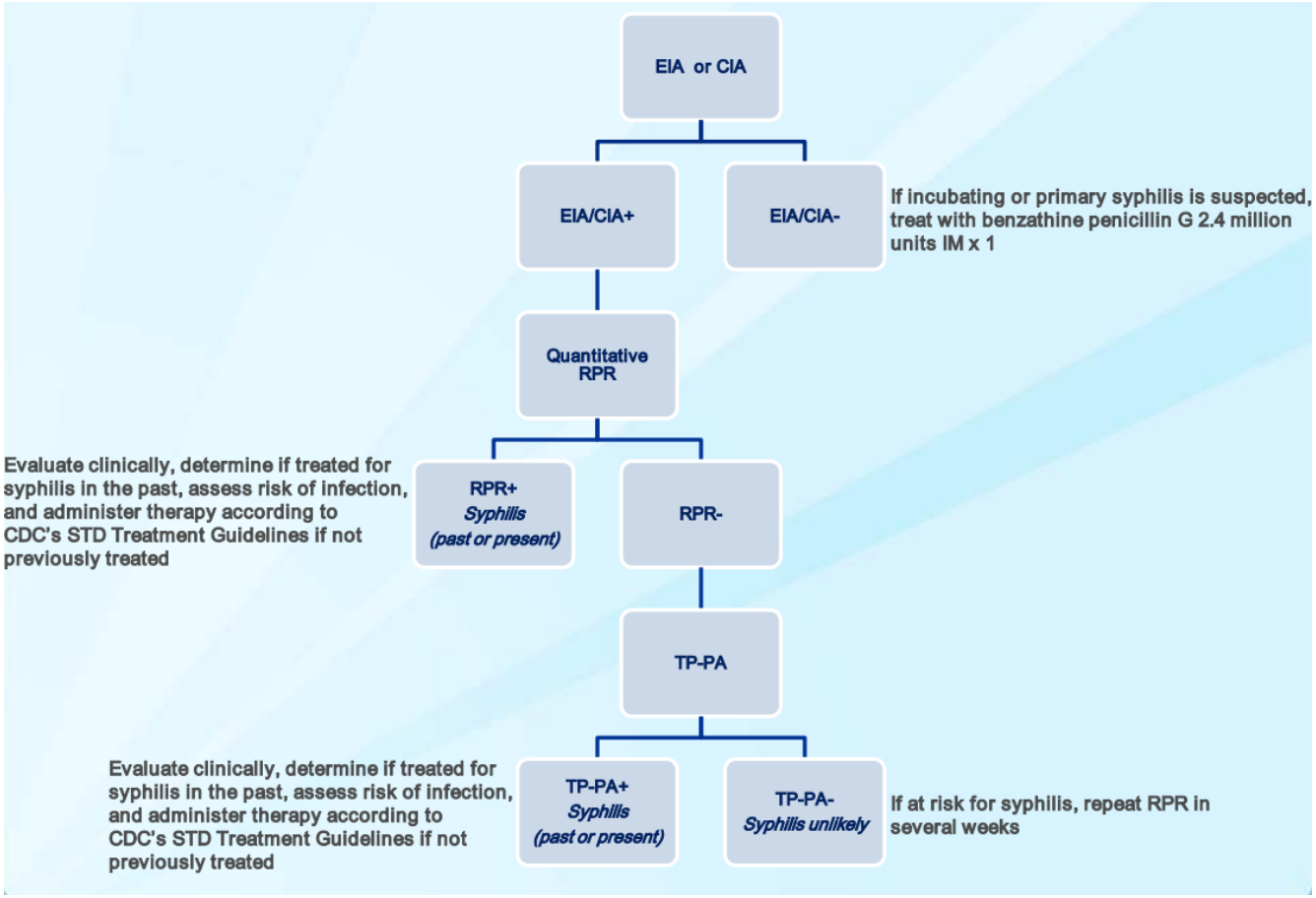
- NON-SPECIFIC ANTIBODY TO LIPOIDAL ANTIGENS
- QUANTITATIVE
- REACTIVITY DECLINES WITH TIME

Treponemal tests (e.g., TPPA, FTA-Abs

- SPECIFIC TO *TP*
- QUALITATIVE
- REACTIVITY PERSISTS OVER LIFETIME

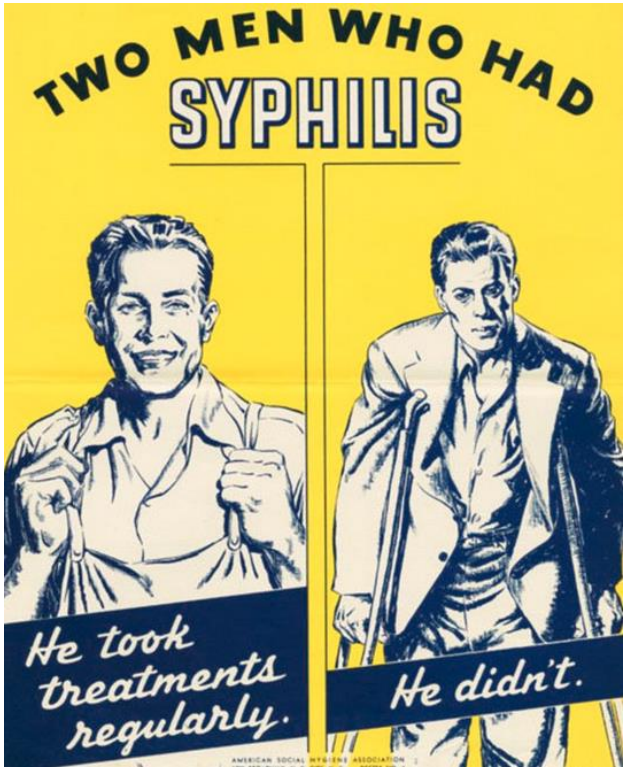
False positive nontreponemal tests can be associated with other infections (e.g. HIV), autoimmune conditions, vaccinations, pregnancy, and older age.

Reverse Sequence Testing Algorithm



***Newer treponemal screening tests:** Enzyme immunoassays (EIA), Chemiluminescence immunoassays (CIA). Microbead immunoassays (MBIA)*

Syphilis Treatment



Early (Primary, Secondary, Latent less than one year): Benzathine penicillin 2.4 m.u. IM once

Late (Latent more than one year, cardiovascular, gummas): Benzathine penicillin 2.4 m.u. IM weekly for three weeks

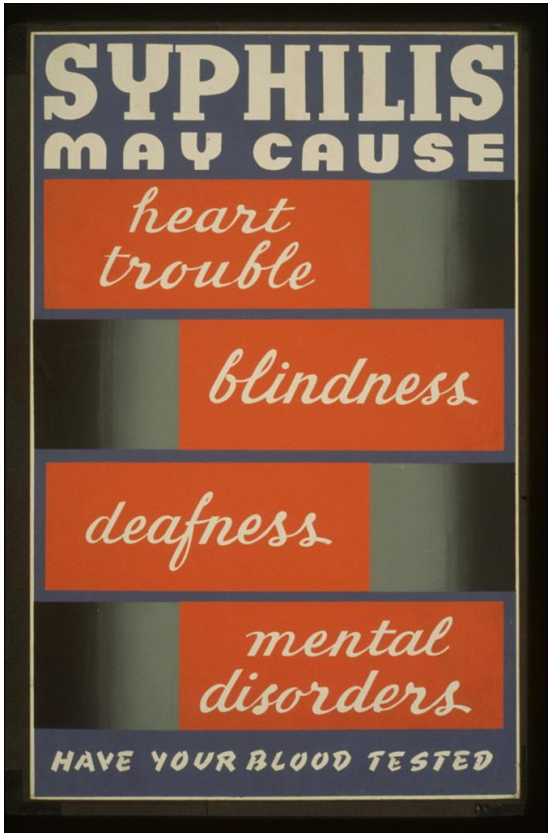
Neurosyphilis: Penicillin G 3-4 m.u. IV every four hours or 24 m.u. continuous infusion for 10-14 days

Congenital: Penicillin G 50,000 units/kg every 8-12 hours for 10-14 days

***Pregnant with syphilis and allergic to penicillin: DESENSITIVE**

***Repeat serologic testing at 6- and 12-months post-treatment (+24 months for latent syphilis, 3-, 6-, 9-, 12-, and 24-months for primary/secondary and 6-, 12-, 18- and 24- months for latent if HIV positive).**

Successful treatment is a 4-fold decline in titers. More frequent follow-up prudent if concern for repeat infection. If concern for treatment failure, CSF examination is recommended



Alternative Syphilis Treatment (Penicillin Allergy)

Early (Primary, Secondary, Latent less than one year): Doxycycline 100mg PO BID for 14 days

Late (Latent more than one year, cardiovascular, gummas): Doxycycline 100mg PO BID for 28 days

Neurosyphilis: Ceftriaxone 1-2g IM or IV for 10-14 days (limited data)

***Pregnant with syphilis and allergic to penicillin: DESENSITIVE**

Chlamydia

Chlamydia Treatment

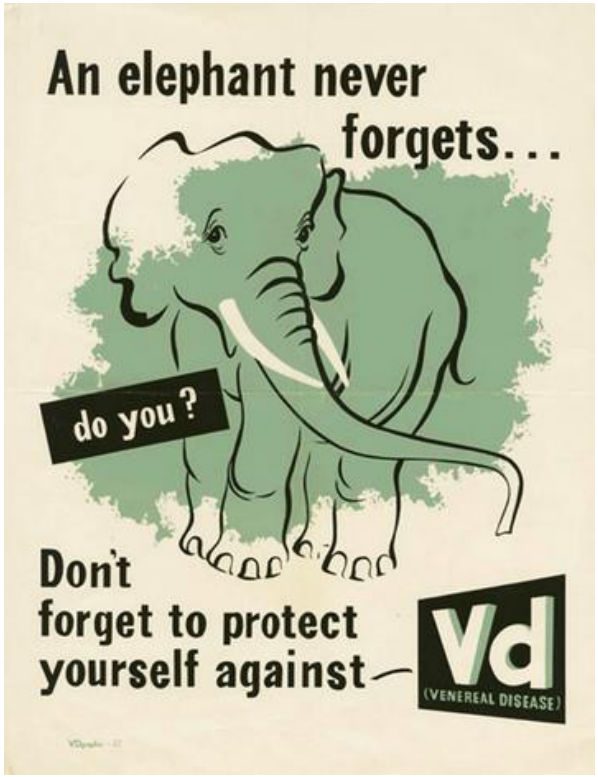
Uncomplicated genital, rectal, or pharyngeal infections

Recommended: Doxycycline
100mg PO BID for seven days

Alternative: Azithromycin
1 gram PO once or Levofloxacin
500mg PO once daily for 7 days

*Doxycycline delayed-release 200 mg, once-daily dosing for 7 days effective for urogenital chlamydia. More costly but lower frequency GI side effects than standard doxycycline.
**In pregnancy, azithromycin 1 gram PO once still recommended (Alternative: amoxicillin 500mg PO three times a day for 7 days.

Gonorrhea



Gonorrhea Treatment

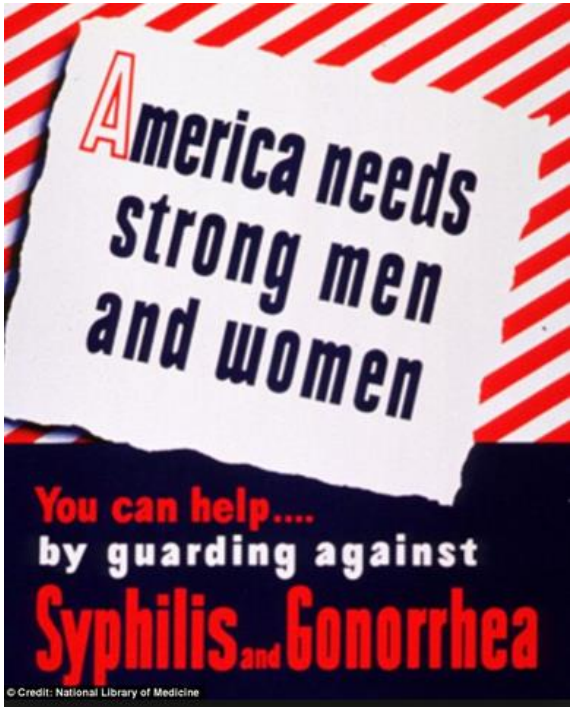
Uncomplicated genital, rectal, or pharyngeal infections

Recommended: Ceftriaxone 500mg IM once † (Monotherapy)

If concern for chlamydia:
Doxycycle 100mg PO BID x 7 days

***2015 CDC Guidelines:** Ceftriaxone 250mg IM once and azithromycin 1g PO once (regardless of chlamydia testing)
****Disseminated GC**: Ceftriaxone 1g IM or IV Q24 hours (Alternative: Cefotaxime or Ceftizoxime 1g IV Q 8 hours).

†Change made December 18, 2020, www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm



Gonorrhea Treatment

Uncomplicated genital, rectal, or pharyngeal infections

If ceftriaxone is unavailable, can do:

Gentamicin 240mg IM + Azithromycin 2 grams PO once (3% vomiting)

or

Cefixime 800mg PO once
(was 400mg PO once)

***Test-of-cure is not needed except for pharyngeal infections (re-test at 7-14 days) or if persistent symptoms (2015: Only re-test if alternative regimen used for pharyngeal infection).**

****In penicillin allergic patients, can perform gyrase A testing to identify cipro susceptibility, and treat with cipro 500mg PO once if sensitive.**

Doxycycline as Post-Exposure Prophylaxis (PEP) to Prevent Bacterial STIs (Syphilis, Gonorrhea, and Chlamydia)

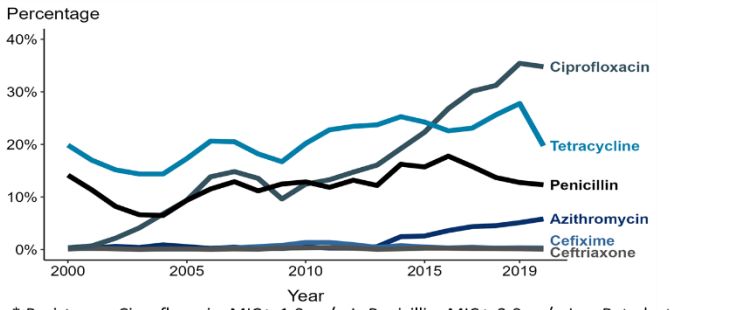
Rationale

- STIs have been significantly increasing;
- Doxycycline has been used for longer-term prophylaxis and treatment in other settings (i.e., malaria, acne, Lyme disease, etc.);
- Generally well-tolerated;
- Low-cost.

Doxycycline

- First-line treatment for chlamydia;
- Second-line treatment for syphilis;
- Some efficacy against gonorrhea.

Neisseria gonorrhoeae — Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2020*



* Resistance: Ciprofloxacin: MIC ≥ 1.0 µg/mL; Penicillin: MIC ≥ 2.0 µg/mL or Beta-lactamase positive; Tetracycline: MIC ≥ 2.0 µg/mL

† Elevated MICs: Azithromycin: MIC ≥ 1.0 µg/mL 29 (2000–2004); ≥ 2.0 µg/mL (2005–2020); Ceftriaxone: MIC ≥ 0.125 µg/mL; Cefixime: MIC ≥ 0.25 µg/mL

DOXYPEP

Doxycycline post-exposure prophylaxis for prevention of STIs among MSM and TGW who are living with HIV or on PrEP (DoxyPEP)

Overview (San Francisco, Seattle)

Open-label, randomized study 2:1 to 200mg doxycycline PEP within 72 hours after sex (and ideally within 24 hours) versus no prophylaxis

Inclusion Criteria

- MSM or TGW
- 1+ STI past 12 mo
- Condomless sex 1+ male past 12 mo
- HIV+ or on PrEP

Primary Outcome

At least one incident STI (gonorrhea, chlamydia, syphilis) during follow-up

Participants

N=501 (327 PrEP, 174 HIV+; Testing Q3 mo)

Results

- Stopped early May 2022 due to effectiveness;
- Overall 65%* reduction in STI incidence/quarter
- Reductions in Chlamydia (74-88%*), Syphilis (77-87%*), Gonorrhea (55-57%*)

*Significant results
**Similar reductions in HIV (62%) and PrEP (66%) groups
***No grade 3+ adverse events; 1.5% discontinued due to intolerance or preference; Patterns of use: <10 doses/month (54%); 10-20 doses/month (30%); 20+ doses/month (16%)

Luetkemeyer et al., NEJM, 2023

Implementation and Unanswered Questions: Doxycycline as PEP

Do people actually want to take it?

Multiple studies demonstrate the willingness of MSM to use doxycycline as PEP (and also as PrEP).

How do we achieve major goals of STI control?

Major goals include reducing the overall number of bacterial STI cases and reducing associated sequelae and complications of STIs.

How to effectively reach people?

Specialty clinics (HIV, STI clinics), FQHCs, primary care clinics, community-based clinics, etc.

How to address disparities?

How do we effectively reach African American/Black and Hispanic/Latinx communities?

Maynard et al., STDs, 2023

Implementation and Unanswered Questions: Doxycycline as PEP

What about cis-gender women?

The dPEP-KE study did not show efficacy in cis-gender women. Was low adherence the issue?

Impact on antimicrobial resistance?

Will we see increasing rates of doxycycline resistance in STIs? (i.e., doxycycline resistance in T. pallidum and C. trachomatis is rare. What about M. genitalium? N. gonorrhoeae?)

Will we see increasing rates of doxycycline resistance in other bacteria? (i.e., community-acquired MRSA, etc.)

Impact on the microbiome?

Will doxycycline as PEP affect the microbiome including metabolic changes?

Maynard et al., STDs, 2023

Doxycycline as PEP: Conclusions

What does the evidence show?

Doxycycline 200mg orally within 24 and up to 72 hours of condomless oral, vaginal or anal sex in MSM/TGW reduces infection with bacterial STIs.

How do we counsel people?

Follow the evidence (CDC interim guidance forthcoming).

Risks versus benefits.

Shared decision making.

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

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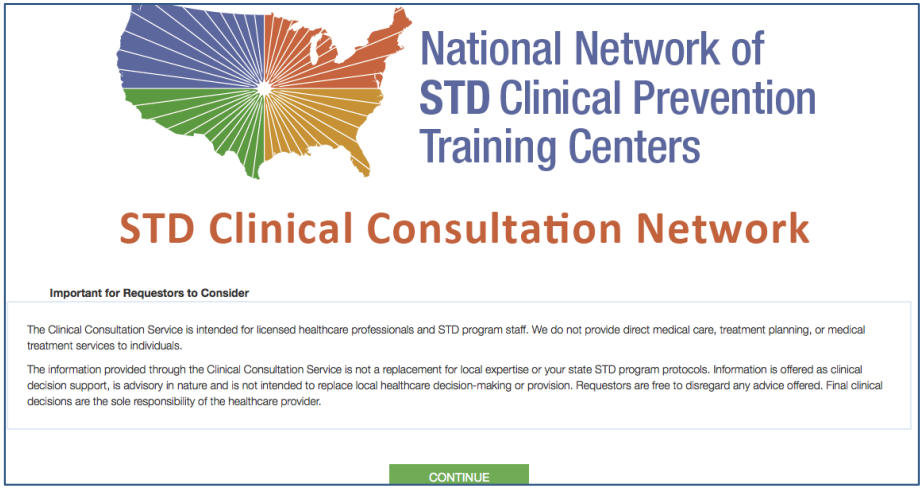

A Focus on Congenital Syphilis & Pregnancy

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Director, Division of Infectious Disease, Women & Infants, and
Care New England Health System

Disclosures

No relevant financial disclosures

Outline

- Congenital syphilis update
- Updates to the 2021 STI Guidelines with a special focus on pregnancy and cis-gender women
- Referral options, resources

Congenital syphilis update

Congenital syphilis (CS) – transmission risk

- When syphilis is transmitted from pregnant patient to fetus
- Can occur at any stage of infection – risk much higher during primary and secondary
  - Early syphilis (60-100% transmission)
  - Early latent (40% transmission)
  - Late latent (8% transmission)
- Untreated fetal infection – 40% result in stillbirth
  - Wide spectrum of disease in infant
- Obstetric complications of CS:
  - Miscarriage, stillbirth, prematurity, low birth weight, death shortly after birth
- Neonatal complications of CS (babies born with CS):
  - Deformed bones, severe anemia, enlarged liver and spleen, jaundice, CNS abnormalities (blindness, deafness), meningitis, skin rashes

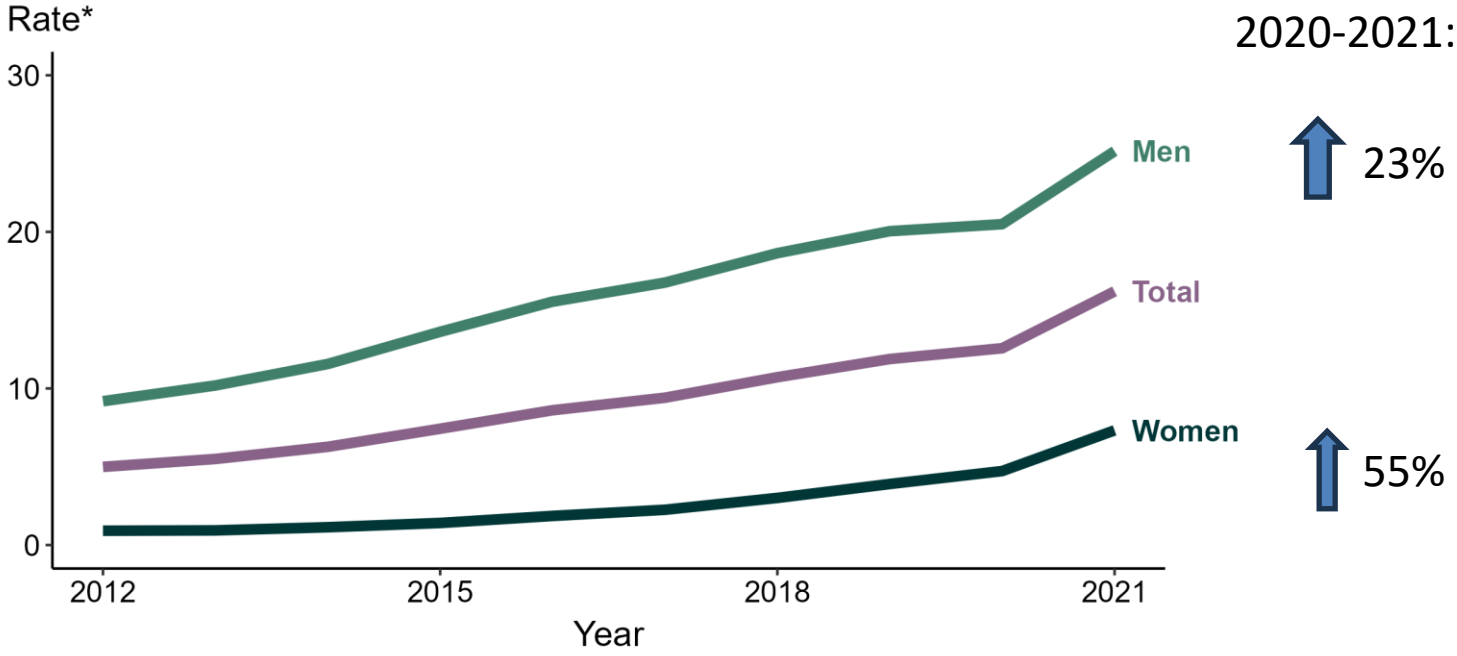
https://www.cdc.gov/std/syphilis/stdfact-congenital-syphilis.htm

Congenital syphilis

- Maternal risk factors for congenital syphilis:
  - Sex with multiple partners
  - Sex in conjunction with drug use or transactional sex
  - Late entry to prenatal care or no prenatal care
  - Methamphetamine or heroin use
  - Incarceration of the woman or her partner
  - Unstable housing or homelessness
- Providers should obtain information concerning ongoing risk behaviors and treatment of sex partners to assess risk for reinfection

https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm

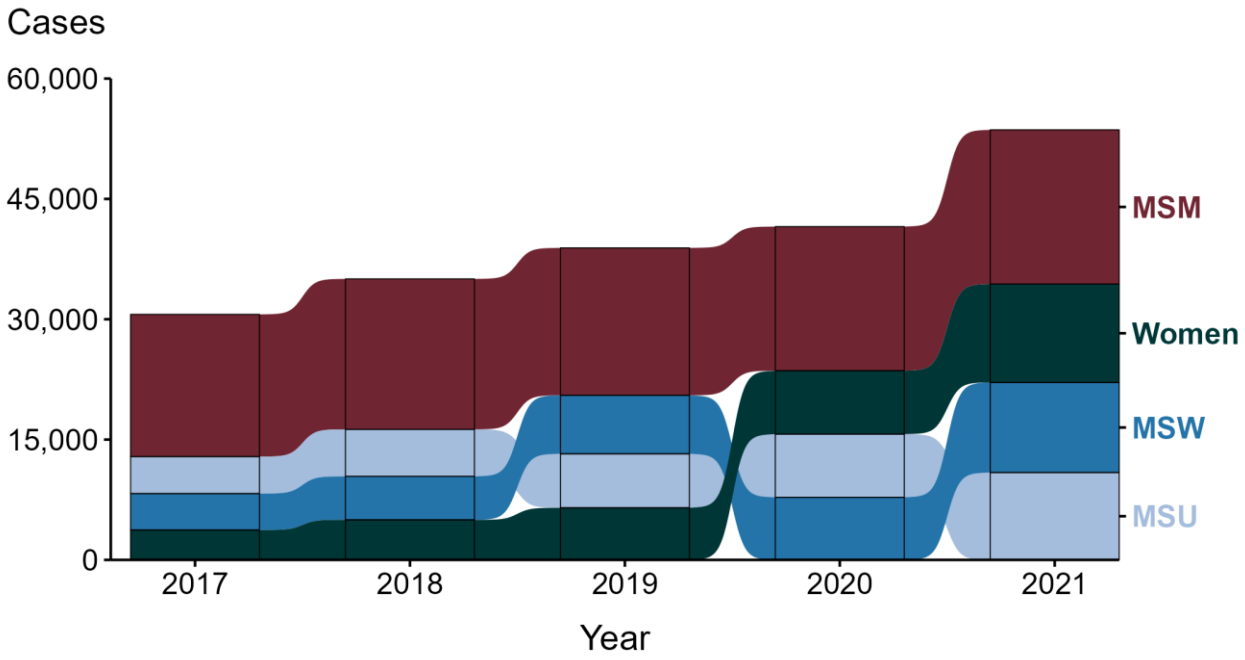
Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2012–2021



* Per 100,000

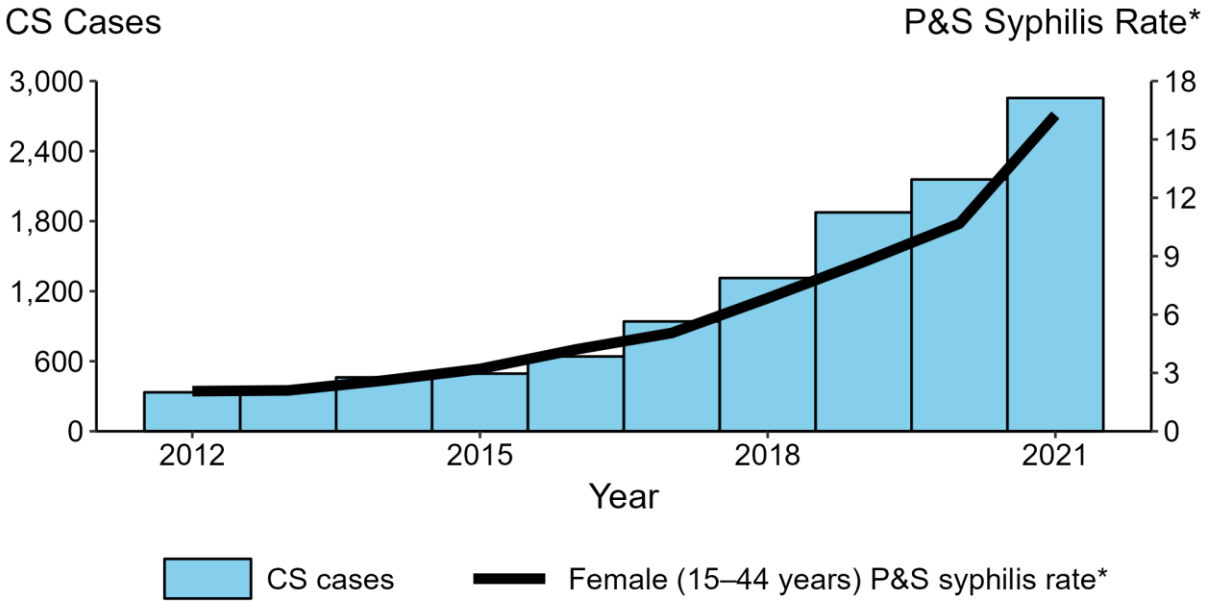
Last 5 years, 217% increase in women, 50% increase in men

Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners, United States, 2017–2021



ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSU = Men with unknown sex of sex partners; MSW = Men who have sex with women only
NOTE: Over the five year period, 0.2% of cases were missing sex and were not included.

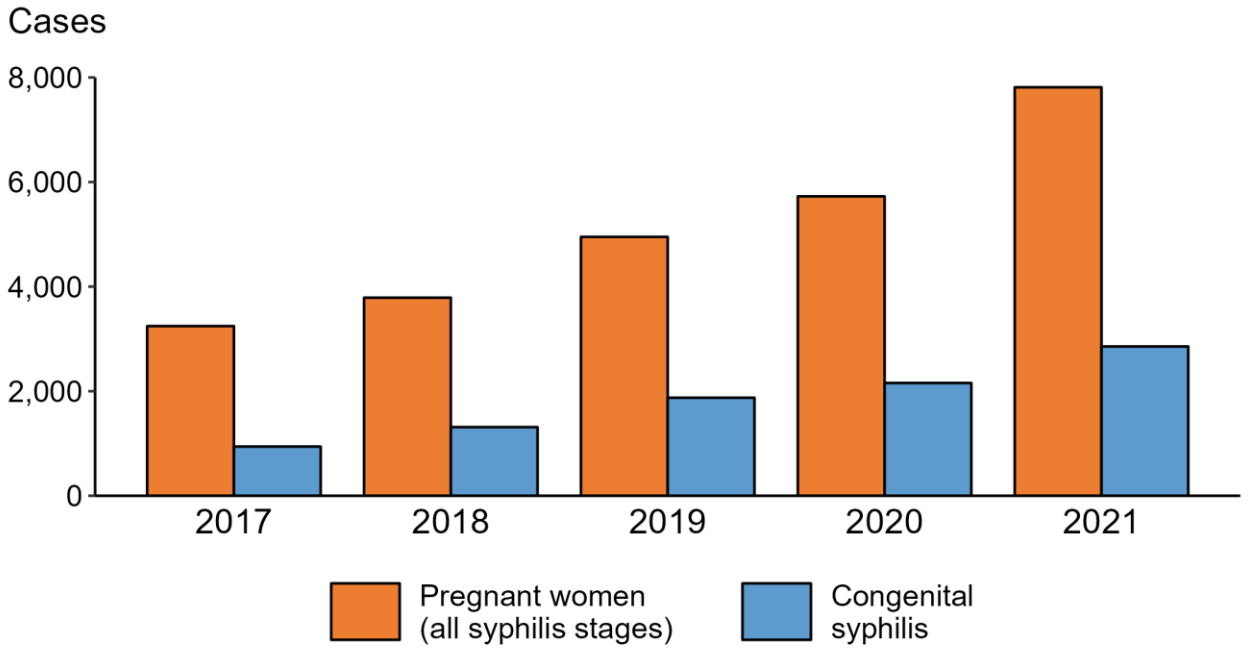
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2012–2021



* Per 100,000

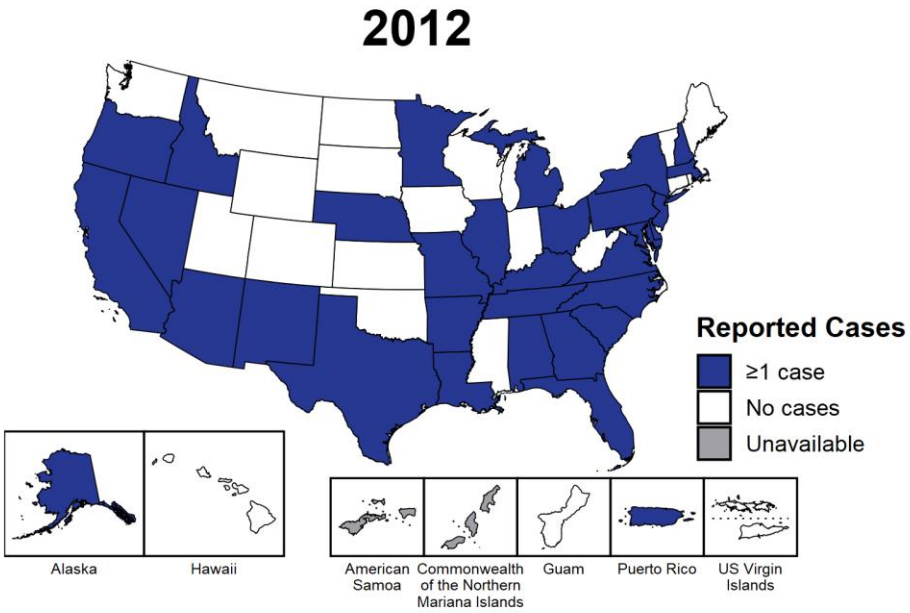
ACRONYMS: CS = Congenital syphilis; P&S Syphilis = Primary and secondary syphilis

Syphilis— Reported Cases of Syphilis (All Stages) among Pregnant Women and Reported Cases of Congenital Syphilis by Year of Birth, United States, 2017–2021

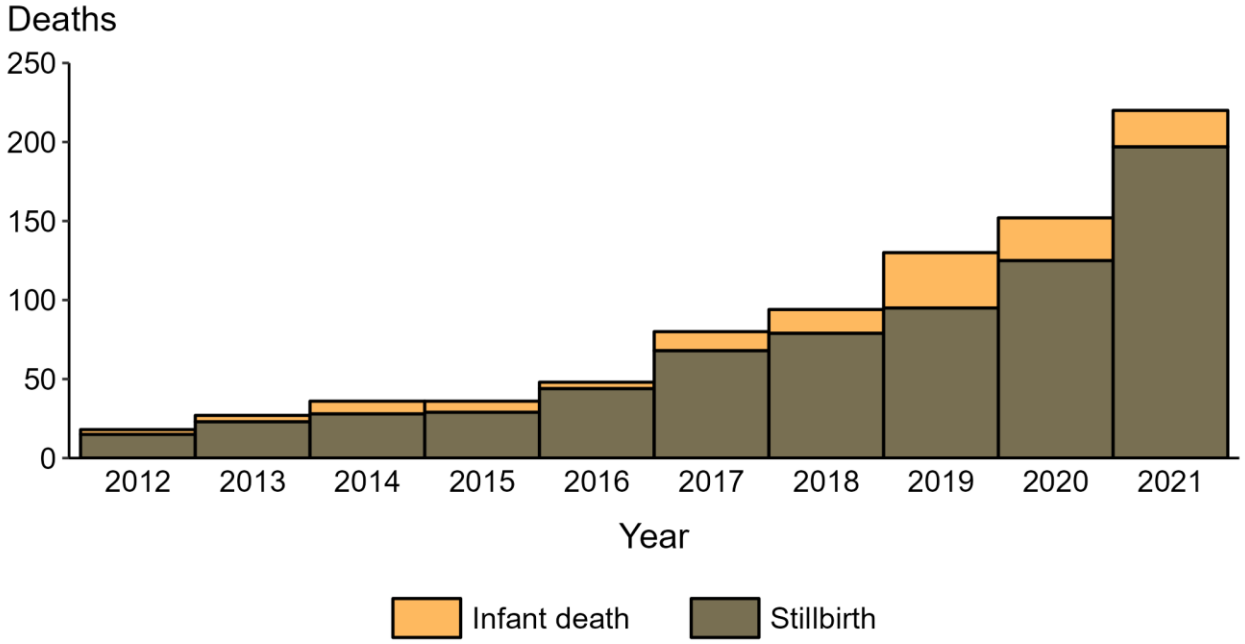


NOTE: The percent of cases missing information on pregnancy status decreased from 14.0% in 2017 to 9.3% in 2021.

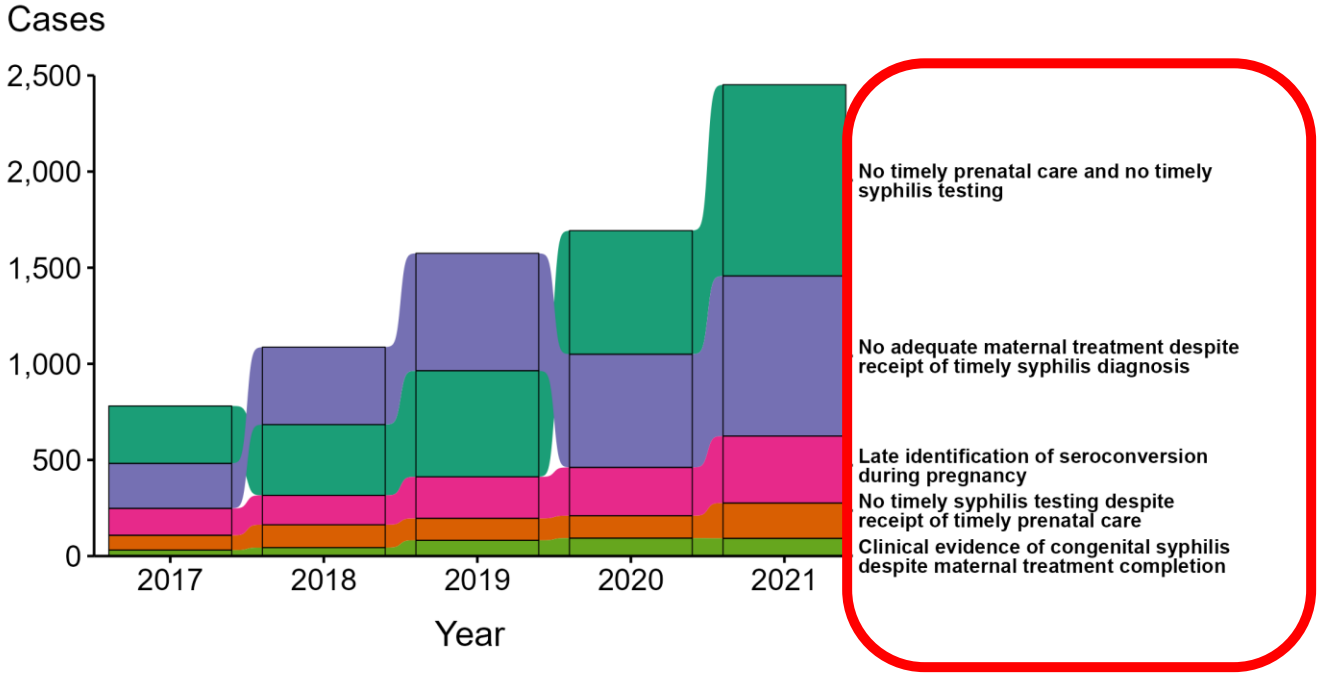
Congenital Syphilis — Reported Cases by Year of Birth and State, United States and Territories, 2012–2021



Congenital Syphilis — Reported Stillbirths and Infant Deaths, United States, 2012–2021



Congenital Syphilis — Missed Prevention Opportunities among Mothers Delivering Infants with Congenital Syphilis, United States, 2017–2021



NOTE: Of the 9,141 congenital syphilis cases reported during 2017 to 2021, 1,553 (17.0%) were not able to have the primary missed prevention opportunity identified due to insufficient information provided to CDC related to maternal prenatal care, testing, or treatment.

Congenital Syphilis

2021

Congenital Syphilis – CDC Fact Sheet

Español (Spanish)

Recently, there has been a sharp increase in the number of babies born with syphilis in the United States. Protect your baby from congenital syphilis by getting tested for syphilis during your pregnancy.

RHODE ISLAND

HIV, Sexually Transmitted Infections, Viral Hepatitis, and Tuberculosis Surveillance Report

Congenital Syphilis

In 2021, among the 11,001 births in Rhode Island, there were less than five infants diagnosed with congenital syphilis. Less than five congenital cases have been reported in Rhode Island over the past 10 years. Nationally, there has been a sharp rise in congenital syphilis. Congenital syphilis cases have more than tripled in recent years in the U.S., with more than 2,000 cases reported in 2020 alone. This is the highest number reported in one year since 1994.

Rising rates of congenital syphilis

The Commonwealth of Massachusetts

Executive Office of Health and Human Services
Department of Public Health

Bu

CHARLES D. BAKER
Governor

KARYN E. POLITO
Lieutenant Governor

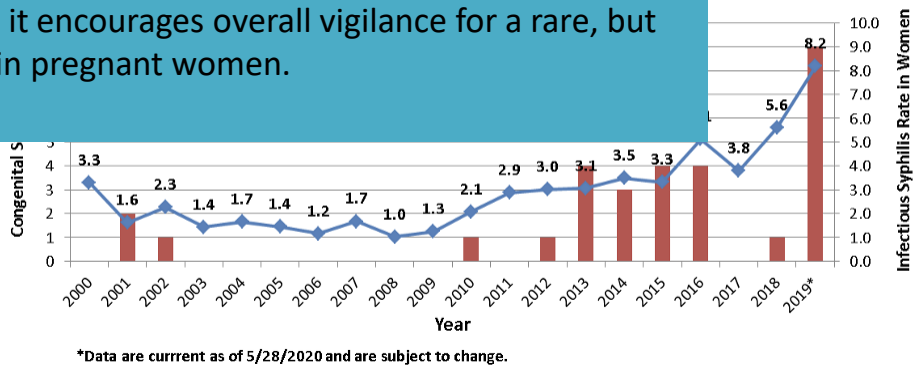
The syphilis rate is rising and projected to exceed 10.0/100,000 women of reproductive age in Massachusetts in 2020. **MDPH is therefore recommending universal syphilis screening early in the 3rd trimester (around 27 - 28 weeks gestation), in addition to routine syphilis screening performed at the first prenatal visit**. Screening again at delivery should be considered in high-risk women. No infant should leave the hospital without the mother's serological status having been documented at least once during pregnancy. Although universal screening during the 3rd trimester may not prevent all cases, it encourages overall vigilance for a rare, but extremely serious occurrence: syphilis in pregnant women.

TO: Maternal and N
FROM: Katherine Hsu,
Lila Coverstone,
Kathleen Roose
DATE: June 30, 2020
RE: Increases in Cor
Universal 3rd Tri

Two stillbirths with syphilis and a congenital syphilis case exhibiting symptoms of rash, jaunc hepatosplenomegaly at birth have been reported to the Massachusetts Department of Publi 2020. One stillbirth occurred in a woman with limited prenatal care who delivered at 28 weeks stillbirth occurred in a woman who delivered at 33 weeks with negative 1st trimester syphilis sc risk to prompt 3rd trimester re-screening, but in retrospect had a rash compatible with seconda weeks. The symptomatic congenital syphilis case was born at 37 weeks to a woman with negat syphilis screening, no history of syphilis symptoms, and no history of risk to prompt 3rd trimest

Infectious syphilis rates in Massachusetts continue to increase. Rates have increased 13-fold

phili
ars)



*Data are currrent as of 5/28/2020 and are subject to change.

Stage of disease	Time	Clinical signs/symptoms
Primary	10-90 days after infection (average 3 weeks)	Chancre (PAINLESS)
Secondary Most infectious – high titers	6 weeks – 6 months	Skin rash (in 75-100%) Mucous membrane ulcerations (5-30%) Fever, LAD, pharyngitis, HA, fatigue
Latent: Early	<12 months	Asymptomatic
Late	> 12 months	Asymptomatic
Late/tertiary (15% of untreated)	10-20 years	Damage to brain, eyes, ears, heart, bone, liver, joints

Syphilis in pregnancy

- Screen everyone at first prenatal visit
- For high prevalence areas, repeat RPR twice in the third trimester and at delivery**
  - 17 states require 3rd trimester testing
- Test all women with stillborn delivery >20wks for syphilis
- If sero-positive, consider infected unless treatment can be documented

** Information about the incidence of syphilis among women is available at the state- and county-level through the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention Atlas and is available at http://gis.cdc.gov/grasp/nchhstpatlas/main.html?value=atlas.

Syphilis - Treatment

- Treat based on stage of disease
- Some evidence for benzathine PCN 2.4 million units IM weekly x 2 for additional fetal treatment (primary, secondary, and early latent)

  ALL MUST BE TREATED WITH PENICILLIN

  If allergic → desensitize to penicillin
- Missed doses >9 days are not acceptable for pregnant women receiving therapy for late latent syphilis
  - Optimal interval is 7 days for pregnant women
  - Offer HIV testing to all diagnosed with syphilis

Maternal Titers After Adequate Syphilotherapy During Pregnancy

Martha W. F. Rac,[1] Stefanie N. Bryant,[1] Joseph B. Cantey,[2] Donald D. McIntire,[1] George D. Wendel Jr,[1] and Jeanne S. Sheffield[1]

[1]Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, and [2]Department of Pediatrics, Parkland Health and Hospital System, Dallas, Texas

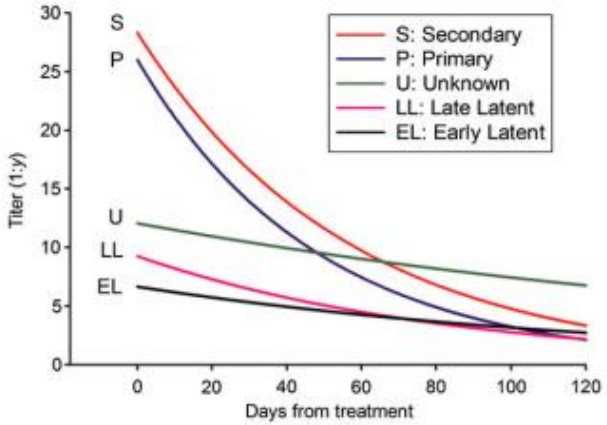


Figure 1. Nontreponemal titer decline after treatment by stage of maternal syphilis.

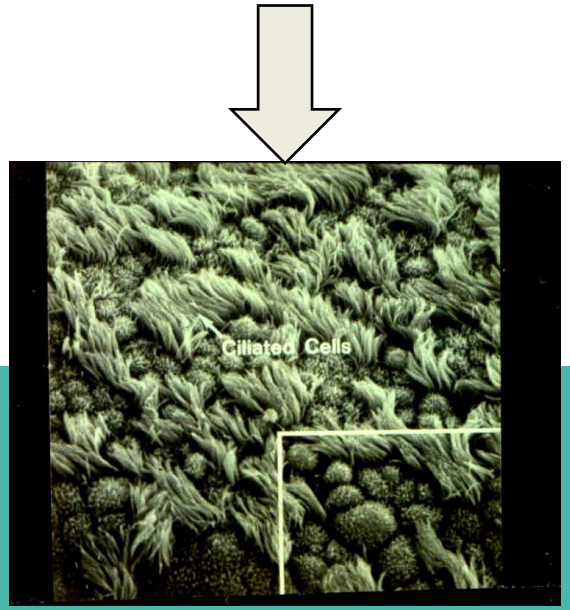
Rac MW et al. CID 2015:60

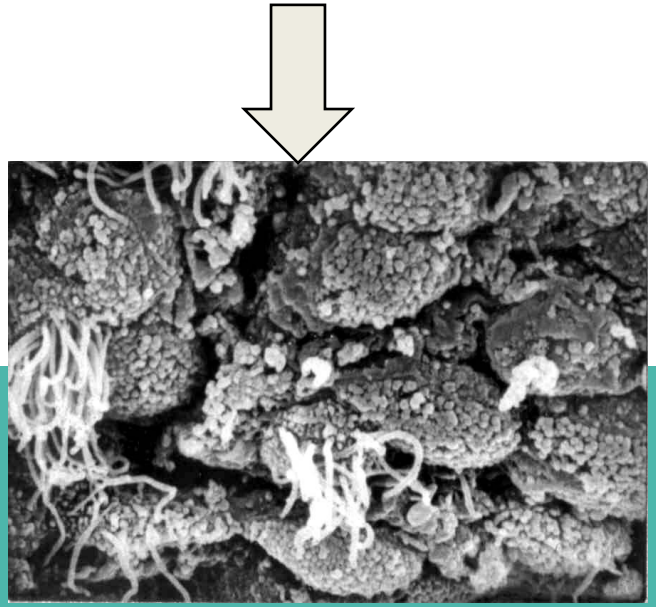
Syphilis pearls and monitoring in pregnancy

- In pregnancy, treat as appropriate for stage of disease
  - Some evidence suggests an additional (second) dose of benzathine penicillin, one week after the first dose,is beneficial even for early stage disease
- Titers should decline 4-fold (2 dilutions: 1:32 to 1:8) in 6-12 months after treatment - many will not have this decline before delivery - a 4-fold increase indicate possible treatment failure
  - Should not recheck titers before 8 weeks after treatment
- Level II US recommended to assess for fetal signs of congenital syphilis (hepatomegaly, ascites, hydrops, fetal anemia, or thickened placenta) - these would indicate a greater risk of treatment failure - 2nd dose can be beneficial for fetal treatment in these cases
- Penicillin for all in pregnancy
- Missed doses (>9 days between doses) not acceptable in pregnancy, 7 days optimal, if missed doses, series must be repeated

Chlamydia Updates

Normal fallopian tube





Sequelae of recurrent infection: Infertilty (20%), ectopic pregnancy (9%), chronic pelvic pain (18%) *

CDC Slide photo files. Scanning electron microscopy photos (1200x) courtesy of D.L. Patton, University of Washington, Seattle, Washington

*Chappell and Wiesenfeld, Clinical Obstet & Gynecol 2012; Westrom, AJOG 1975; Westrom, Sex Transm Dis 1992

Chlamydia treatment

Recommended Regimens for Chlamydial Infection Among Adolescents and Adults

Doxycycline 100 mg orally 2 times/day for 7 days

Alternative Regimens

Azithromycin 1 g orally in a single dose
OR
Levofloxacin 500 mg orally once daily for 7 days

CDC STI Treatment Guidelines, 2021 update

Rectal chlamydia in women?

Evidence for Increased Chlamydia Case Finding After the Introduction of Rectal Screening Among Women Attending 2 Canadian Sexually Transmitted Infection Clinics

Jennifer Gratrix,[1] Ameeta E. Singh,[2,6] Joshua Bergman,[2] Caroline Egan,[3] Sabrina S. Plitt,[4] Justin McGinnis,[5] Christopher A. Bell,[6,7] Steven J. Drews,[8] and Ron Read[3]

- Chlamydia was detected at the anorectal site among 33%-83% of women who had urogenital chlamydia infection, and its detection was not associated with report of receptive anorectal sexual activity

Effectiveness of doxycycline vs azithromycin in women

Treatment Effectiveness of Azithromycin and Doxycycline in Uncomplicated Rectal and Vaginal *Chlamydia trachomatis* Infections in Women: A Multicenter Observational Study (FemCure)

Nicole H. T. M. Dukers-Muijrers,[1,2] Petra F. G. Wolffs,[2] Henry de Vries,[3,4,5] Hannelore M. Götz,[5,6,7] Titia Heijman,[3] Sylvia Bruisten,[3,4] Lisanne Eppings,[1] Arjan Hogewoning,[3,4] Mieke Steenbakkers,[1] Mayk Lucchesi,[2] Maarten F. Schim van der Loeff,[3,4] and Christian J. P. A. Hoebe[1,2]

- Prospective, multicenter cohort (FemCure)
- Treatment: doxy 100 BID x 7 days for rectal CT-positive women
- Azithro 1gm single dose for vaginal CT-positive women (rectally untested or negative)
- Self-collected vaginal and rectal swabs at enrollment and during 4 wks F/U
- Endpoint: microbiologic cure by negative NAAT at 4 weeks

Dukers-Muijrers NHTM, Wolffs PFG, De Vries H, et al. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal Chlamydia trachomatis infections in women: a multicentre observational study (FemCure). Clin Infect Dis. 2019;69(11):1946-54

Effectiveness of doxy vs azithro in women

Table 2. Proportions and Differences of Microbiological Cure for Azithromycin- or Doxycycline-treated Rectal and Vaginal *Chlamydia trachomatis* Infections, and the Treatment Effect (ie, the Odds of Azithromycin Compared to Doxycycline in Not Reaching Microbiological Cure) in the Main Population and the Restricted Subset

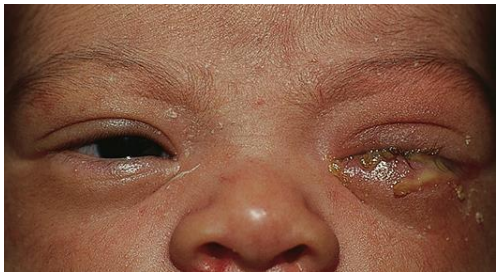
	Proportion Cured							
	Azithromycin		Doxycycline		Difference in % Cured		Treatment Effect	
Patients	no./No.	% (95% CI)	no./No.	% (95% CI)	% (95% CI)	*P* Value[a]	OR (95% CI)	aOR (95% CI)
Rectal chlamydia								
All patients	164/209	78.5 (72.6–83.7)	126/132	95.5 (91.0–98.2)	17.0 (9.6–24.7)	< .001	5.76 (2.38–13.93)	9.38 (3.24–27.17)
Subset[b]	89/113	78.8 (70.6–85.6)	68/70	97.1 (91.4–99.5)	18.4 (8.7–27.5)	< .001	9.17 (2.09–40.14)	18.51 (3.20–106.96)
Vaginal chlamydia								
All patients	246/263	93.5 (90.1–96.1)	125/131	95.4 (90.9–98.2)	1.9 (–3.6 to 6.7)	.504	1.44 (.55–3.74)	1.40 (.49–3.96)
Subset[b]	134/143	93.7 (88.9–96.9)	69/72	95.8 (89.5–98.3)	2.1 (–6.1 to 9.1)	.755	1.55 (.41–5.89)	0.89 (.19–4.11)

- Effectiveness of doxy is high, and exceeds that of azithromycin for the treatment of rectal chlamydia infections in women

Dukers-Muijrers NHTM, Wolffs PFG, De Vries H, et al. Treatment effectiveness of azithromycin and doxycycline in uncomplicated rectal and vaginal Chlamydia trachomatis infections in women: a multicentre observational study (FemCure). Clin Infect Dis. 2019;69(11):1946-54

Chlamydia
Obstetric and Fetal Outcomes

Conjunctivitis neonatorum



Can be transmitted to the neonate at birth (50%)

- From infected cervix

Neonatal conjuntivitis (20-50%)

- Develops 5-12 days after birth

Neonatal pneumonia (5-30%)

- Subacute, afebrile
- Onset 1-3 months after birth

Rare causes of transmission via intact membranes (transmembrane or transplacental)

Presumptive treatment not effective so identifying the treating mother is best way to prevent infant disease

The topical erythromycin is for gonococcal conjunctivitis

Chlamydia Treatment: Pregnancy

Recommended regimen:

- Azithromycin 1g orally in a single dose

Doxycycline relatively contraindicated

Alternative regimen:

- Amoxicillin 500mg orally TID x 7 days

1) TEST OF CURE to document eradication (preferably by NAAT) 4 weeks after completion of therapy
2) Test for reinfection 3 mo after treatment

Persistence of chlamydia in pregnancy

High rates of persistent and recurrent chlamydia in pregnant women after treatment with azithromycin

Jodie Dionne-Odom, MD, MSPH,
Division of Infectious Diseases, Department of Medicine, Center for Women's Reproductive Health, University of Alabama at Birmingham, Birmingham, Alabama.

Akila Subramaniam, MD, MPH,
Center for Women's Reproductive Health, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Alabama at Birmingham, Birmingham, Alabama.

Kristal J. Aaron, DrPH, MPH,
Division of Infectious Diseases, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama.

William M. Geisler, MD, MPH,
Division of Infectious Diseases, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama.

Alan T. N. Tita, MD, PhD,
Center for Women's Reproductive Health, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Alabama at Birmingham, Birmingham, Alabama.

Jeanne Marrazzo, MD, MPH
Division of Infectious Diseases, Department of Medicine, Center for Women's Reproductive Health, University of Alabama at Birmingham, Birmingham, Alabama.

1-in-4 women with chlamydia in pregnancy, treated with 1 g azithro, are observed to have persistent positivity on follow-up testing

Azithromycin, still first line

Design: Retrospective cohort, urogenital chlamydia in pregnancy
Outcomes: persistence, recurrence, clearance

Am J Obstet Gynecol MFM. 2020 November ; 2(4): 100216. doi:10.1016/j.ajogmf.2020.100216

Chlamydia treatment - take home messages

- Azithro maintains high efficacy for urogenital chlamydia in women
- Concern regarding effectiveness of azithromycin for concomitant rectal chlamydia, which can occur commonly among women and cannot be predicted by reported sexual activity
- Inadequately treated rectal chlamydia may increase risk of transmission and place women at risk for repeat urogenital chlamydia infection through autoinoculation from the anorectal site
- Doxy available in delayed release 200mg once daily x 7 days - more expensive but less side effects than doxy 100 BID x 7 days
- Levofloxacin 500 daily x 7 days effective but expensive
- Pregnancy azithromycin 1gm po x 1
- Ability to dispense all doses on site is important, DOT single dose in persons for whom adherence to multiday dosing is a considerable concern

Gonorrhea

Gonorrhea

Obstetric and Fetal Outcomes

Maternal adverse effects:

- Spontaneous abortion
- Premature rupture of membranes
- Intra-amniotic infection
- Preterm birth
- Post partum endometritis

Recommended Regimen to Prevent Ophthalmia Neonatorum Caused by *N. gonorrhoeae*
Erythromycin 0.5% ophthalmic ointment in each eye in a single application at birth

Neonatal adverse outcomes:

- Fetal risk generally via contact with infected cervix
  - Generally, an acute illness that occurs 2-5 days after delivery
- **Most severe:** Neonatal sepsis (can include arthritis and meningitis), opthalmia neonatorum
- **Less severe:** rhinitis, vaginitis, urethritis, and scalp infection at site of scalp electrodes

Gentamicin in pregnancy

"Gentamicin use is cautioned during pregnancy because of risk for neonatal birth defects, nephrotoxicity, or ototoxicity." (2021 CDC guidelines)

Case-control epidemiological study of IV gentamicin in pregnancy did not find increased teratogenic risk[1]

Ototoxicity and nephrotoxicity theoretical fetal risk – have not been documented clinically

Elimination could be decreased in pre-eclampsia

- larger volume of distribution in pregnancy, renal dysfunction may cause delayed clearance

Standard antibiotic used in chorioamnionitis

Theoretic risk, however, no evidence that drug should be avoided if clear indications for its use

Czeizel AE, Rockenbauer M, Olsen J, Srensen HT: A teratological study of aminoglycoside antibiotic treatment during pregnancy. Scand J Infect Dis 2000;32:309-13. 2. Regev RH, Litmanowitz I, Arnon S et al: Gentamicin serum concentrations in neonates born to gentamicin-treated mothers. Pediat Infect Dis J 19:890-1, 2000

Trichomonas

Trichomonas updates

Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial

Patricia Kissinger, Christina A Muzny, Leandro A Mena, Rebecca A Lillis, Jane R Schwebke, Laura Beauchamps, Stephanie N Taylor, Norine Schmidt, Leann Myers, Peter Augostini, William E Secor, Martina Bradic, Jane M Carlton, David H Martin

- Multicenter, open-label, RCT at 3 sexual health clinics in the US
- Randomized to 2g metronidazole in a single dose or 500mg BID x 7 days
- Primary outcome was *T vaginalis* at test of cure (TOC) 4 weeks after treatment
- 7 day group less likely to be TV positive at TOC (11% vs 19%, RR 0.55, 95%CI 0.34-0.70, p<0.0001)
  - BV status had no significant effect on RR
  - Self-reported adherence was 96% in 7-day group, and 99% in single dose group
  - Side effects similar by group (nausea 23%, HA 7%, vomiting 4%)

Kissinger et al. Lancet Infect Dis 2018;18:1251-59

Trichomonas reminders

- Because of the high rate of reinfection regardless of partner treatment, patients with TV should be retested <3 months after infection (and if not possible, at next presentation for care in the next 12 months)
- Refer all partners for presumptive treatment
- Symptomatic pregnant women, regardless of trimester should be tested and treated with metronidazole (tinidazole avoided in pregnancy)
    - The benefit of routine screening in asymptomatic pregnant women has not been established
- HIV infected, always use metronidazole 7 days (not single dose)
- Abstaining from alcohol after metronidazole or tinidazole is not needed
    - Prior studies based on animal studies and case histories - reports may be the result of alcohol or metronidazole side effects independently
    - Metronidazole does not inhibit acetaldehyde dehydrogenase like disulfiram

Pelvic Inflammatory Disease

PID Updates - addition of metronidazole for PID

Recommended Parenteral Regimens for Pelvic Inflammatory Disease
Ceftriaxone 1 g IV every 24 hours PLUS
Doxycycline 100 mg orally or IV every 12 hours PLUS
Metronidazole 500 mg orally or IV every 12 hours
OR
Cefotetan 2 g IV every 12 hours PLUS
Doxycycline 100 mg orally or IV every 12 hours
OR
Cefoxitin 2 g IV every 6 hours PLUS
Doxycycline 100 mg orally or IV every 12 hours

Data behind treatment regimens for PID

A Randomized Controlled Trial of Ceftriaxone and Doxycycline, With or Without Metronidazole, for the Treatment of Acute Pelvic Inflammatory Disease

Harold C. Wiesenfeld,[1,2] Leslie A. Meyn,[1,2] Toni Darville,[3] Ingrid S. Macio,[2] and Sharon L. Hillier[1,2]

[1]Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, [2]Magee-Womens Research Institute, Pittsburgh, Pennsylvania, USA, and [3]Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

- Study designed to answer the question of whether adding metronidazole improves clinical and microbiologic cure in women with acute PID
- Randomized 233 women to standard of care (ceftriaxone/doxy) or standard of care + metronidazole and measured responses at 3 and 30 days

Weisenfeld et al. CID 2021;72(7):1181-9

RCT ctx/doxy +/- metronidazole RESULTS

- Clinical improvement was high in the two groups at 3 days (83% with metronidazole v 80% without, P=0.74) and 30 days (97% with metronidazole vs 90% without, P=0.13)
- Only a small proportion of women (22%) tested positive for *C .trachomatis* or *N. gonorrhea* (as with other trials, i.e. PEACH trial* - 35%)
- Rates of CT and GC did not differ among groups at 30 days, however rates of BV, and endometrial cultures for anaerobic organisms were significantly lower in the metronidazole arm, rates of *T. vaginalis* trend to lower as well
    - Anaerobic organisms 8% vs 21%, P<0.05), *M genitalium* reduced (4% vs 14%, P<0.05), BV (20% vs 54%, P<0.001), *T. vaginalis* (5% vs 12%, P=0.10)
- Pelvic tenderness less common among women with metronidazole (9% vs 20%), P<0.05)
- Adverse events similar in each treatment arm

Weisenfeld et al. CID 2021;72(7):1181-9 *Ness et al Control Clin Trials. 1998. Oct;19(5):499-514

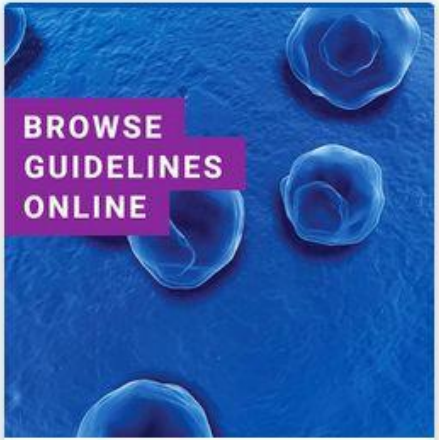
Resources

STI Treatment Guidelines Update

CDC's Sexually Transmitted Infections (STI) Treatment Guidelines, 2021 provides current evidence-based prevention, diagnostic and treatment recommendations that replace the 2015 guidance. The recommendations are intended to be a source for clinical guidance. Healthcare providers should always assess patients based on their clinical circumstances and local burden.

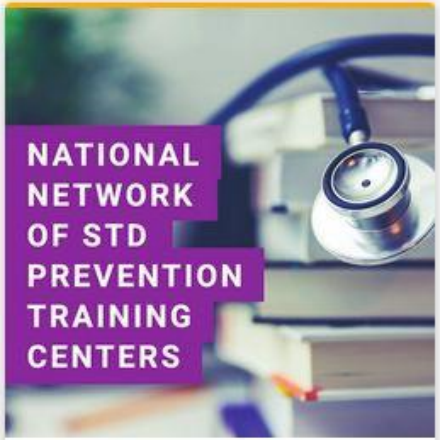
https://www.cdc.gov/std/default.htm

Many resources available



View the full STI Treatment Guidelines.

Access print-friendly versions of the wall chart, pocket guide, and guidelines.



Explore STD trainings, technical assistance, clinical consultation services, and more.

Learn about recommendations and tools to help healthcare settings improve STD care services.

Ratelle STD/HIV Prevention Training Center

Sylvie Ratelle
STD/HIV Prevention Training Center

Meet Our Faculty

Kevin Ard
MD, MPH

Dr. Kevin L. Ard, MD, MPH is a faculty member in the Division of Infectious Diseases at Massachusetts...

Erica Hardy
MD, MMSc

Dr. Hardy is an Assistant Professor of Medicine and Obstetrics and Gynecology, in the Divisions of...

Katherine Hsu
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Katherine Hsu, MD, MPH is the Medical Director for the Division of STD Prevention & HIV/AIDS Surveillance,...

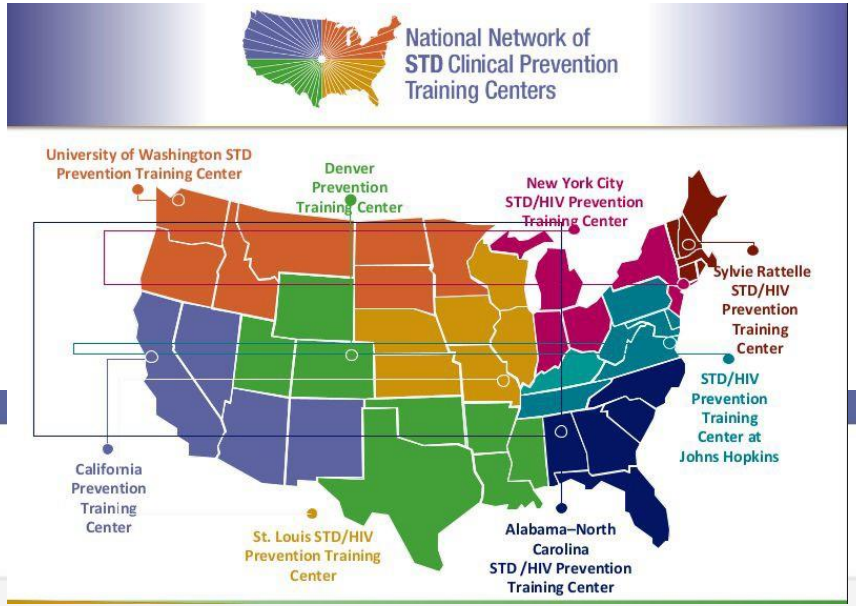
Philip Chan
MD, MS

Dr. Chan is an Associate Professor in the Department of Medicine and School of Public Health at Brown...

Zoon Wangu
MD, FAAP

Dr. Wangu is an Assistant Professor of Pediatrics at UMass Medical School and attending physician...

https://www.STDCCN.org



STD Clinical Consultation Network

NNPTC National Network of STD Clinical Prevention Training Centers

The Clinical Consultation Service is intended for licensed healthcare professionals and STD program staff. We do not provide direct medical care, treatment planning, or medical treatment services to individuals. Consultations are based on information provided by the caller without the benefit of a direct evaluation/examination of the patient, and as such, do not constitute medical advice, are intended to be used only as a guide.

The information provided through the Clinical Consultation Service is not a replacement for local expertise or your state STD program protocols. Information is offered as clinical decision support, is advisory in nature and is not intended to replace local healthcare decision-making or provision. Requestors are free to disregard any advice offered. Final clinical decisions are the sole responsibility of the healthcare provider.

Please note, consults placed after 4 pm may not be triaged until the next business day and responses may be delayed during holiday periods.

CONTINUE

Resources

- Women & Infants
  - Obstetrics and Gynecology Care Center
    https://www.womenandinfants.org/services/obstetrics-gynecology-care
  - Reproductive Infectious Disease Consultation
    - https://www.womenandinfants.org/services/infectious-disease
    - 401-453-7950 phone, 401-453-7748 fax
  - Maternal Fetal Medicine
    - https://www.womenandinfants.org/services/infectious-disease
  - Emergency Care for Women
    - https://www.womenandinfants.org/services/emergency-care

THANK YOU!

erica_hardy@brown.edu

Evaluation & CME Credits

Please complete a session evaluation! Claim CME credit here:

https://www.surveymonkey.com/r/Team-Based-Care-CME-evaluation

Application for CME credit has been filed with the American Academy of Family Physicians. Determination of credit is pending.

RIGEC
Rhode Island Geriatric Education Center

Geriatric Education Series

CEU Webinar

Social Isolation and Loneliness in Older Adults

Tuesday, September 19, 2023 | 8-9 AM ET

Speaker:

Max Zubatsky, Ph.D.
Associate Professor, Program Director
Medical Family Therapy Program
The Memory Clinic Director
St. Louis University School of Medicine

Click Here TO REGISTER

Learning Objectives:

After attending this webinar, participants will be able to:

1. Describe the risks and effects of social isolation and loneliness in older adults
2. Identify ways for to assess and monitor loneliness and social isolation in clinical practice
3. List practices and interventions that can be used to reduce social isolation.

CONTINUING EDUCATION

This activity has been submitted for 1.0 contact hour of continuing education in nursing, social work and mental health counseling.

CARE TRANSFORMATION COLLABORATIVE RHODE ISLAND

pcmh kids patient-centered medical home

ADVANCING INTEGRATED HEALTHCARE

Next Month: Join us for a presentation from the RI Geriatric Education Center

Social Isolation and Loneliness in Older Adults

Tues, September 19 8-9am

Register here: https://uri-edu.zoom.us/meeting/register/tJIkceutrzIsEtF-NZJcOwK9NQRvPOAP-S4_#/registration

THANK YOU

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