
STI 2016

Emerging Crises, Enduring Concerns

Bradley Stoner, MD, PhD

Associate Professor

Washington University in St. Louis

Medical Director, St. Louis STD/HIV Prevention Training Center

U.S. | NATIONAL BRIEFING | HEALTH

Spike Seen in Reported Cases of Sexually Transmitted Diseases

By DONALD G. McNEIL Jr. NOV. 17, 2015

- Syphilis (P&S)  15.1% in US
- Gonorrhea  5.1% in US
- Chlamydia  2.8% in US

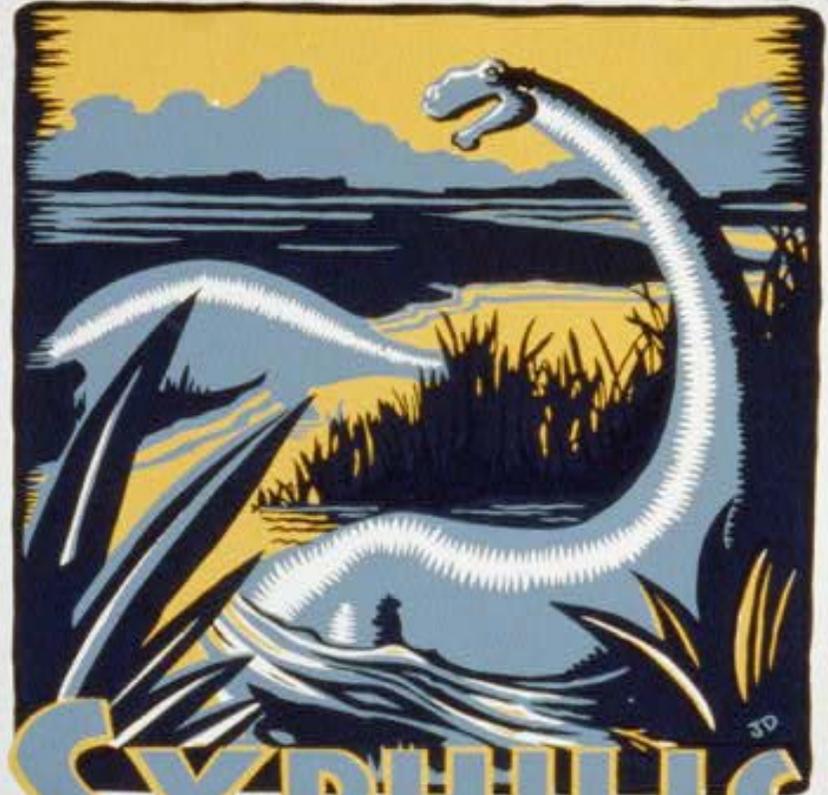
THE ENEMY IS SYPHILIS



Enlist employees in a campaign against it

1940-1941 THE WPA ART PROJECT ONE 202

AS OLD AS CREATION



SYPHILIS

IS NOW CURABLE

CONSULT YOUR PHYSICIAN

TOWN OF KEMPSTEAD
WH. RUNCIE M.D. HEALTH OFFICER

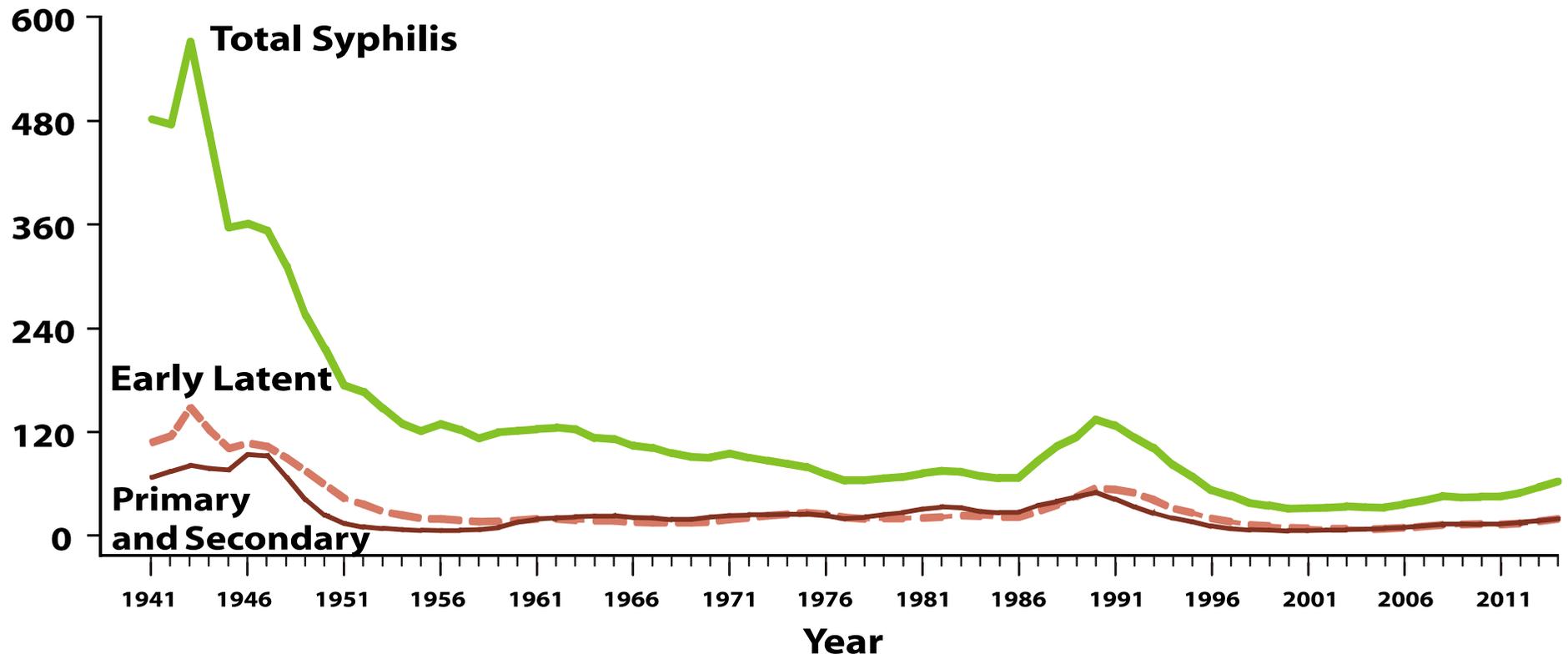
FEDERAL ART PROJECT

Syphilis

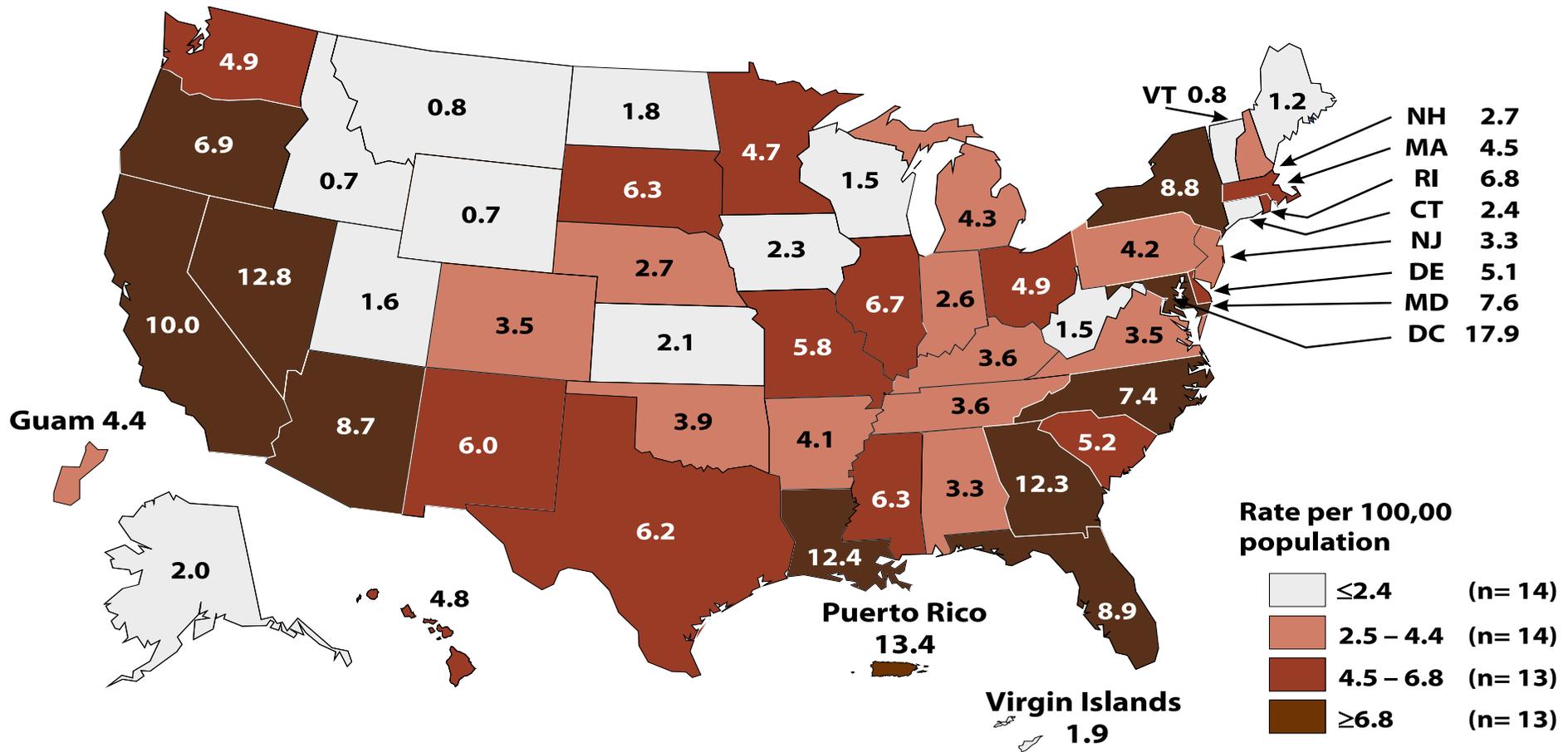
- ◆ High rates among men who have sex with men (MSM)
 - » many of whom are HIV+

Syphilis — Reported Cases by Stage of Infection, United States, 1941–2014

Cases (in thousands)



Primary and Secondary Syphilis—Rates of Reported Cases by State, United States and Outlying Areas, 2014

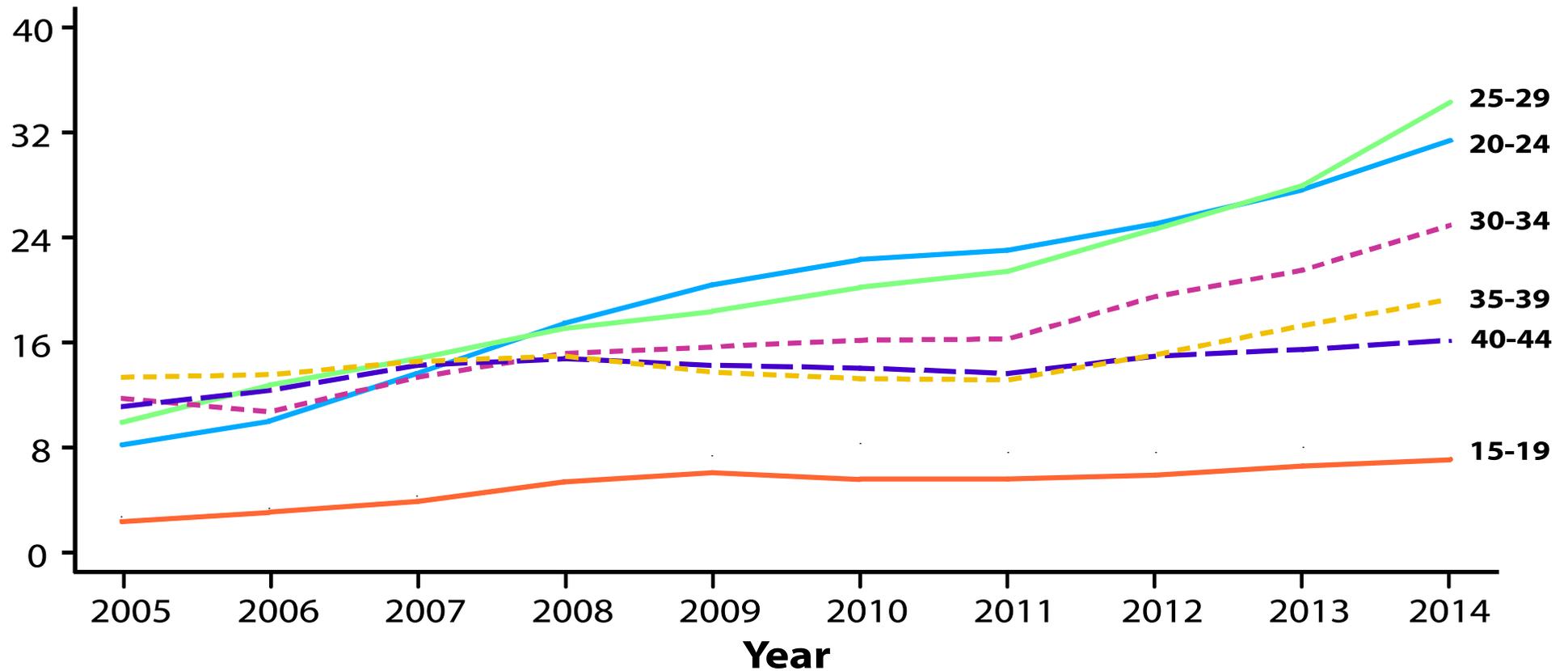


NOTE: The total rate of primary and secondary syphilis for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 6.4 per 100,000 population.

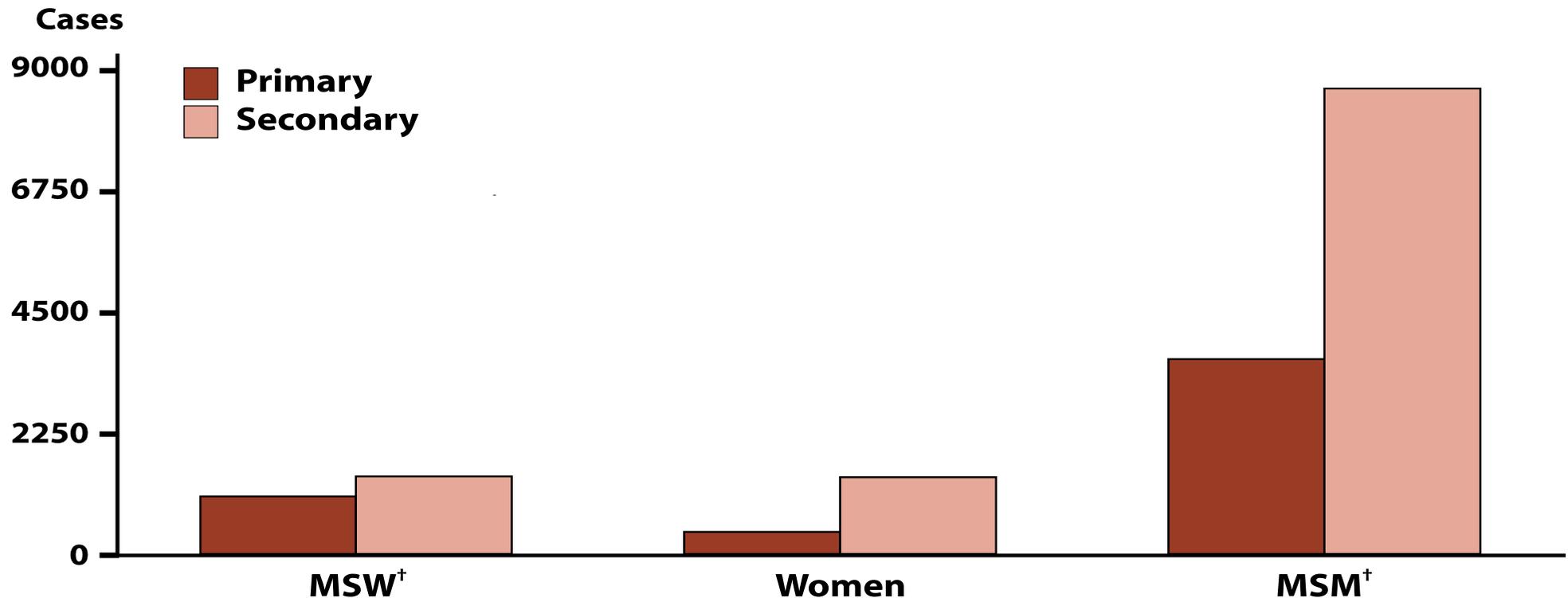


Primary and Secondary Syphilis — Rates of Reported Cases Among Men Aged 15–44 Years by Age, United States, 2005–2014

Rate (per 100,000 population)



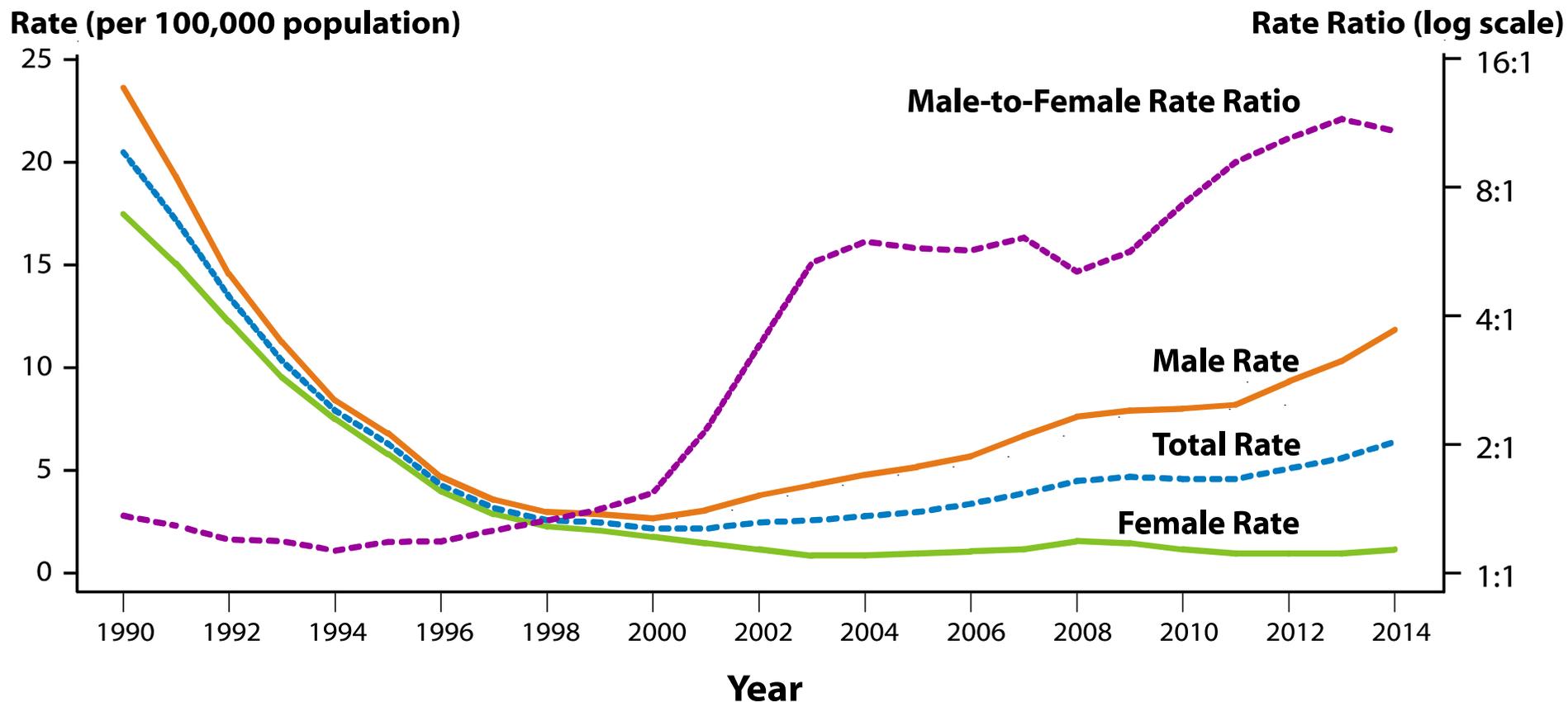
Primary and Secondary Syphilis — Reported Cases* by Stage, Sex, and Sexual Behavior, 2014



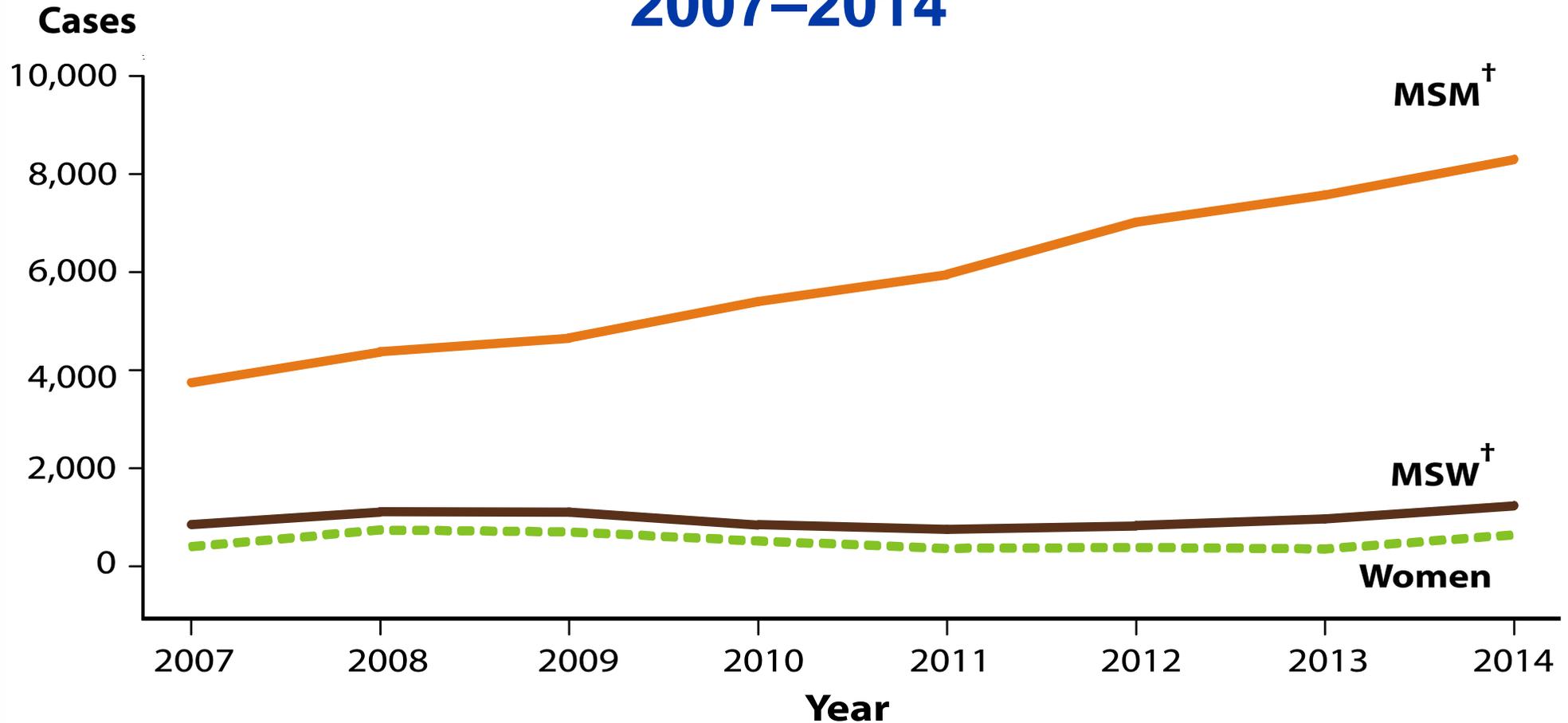
*Of the reported male cases of primary and secondary syphilis, 18.8% were missing sex of sex partner information.

†MSW=men who have sex with women only; MSM=men who have sex with men.

Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2014



Primary and Secondary Syphilis — Reported Cases by Sex and Sexual Behavior, 27 Areas*, 2007–2014

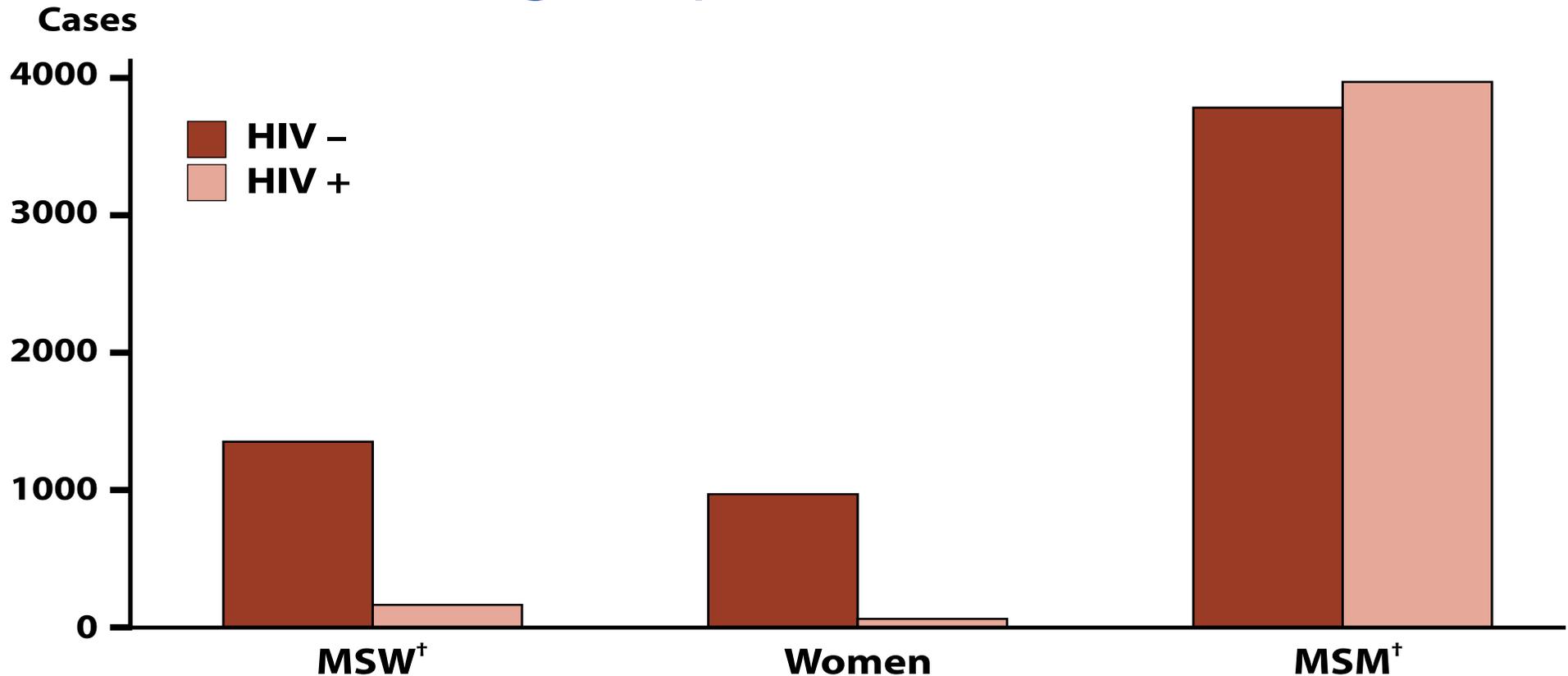


*27 states reported sex of partner data for 70% of reported cases of primary and secondary syphilis for each year during 2007–2014.

† MSM = men who have sex with men; MSW = men who have sex with women only.



Primary and Secondary Syphilis — Reported Cases by Sex, Sexual Behavior, and HIV Status (Positive or Negative), 26 Areas*, 2014*



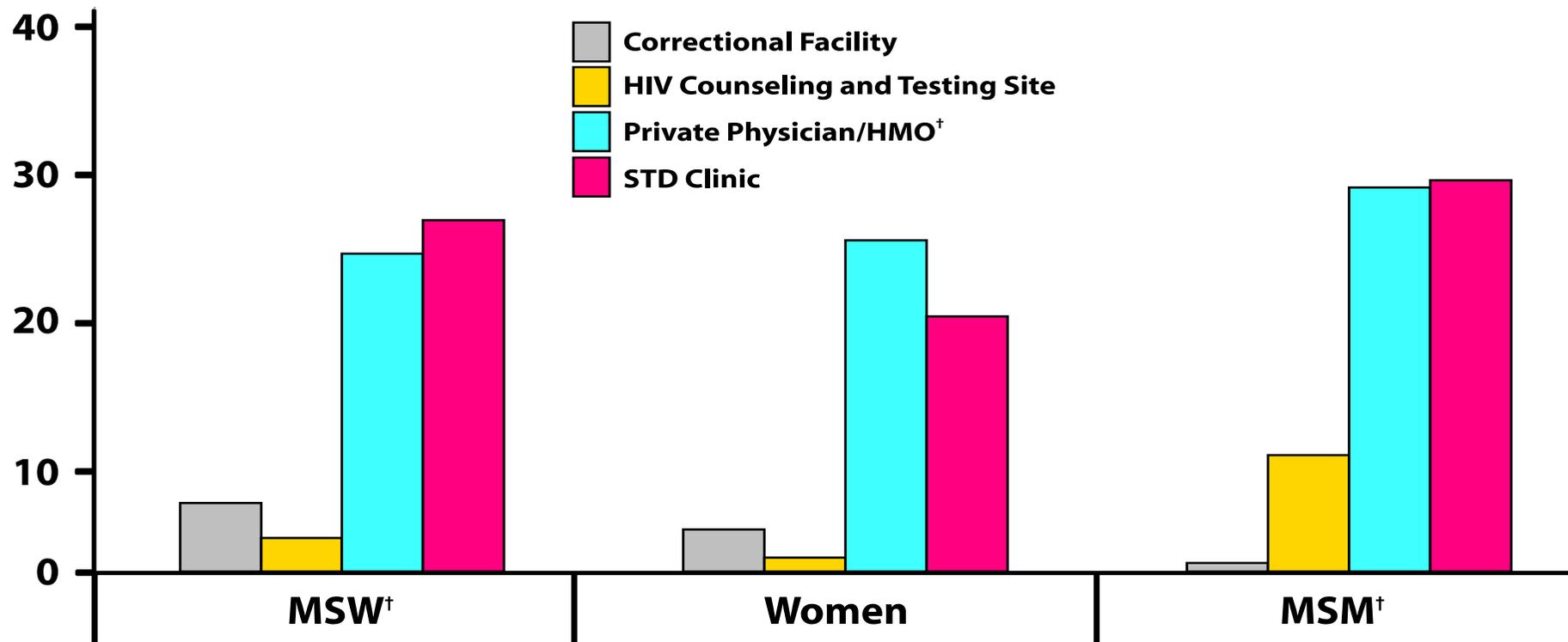
*26 states reported both sex of sex partner and HIV status for 70% of reported cases of primary and secondary syphilis during 2014.

† MSW = men who have sex with women only; MSM = men who have sex with men.



Primary and Secondary Syphilis — Percentage of Reported Cases* by Sex, Sexual Behavior, and Selected Reporting Sources, 2014*

Percentage



* Of all primary and secondary syphilis cases, 6.7% had a missing or unknown reporting source. Among all cases with a known reporting source the reporting source categories presented represent 62.0% of cases; 38.0% were reported from sources other than those shown.

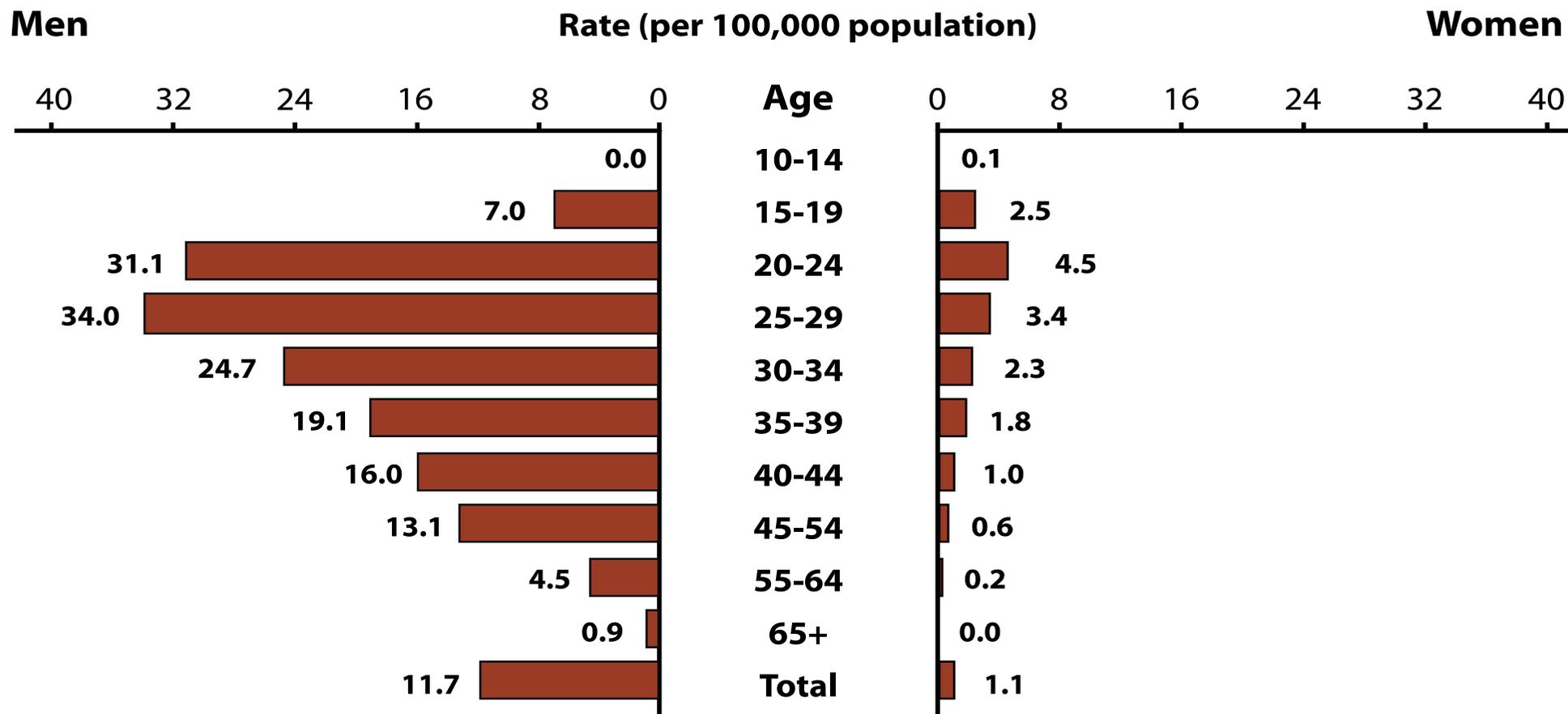
† HMO = health maintenance organization; MSM = men who have sex with men; MSW = men who have sex with women only.



Syphilis

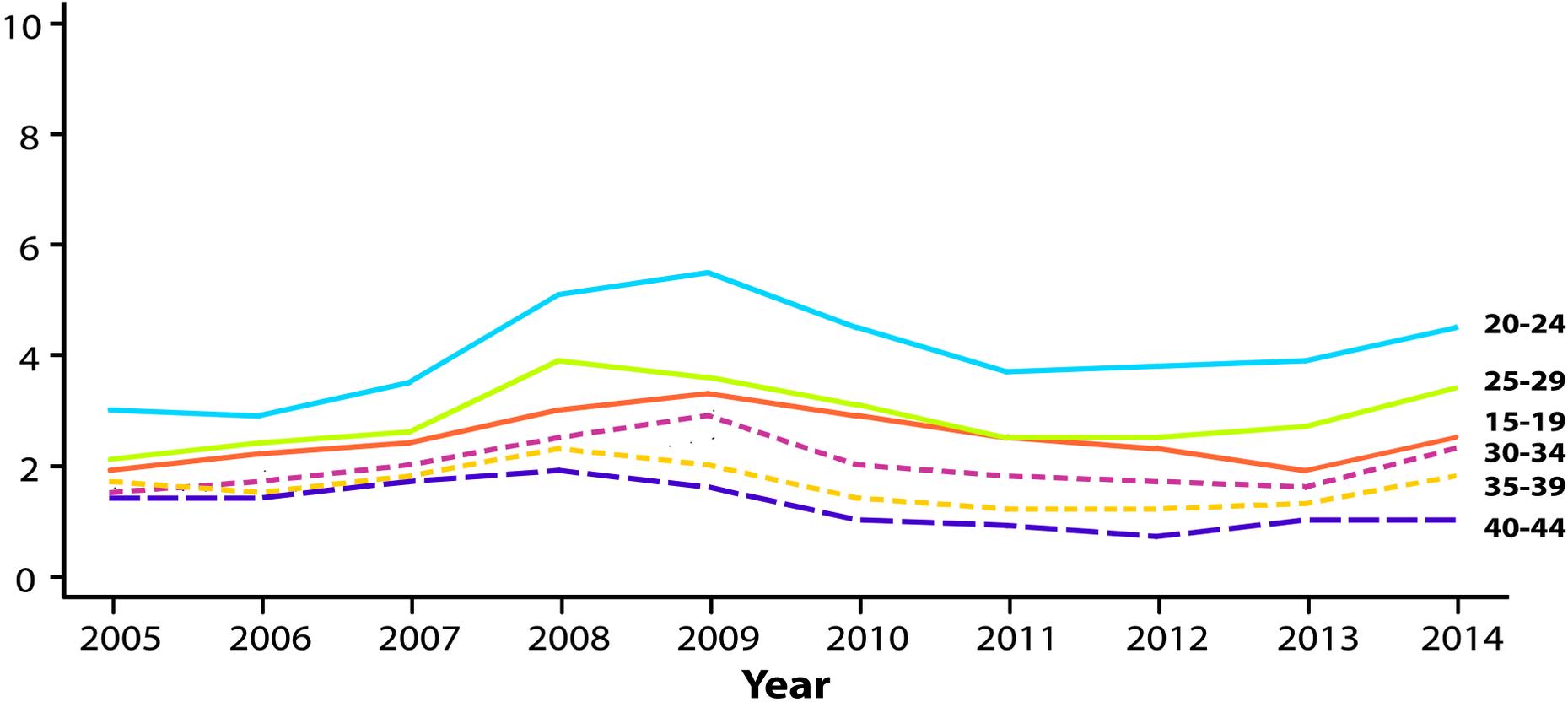
- ◆ High rates among men who have sex with men (MSM)
 - » many of whom are HIV+
- ◆ Low-level (but increasing) heterosexual transmission
 - » rising rates of congenital syphilis

Primary and Secondary Syphilis — Rates of Reported Cases by Age and Sex, United States, 2014



Primary and Secondary Syphilis — Rates of Reported Cases Among Women Aged 15–44 Years by Age, United States, 2005–2014

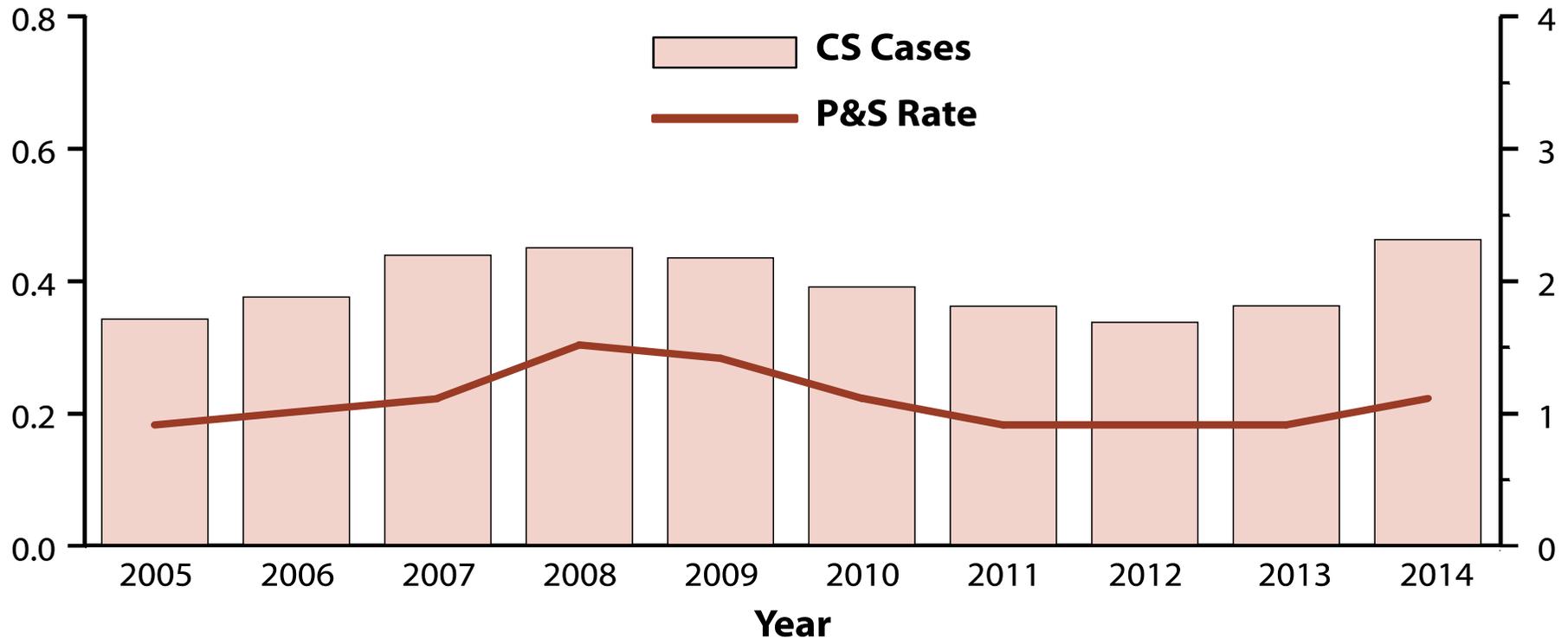
Rate (per 100,000 population)



Congenital Syphilis — Reported Cases by Year of Birth and Rates of Primary and Secondary Syphilis Among Women, United States, 2005–2014

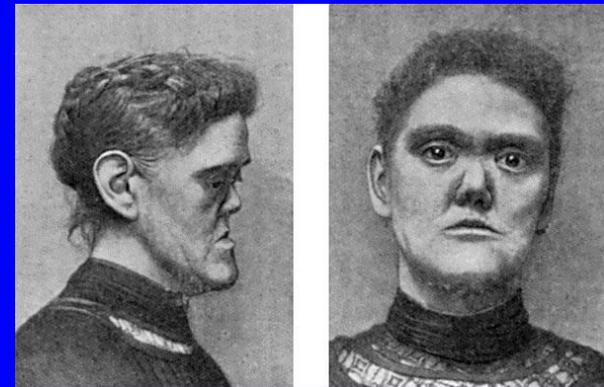
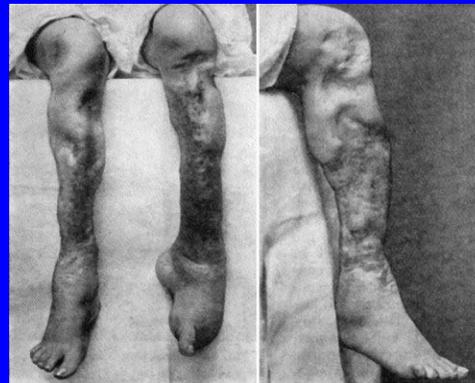
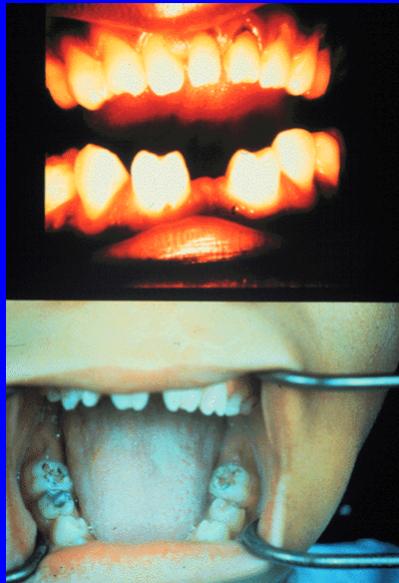
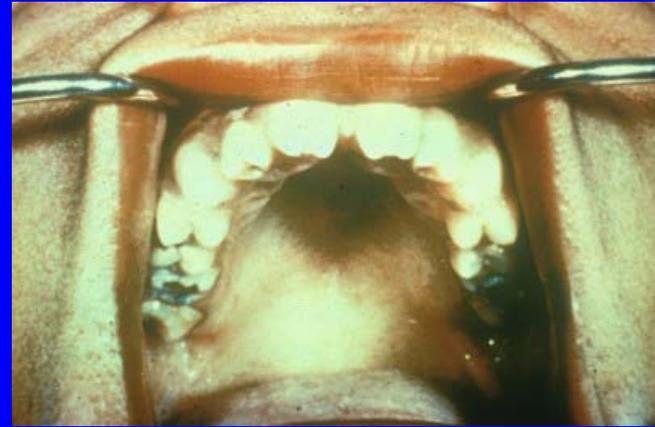
CS* cases (in thousands)

P&S* rate (per 100,000 women)

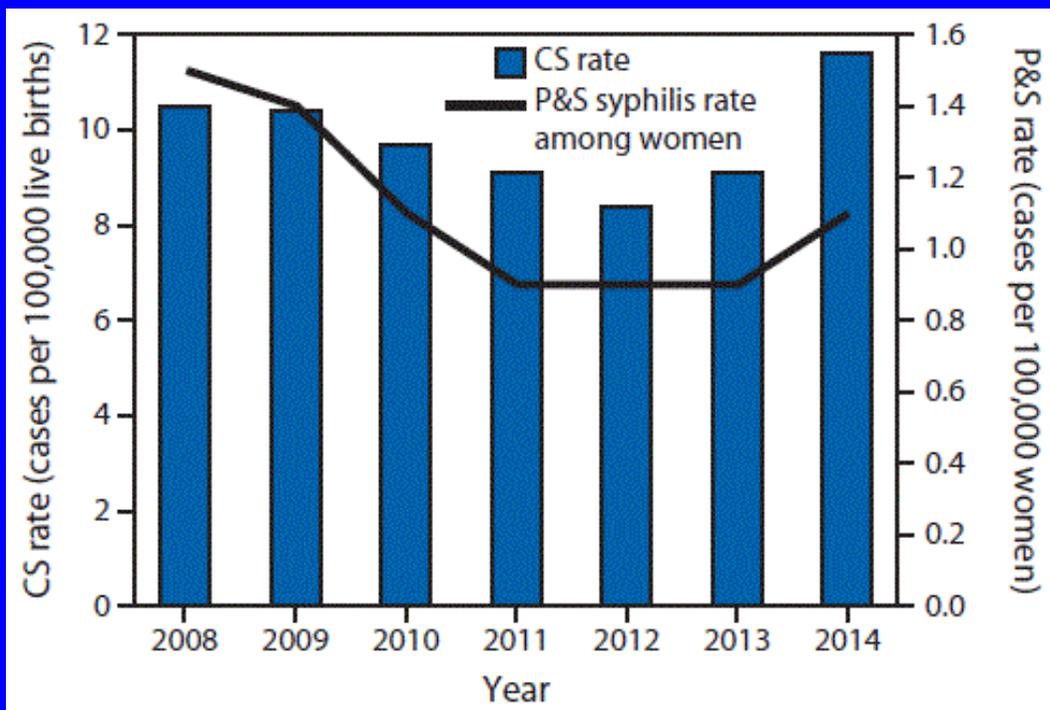


* CS=congenital syphilis; P&S=primary and secondary syphilis.

Congenital syphilis



Increase in Incidence of Congenital Syphilis — United States, 2012–2014



CS rates increased 38% over a two-year period

- No prenatal care in 21% of mothers
- Among those receiving prenatal care
 - 7% never tested for syphilis
 - 17% tested negative early in pregnancy, then acquired syphilis
 - 30% inadequately treated

Congenital syphilis prevention

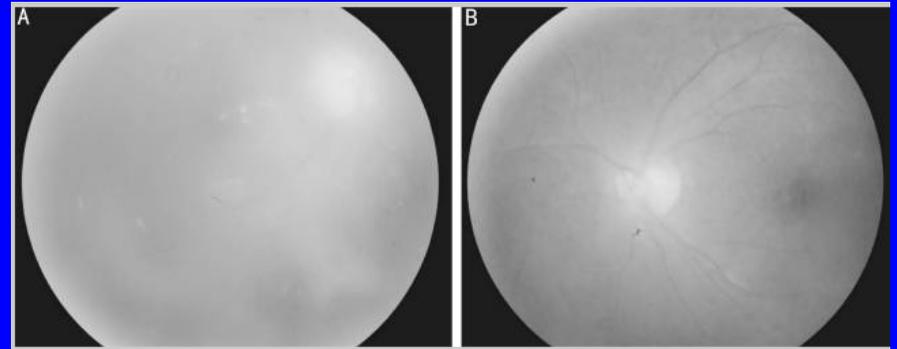
- ◆ Screen all women in early pregnancy
- ◆ Screen again twice in third trimester “for communities and populations in which the prevalence of syphilis is high, and for women at high risk of infection”
 - ◆ Screen at 28-32 weeks
 - ◆ Screen again at delivery

Syphilis

- ◆ High rates among men who have sex with men (MSM)
 - » many of whom are HIV+
- ◆ Low-level (but increasing) heterosexual transmission
 - » rising rates of congenital syphilis
- ◆ Increasing rates of ocular syphilis

Ocular (ophthalmic) syphilis

- Increasingly reported among MSM
 - Most common: posterior uveitis / pan-uveitis
 - May also include
 - Anterior uveitis
 - Optic neuropathy
 - Retinal vasculitis
 - Interstitial keratitis



Notes from the Field

A Cluster of Ocular Syphilis Cases — Seattle, Washington, and San Francisco, California, 2014–2015

12 cases reported in 3 mos.

(Dec. 2014 – Mar. 2015)

- 11 males (92%)

- 10 HIV+ (83%)

Symptoms included

- vision loss
- flashing lights
- blurry vision



Sexually Transmitted Diseases (STDs)

[Sexually Transmitted Diseases \(STDs\)](#) > [Syphilis](#) > [Treatment and Care](#)

Clinical Advisory: Ocular Syphilis in the United States

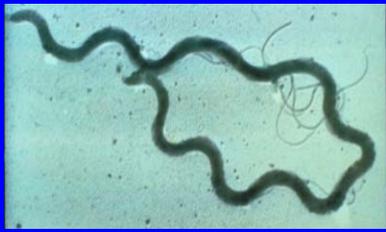


Since December 2014, 24 cases of ocular syphilis have been reported from California and Washington, with several other states reporting potential cases. The majority of cases have been among HIV-infected MSM; a few cases have occurred among HIV-uninfected persons including heterosexual men and women. Several of the cases have resulted in significant sequelae including blindness.

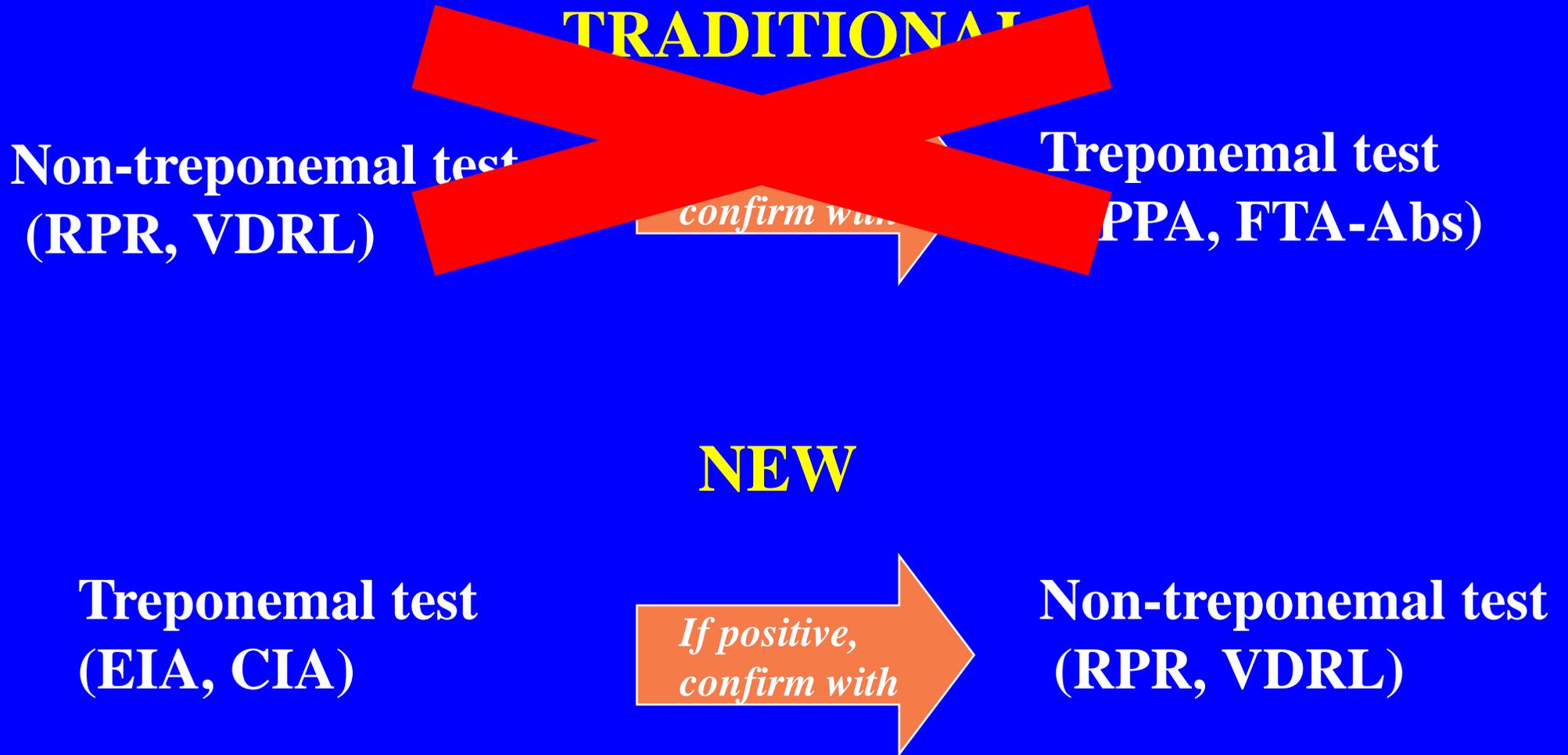
Neurosyphilis can occur during **any** stage of syphilis including primary and secondary syphilis. Ocular syphilis, a clinical manifestation of neurosyphilis, can involve almost any eye structure, but posterior uveitis and panuveitis are the most common. Additional manifestations may include anterior uveitis, optic neuropathy, retinal vasculitis and interstitial keratitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness. While previous research supports evidence of neuropathogenic strains of syphilis, it remains unknown if some *Treponema pallidum* strains have a greater likelihood of causing ocular infections.

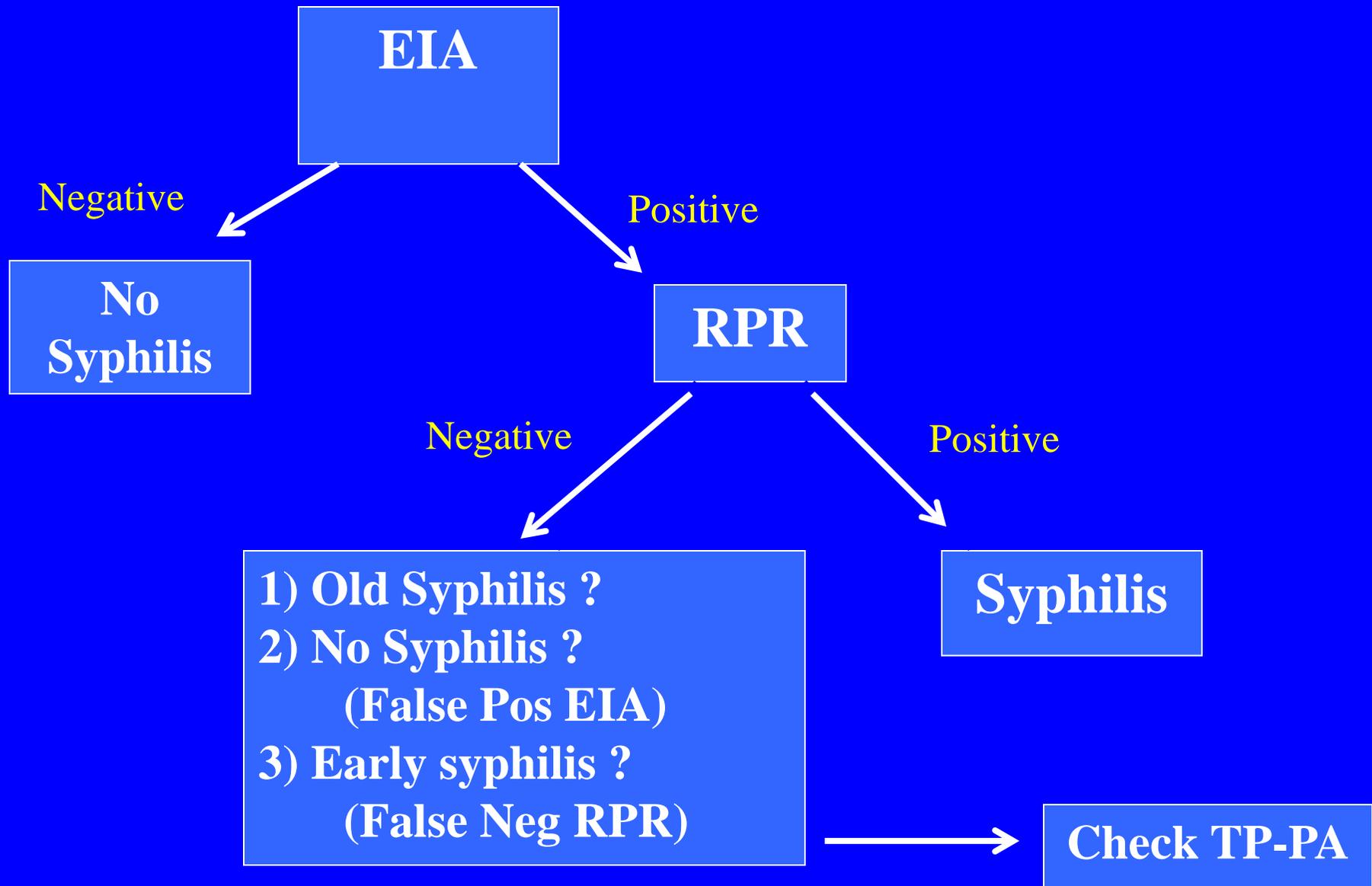
Syphilis – other concerns

- ◆ Reverse-sequence serologic testing
- ◆ Rolling penicillin shortages



Syphilis Screening Paradigm





Penicillin Shortage Spells Major Concerns For Pregnant Women



Could Be A Problem Syphilis

Bicillin L-A, the only recommended treatment for pregnant women with syphilis, is on backorder because of a manufacturing delay.

Syphilis Rates On the Rise Amid Treatment Shortage

Beni Enas | June 23, 2016 1:48 pm



**Centers for Disease
Control and Prevention**
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of STD Prevention

Bicillin-LA (benzathine penicillin G) Shortage

Message from CDC regarding the recent shortage of Penicillin G benzathine in the United States

Penicillin G benzathine is the recommended treatment for syphilis and the only recommended treatment for pregnant women infected or exposed to syphilis. Pfizer, the sole manufacturer of Bicillin L-A[®] (penicillin G benzathine) in the United States is experiencing a manufacturing delay of this product. CDC is working with FDA's Drug Shortage Staff and Pfizer to address this situation.

Until normal quantities of Bicillin L-A® (penicillin G benzathine) are available, CDC suggests the following:

1. Refrain from the use of Bicillin L-A® (penicillin G benzathine) for treatment of other infectious diseases (e.g., streptococcal pharyngitis) where other effective antimicrobials are available.
2. Adhere to the recommended dosing regimen of 2.4 million units of penicillin G benzathine IM for the treatment of primary, secondary and early latent syphilis (i.e., early syphilis) as outlined in the [2015 STD Treatment Guidelines](#). Additional doses to treat early syphilis do not enhance efficacy, including in patients living with HIV infection.
3. Contact your pharmacists/distributors to procure Bicillin L-A® (penicillin G benzathine), if you do not have product readily available. If product reaches a critical supply level of three weeks or less, contact Pfizer. The company contact information can be found on the [FDA's Drug Shortage Website](#) [↗](#). Also, alert your state or local STD Prevention Program of any shortage of Bicillin L-A® (penicillin G benzathine) as they are informing CDC of any shortages.
4. Direct questions about syphilis clinical management to an infectious disease specialist or the on-line National Network of STD Clinical Prevention Training Centers (NNPTC) STD Clinical Consultation Network (<https://www.stdccn.org> [↗](#)).



Pfizer Inc
275 North Field Drive
Lake Forest, IL 60045
Email: pfizerinjectables@pfizer.com

Pfizer Essential Health

September 2, 2016

BICILLIN® L-A (penicillin G benzathine injectable suspension)
BICILLIN® C-R (penicillin G benzathine and penicillin G procaine injectable suspension)
PENICILLIN G PROCAINE (penicillin G procaine injectable suspension)

SUPPLY UPDATE

NDC#	Presentation	Allocation % range (of normal demand)	Next Anticipated Delivery
60793-0700-10	BICILLIN L-A Pediatric 600,000 Units/1 mL; 1 mL Prefilled Syringe	30% - 40%	Oct-16
60793-0701-10	BICILLIN L-A 1,200,000 Units/2 mL; 2 mL Prefilled Syringe	45% - 55%	Oct-16
60793-0702-10	BICILLIN L-A 2,400,000 Units/4 mL; 4 mL Prefilled Syringe	48% - 58%	Nov-16

Syphilis - treatment

- ◆ Early syphilis (primary, secondary, early latent)
 - Benzathine PCN-G 2.4 mU IM x 1 dose
- ◆ Late syphilis (> 1 year or unknown duration)
 - Benzathine PCN-G 2.4 mU IM q week x 3 doses

Syphilis – penicillin allergy

- Doxycycline 100mg po bid (or tetracycline 500mg po qid)
 - ✓ Treat for 2 weeks for early syphilis
 - ✓ Treat for 4 weeks for late syphilis



**PENICILLIN
CURES
GONORRHEA**
THE ONLY CURE AVAILABLE

IN 4 HOURS

SEE YOUR DOCTOR TODAY

**WE NOW HAVE PENICILLIN
FOR YOUR TREATMENT**

NOT!

What Kind of Mess Have
We Gotten Ourselves Into?

(MDR-GC)



Perspective
FEBRUARY 9, 2012

Cephalosporin Susceptibility Among *Neisseria gonorrhoeae* Isolates — United States, 2000–2010

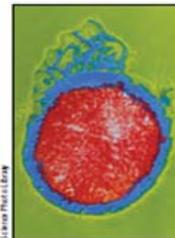
The Emerging Threat of Untreatable Gonococcal Infection

Gail A. Bolan, M.D., P. Frederick Sparling, M.D., and Judith N. Wasserheit, M.D., M.P.H.

It is time to sound the alarm. During the past decade, the wily gonococcus has become less susceptible to our last line of antimicrobial defense, threatening our ability to cure gonorrhea and prevent severe sequelae.

Gonorrhea is the second most commonly reported communicable disease in the United States. Control and Prevention (CDC) now limited to third-generation cephalosporins?

Gonorrhoea—old disease, new threat



Neisseria gonorrhoeae

See World Report page 2229
For the 29th International AIDS Conference see <http://www.aids2012.org/>
For WHO's Global Action Plan to control the spread and impact of antimicrobial resistance in *Neisseria gonorrhoeae* see http://whqlibdoc.who.int/publications/2012/9789241503501_eng.pdf

Delegates at the 29th International AIDS Conference in Washington, DC, next month might consider how, in three decades, their field has changed. The progress from the first case reports, to fearful recognition of the extent of the HIV epidemic, to a point at which "an AIDS-free generation" is talked about represents a remarkable success story. Recognition of this achievement, however, must not turn to complacency; nor should it engender forgetfulness about other sexually transmitted infections (STIs).

As medical science solves problems, it also creates new challenges. Such is the case with *Neisseria gonorrhoeae*. It is deeply concerning that in Australia, France, Japan, Norway, Sweden, and the UK, cases of gonorrhoea have been reported that are cephalosporin-resistant—and thus effectively untreatable. This resistance, accompanied by a high incidence of infections and possibly less noticeable symptoms, bodes ill for the future: fertility problems, ectopic pregnancies, stillbirth, spontaneous abortion, premature deliveries, and severe neonatal eye infections resulting in blindness might be its legacy.

It is essential that steps are taken now in accordance with WHO's Global Action Plan. Health-care workers must be vigilant and prescribe antibiotics appropriately. As with all cases of emerging antibiotic-resistant infections, research into new alternatives for treatment must be prioritised. And public health agencies should strengthen surveillance efforts, as well as targeting safer-sex educational programmes at key groups including young people, men who have sex with men, and sex workers. The growing threat of cephalosporin-resistant gonorrhoea also indicates that it is time to break down the barriers between the efforts against HIV, and those against other STIs. As the at-risk groups and means of prevention are so similar, and as untreated gonococcal infection can significantly increase the risk of HIV infection and transmission, it would seem a logical step. Without new ways of thinking, the health of future generations will be blighted by a disease whose worst effects were—not so long ago—thought to have been consigned to history. ■ *The Lancet*

DRUG-RESISTANT NEISSERIA GONORRHOEAE

THREAT LEVEL
URGENT



This bacteria is an immediate public health threat that requires urgent and aggressive action.

246,000
DRUG-RESISTANT
GONORRHEA INFECTIONS



188,600 RESISTANCE TO
TETRACYCLINE

11,480 REDUCED SUSCEPTIBILITY
TO CEFIXIME

3,280 REDUCED SUSCEPTIBILITY
TO CEFTRIAZONE

2,460 REDUCED SUSCEPTIBILITY
TO AZITHROMYCIN



820,000 GONOCOCCAL INFECTIONS
PER YEAR

Neisseria gonorrhoeae causes gonorrhea, a sexually transmitted disease that can result in discharge and inflammation at the urethra, cervix, pharynx, or rectum.

RESISTANCE OF CONCERN

N. gonorrhoeae is showing resistance to antibiotics usually used to treat it. These drugs include:

- cefixime (an oral cephalosporin)
- ceftriaxone (an injectable cephalosporin)
- azithromycin
- tetracycline

PUBLIC HEALTH THREAT

Gonorrhea is the second most commonly reported notifiable infection in the United States and is easily transmitted. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. Because some drugs are less effective in treating gonorrhea, CDC recently updated its treatment guidelines to slow the emergence of drug resistance. CDC now recommends only ceftriaxone

plus either azithromycin or doxycycline as first-line treatment for gonorrhea. The emergence of cephalosporin resistance, especially ceftriaxone resistance, would greatly limit treatment options and could cripple gonorrhea control efforts.

In 2011, 321,849 cases of gonorrhea were reported to CDC, but CDC estimates that more than 800,000 cases occur annually in the United States.

	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

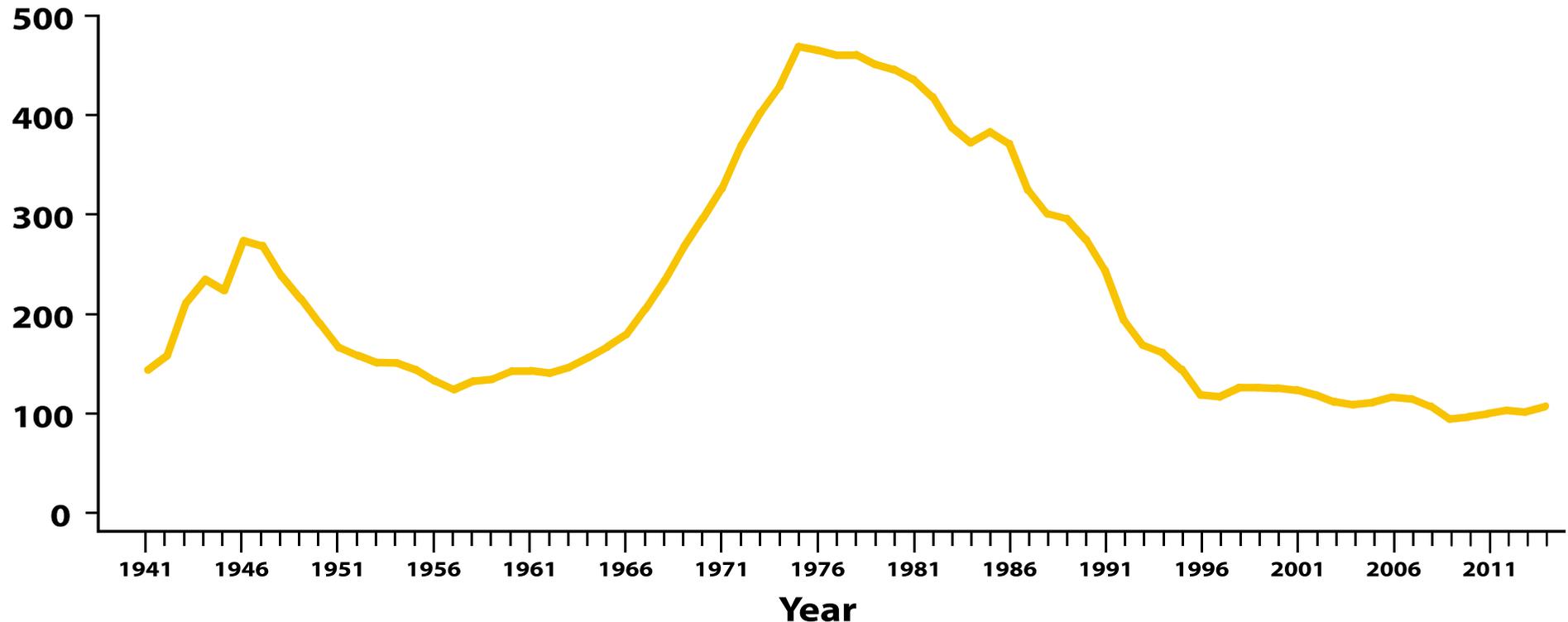
Source: The Gonococcal Infection Surveillance Project (GISP)-6,000 isolates tested for susceptibility in 2011. For more information about data methods and references, please see technical appendix.



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

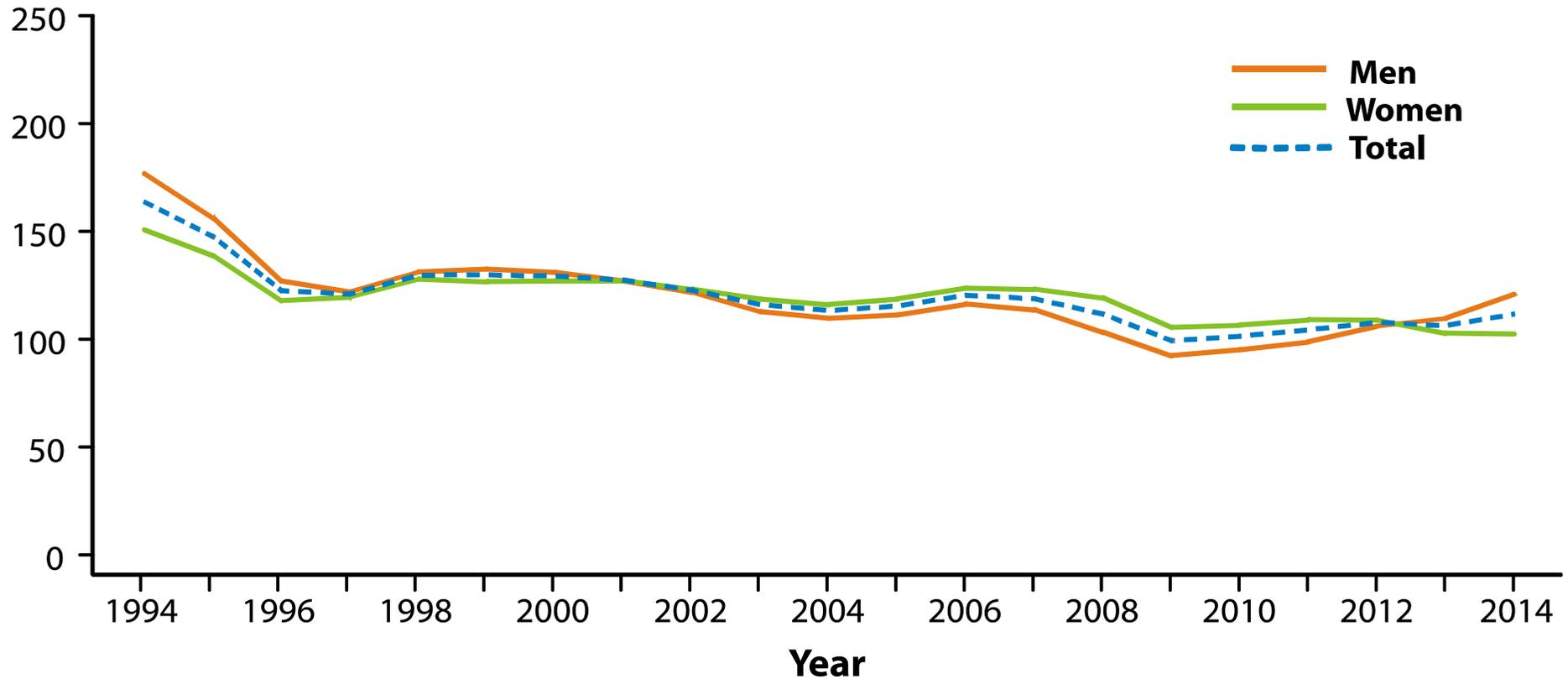
Gonorrhea — Rates of Reported Cases by Year, United States, 1941–2014

Rate (per 100,000 population)

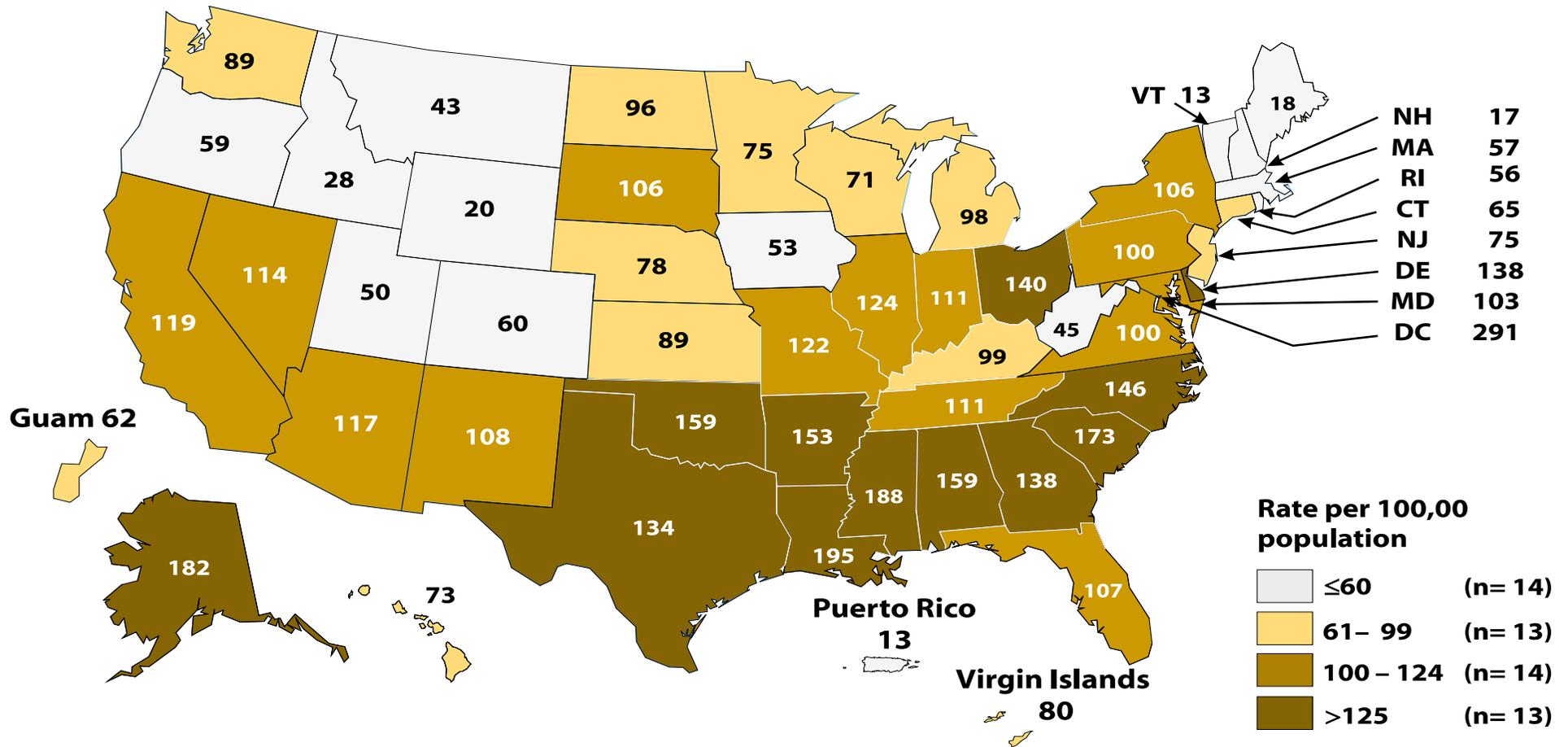


Gonorrhea — Rates of Reported Cases by Sex, United States, 1994–2014

Rate (per 100,000 population)



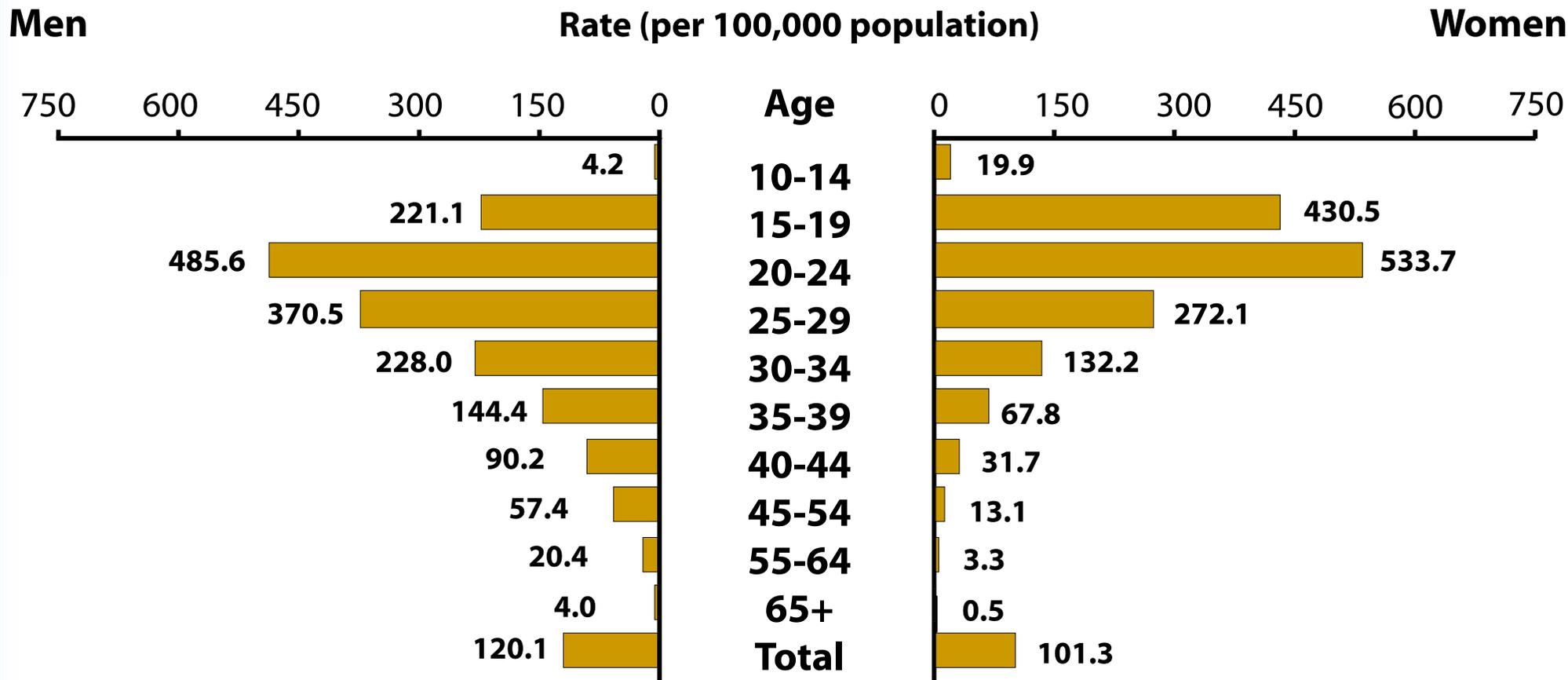
Gonorrhea — Rates of Reported Cases by State, United States and Outlying Areas, 2014



NOTE: The total rate of reported cases of gonorrhea for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 109.6 per 100,000 population.

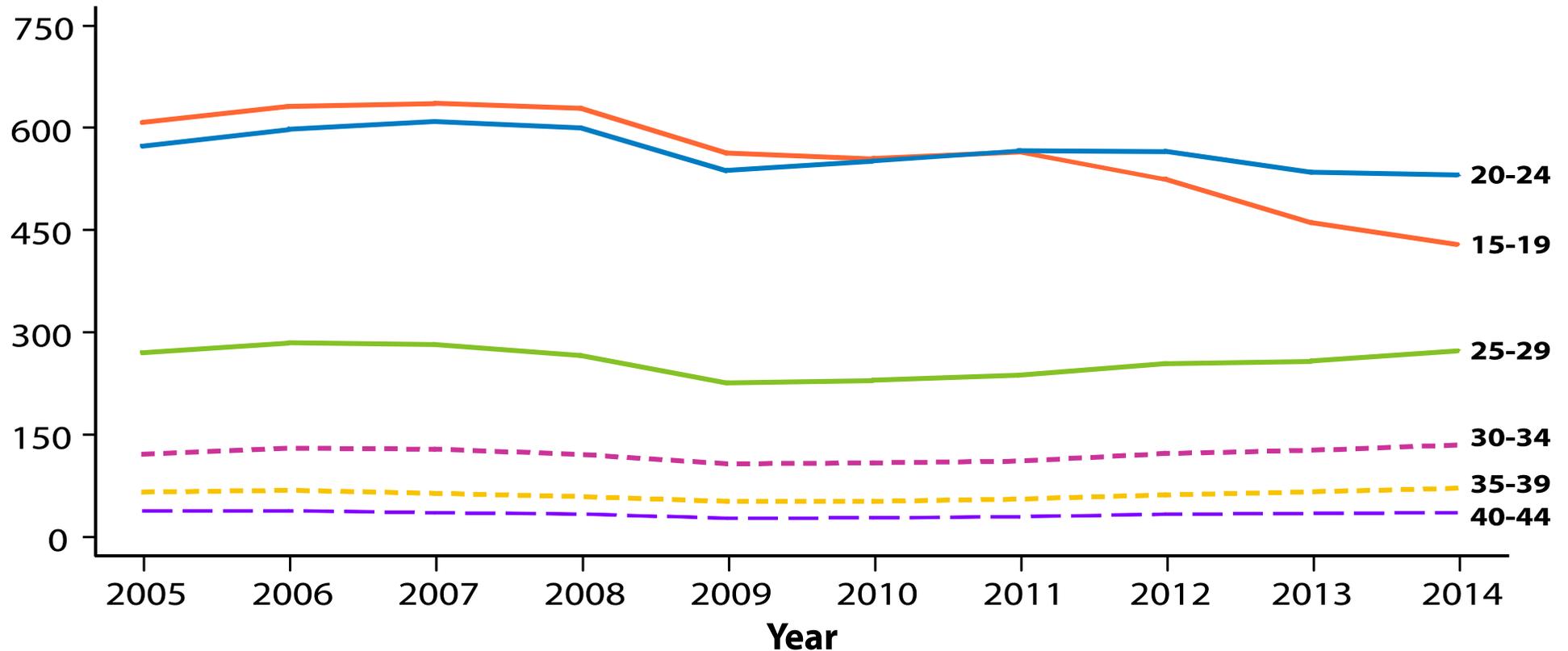


Gonorrhea — Rates of Reported Cases by Age and Sex, United States, 2014



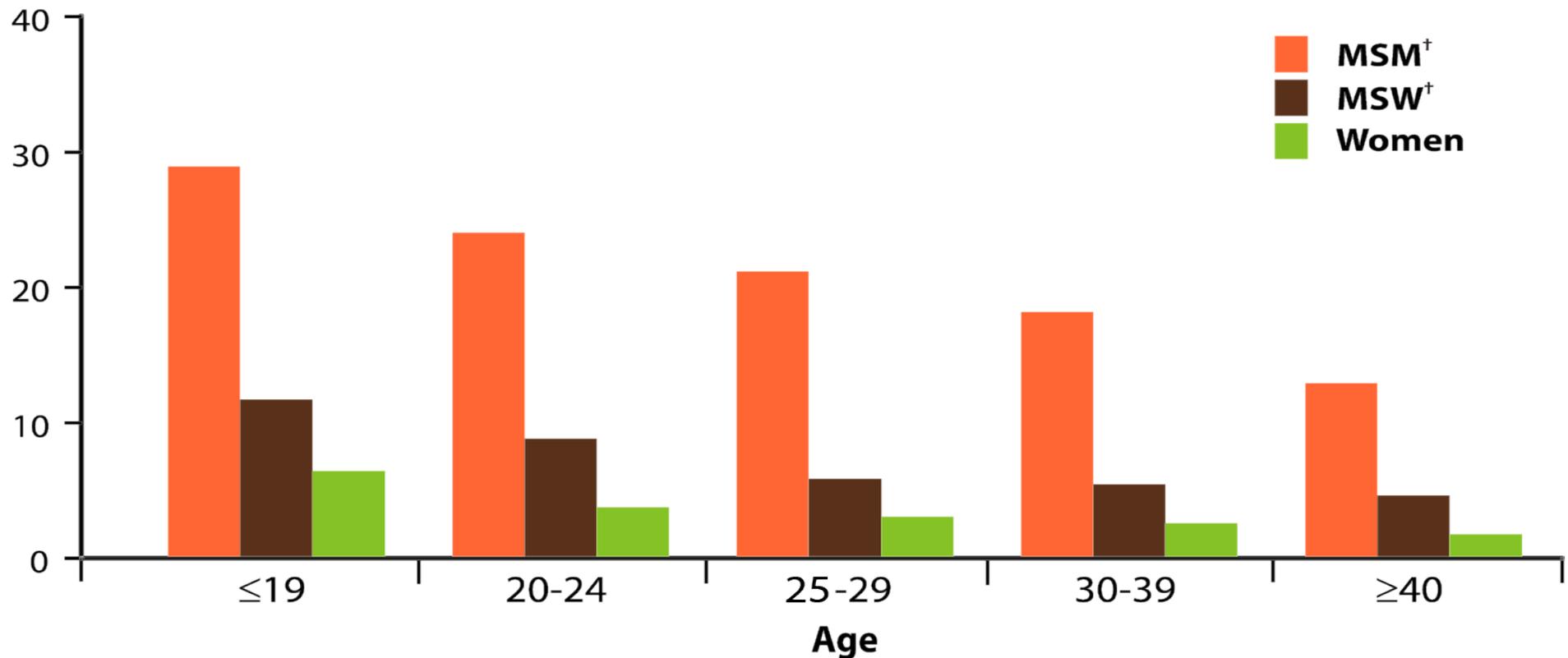
Gonorrhea — Rates of Reported Cases Among Women Aged 15–44 Years by Age, United States, 2005–2014

Rate (per 100,000 population)



Gonorrhea — Proportion of STD Clinic Patients* Testing Positive by Age, Sex, and Sexual Behavior, STD Surveillance Network (SSuN), 2014

Percentage



* Only includes patients tested for gonorrhea.

† MSM = men who have sex with men; MSW = men who have sex with women only.

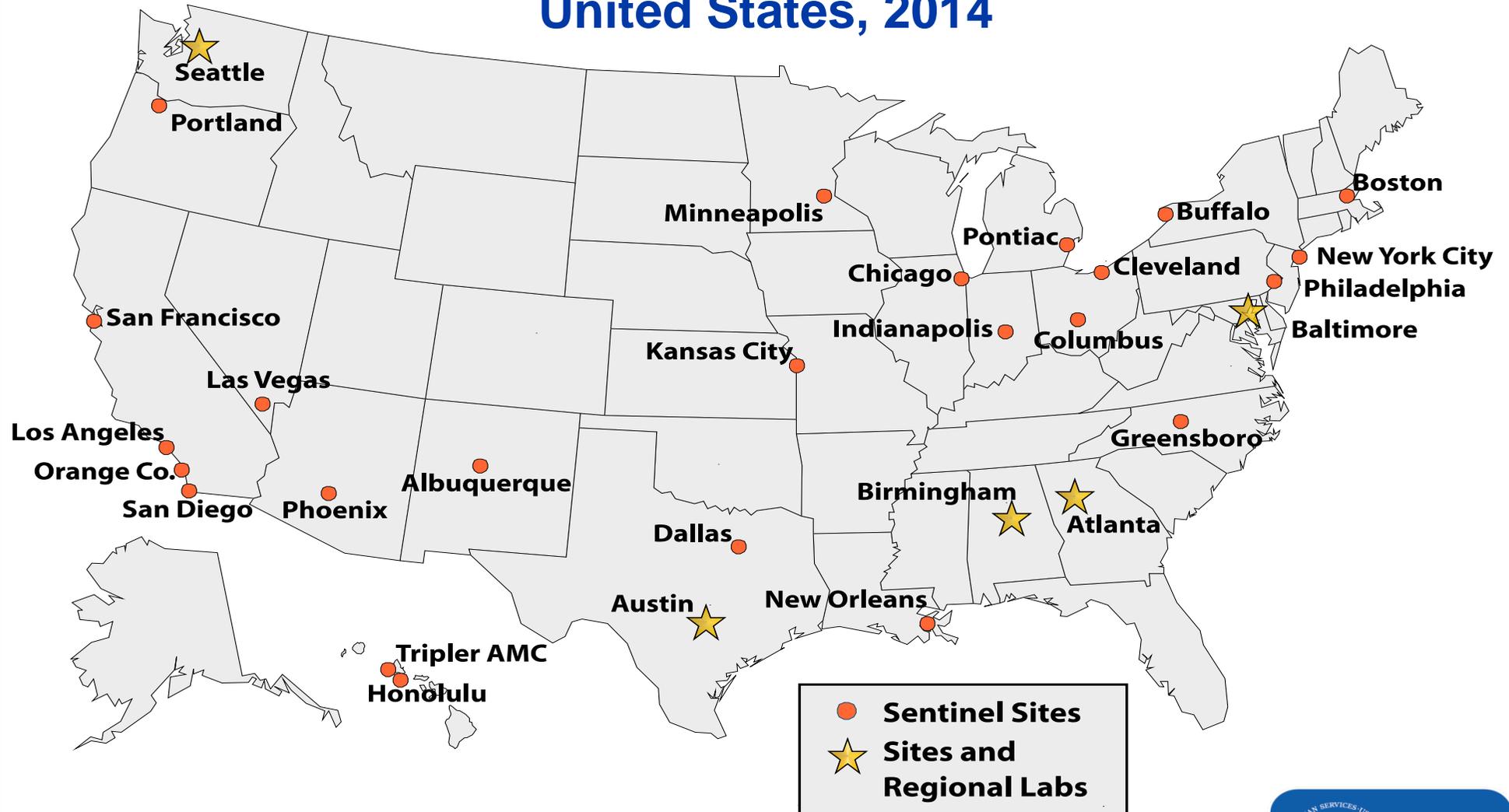
NOTE: Includes the six jurisdictions (Baltimore, Los Angeles, New York City, Philadelphia, San Francisco and Seattle) that contributed data for all of 2014.



Keeping tabs on gonorrhea resistance

- ◆ GISP = Gonococcal Isolate Surveillance Project
 - Sentinel sites across the US
 - Monitor resistance trends

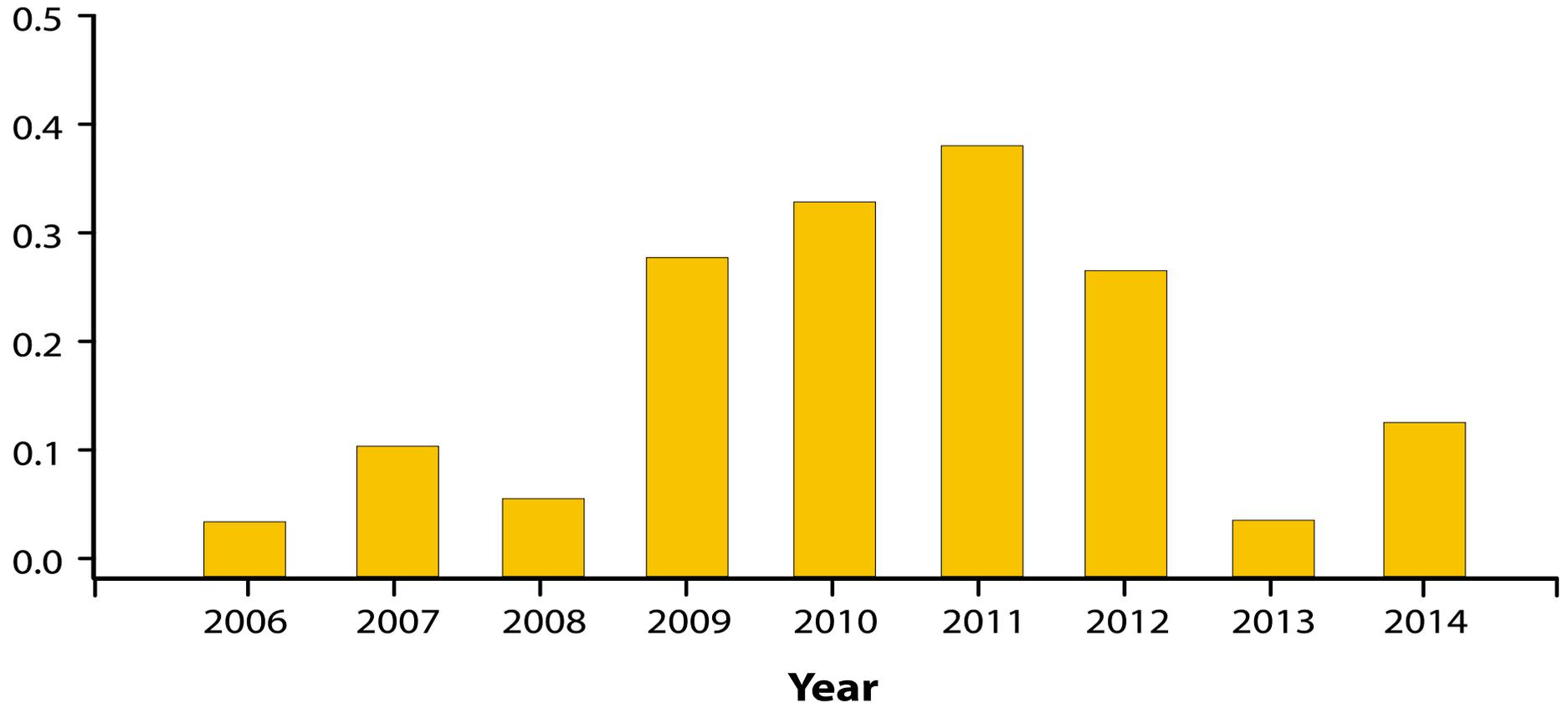
Location of Participating Sentinel Sites and Regional Laboratories, Gonococcal Isolate Surveillance Project (GISP), United States, 2014



NOTE: Austin is a regional laboratory only.

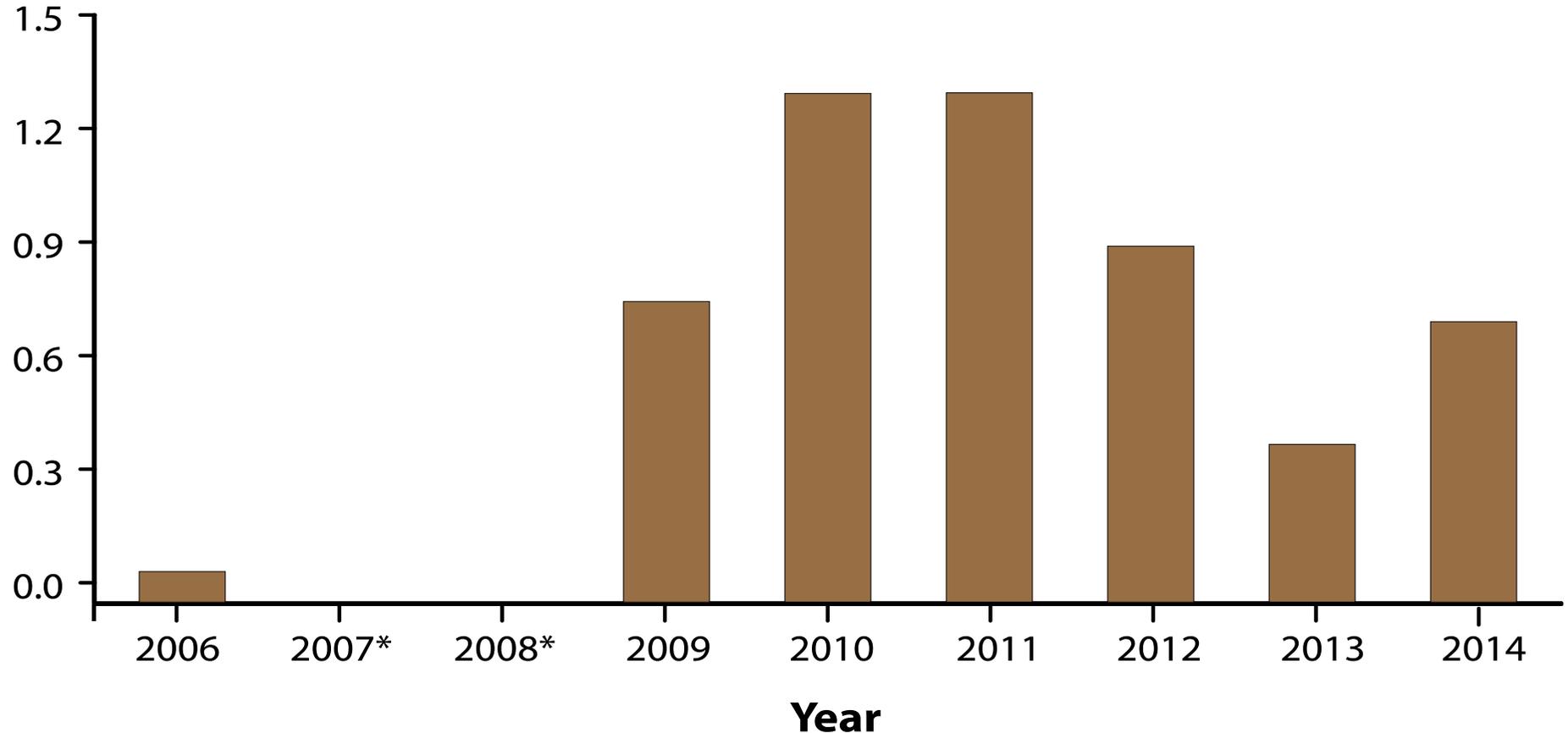
Neisseria gonorrhoeae — Percentage of Isolates with Elevated Ceftriaxone Minimum Inhibitory Concentrations (MICs) (≥ 0.125 $\mu\text{g/ml}$), Gonococcal Isolate Surveillance Project (GISP), 2006 – 2014

Percentage



Neisseria gonorrhoeae — Percentage of Isolates with Elevated Cefixime Minimum Inhibitory Concentrations (MICs) (≥ 0.25 $\mu\text{g/ml}$), Gonococcal Isolate Surveillance Project (GISP), 2006 – 2014

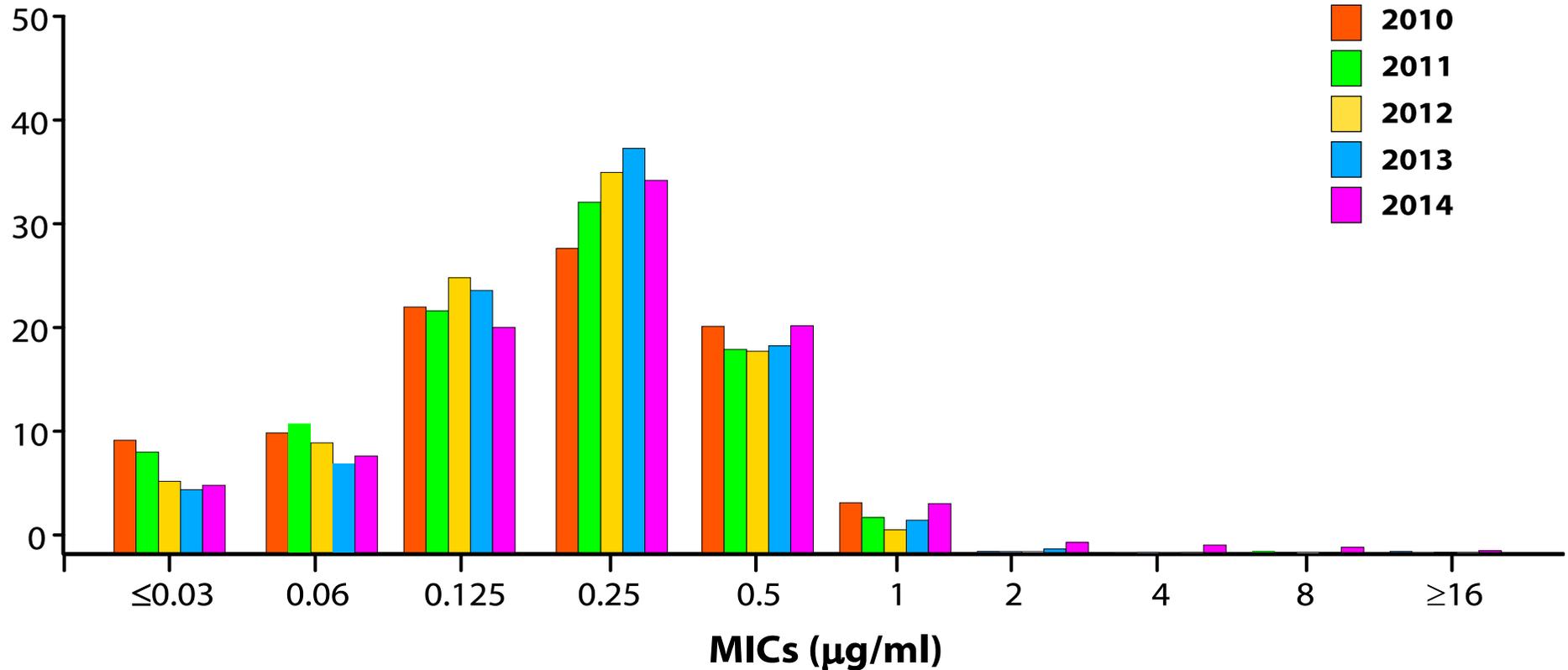
Percentage



*Isolates not tested for cefixime susceptibility in 2007 and 2008.

Neisseria gonorrhoeae — Distribution of Azithromycin Minimum Inhibitory Concentrations (MICs), (Gonococcal Isolate Surveillance Project (GISP), 2010–2014

Percentage



Morbidity and Mortality Weekly Report (*MMWR*)

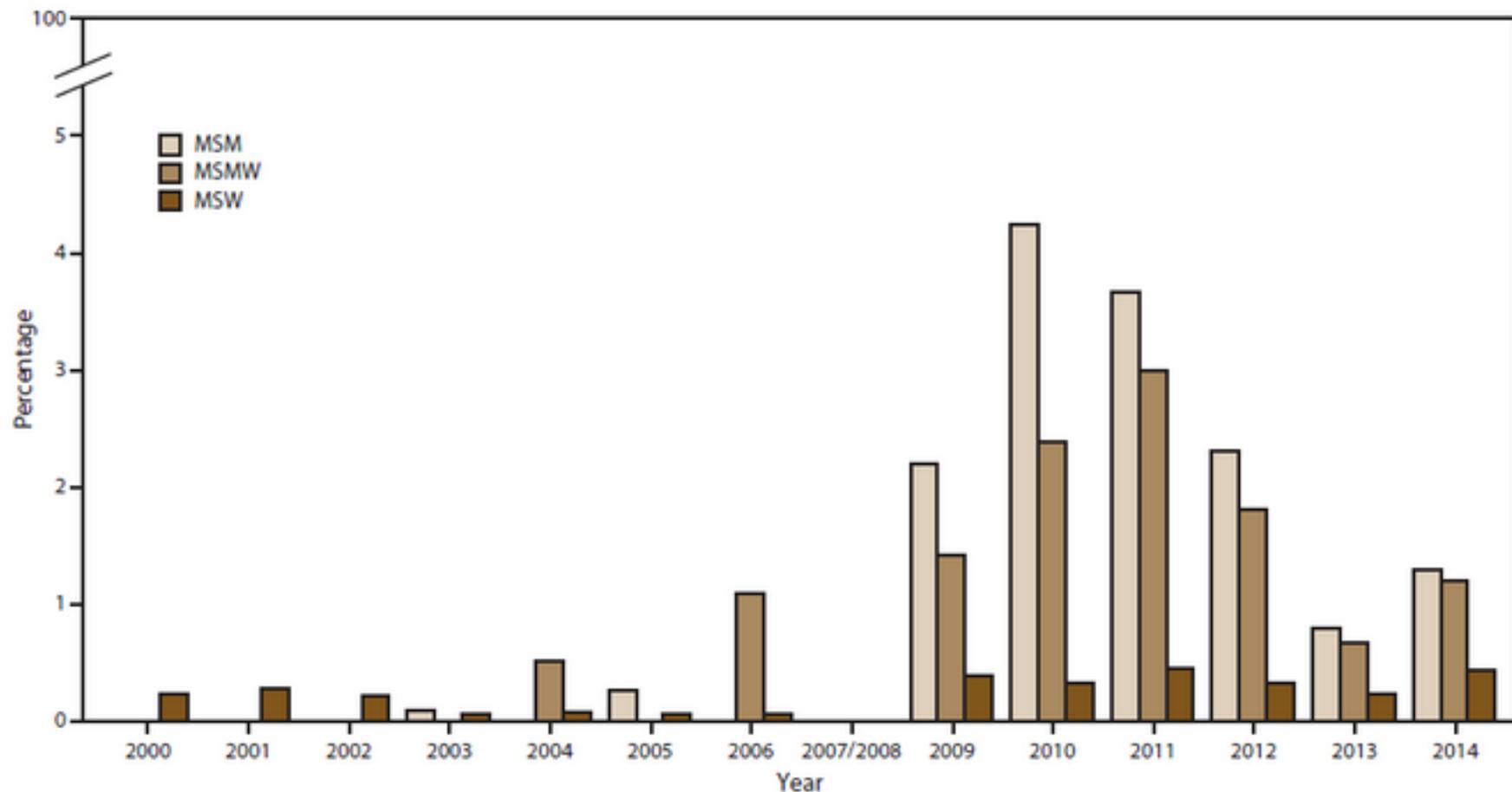
[CDC](#) > [MMWR](#)

Neisseria gonorrhoeae Antimicrobial Susceptibility Surveillance United States, 2014

Surveillance Summaries / July 15, 2016 / 65(7);1-19

- ◆ Reduced susceptibility to cefixime
 - » but rates are stable (good news)
- ◆ Reduced susceptibility to azithromycin
 - » and rates are increasing (bad news)

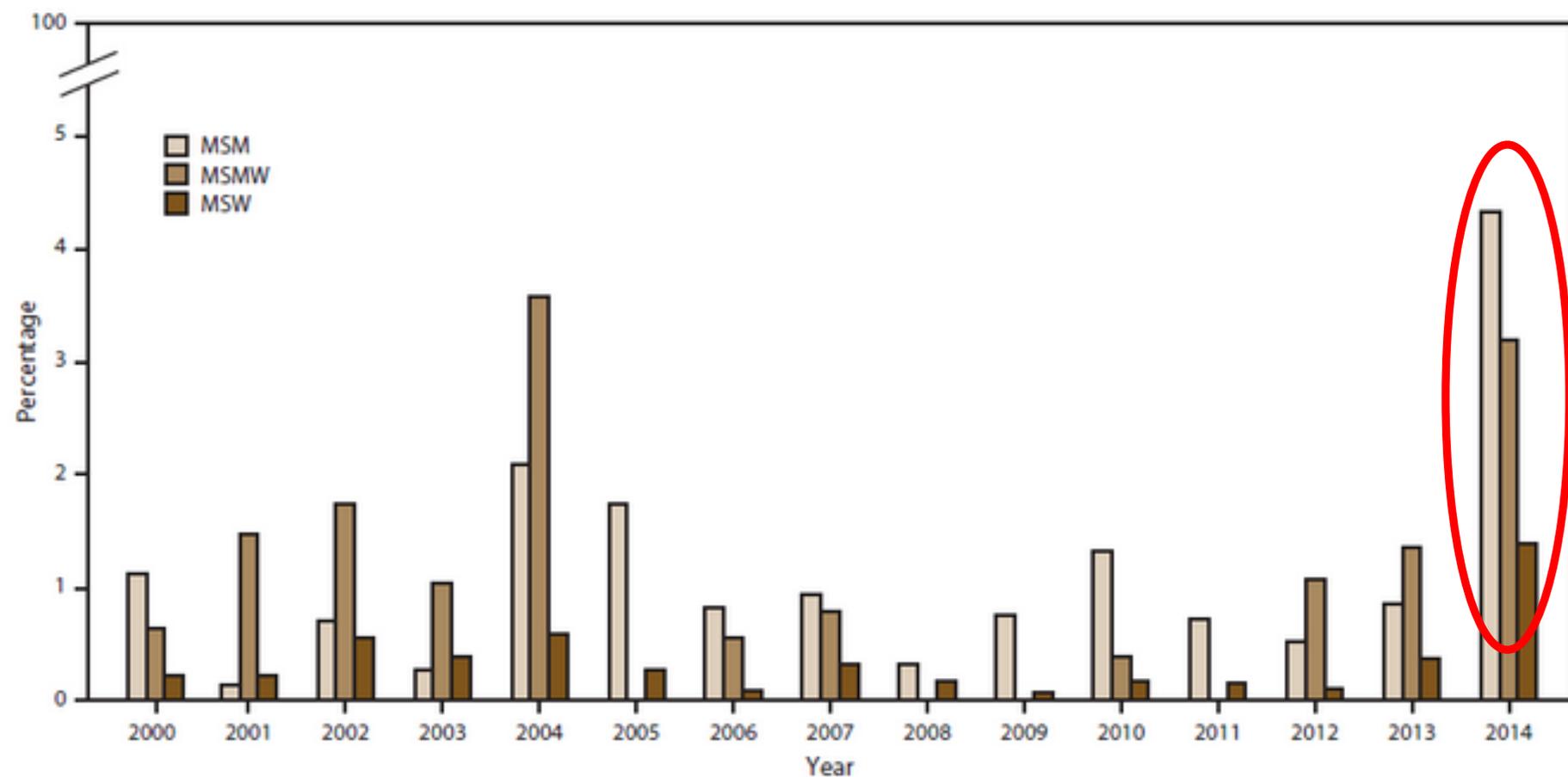
FIGURE 6. Percentage of *Neisseria gonorrhoeae* isolates with reduced cefixime susceptibility,* by sex of sex partner and year Surveillance Project, United States, 2000–2014



Abbreviations: MSM = men who have sex with men; MSMW = men who have sex with men and women; MSW = men who have sex with women.

* Minimum inhibitory concentration (MIC) ≥ 0.25 µg/mL. Cefixime susceptibility was not tested in 2007 and 2008.

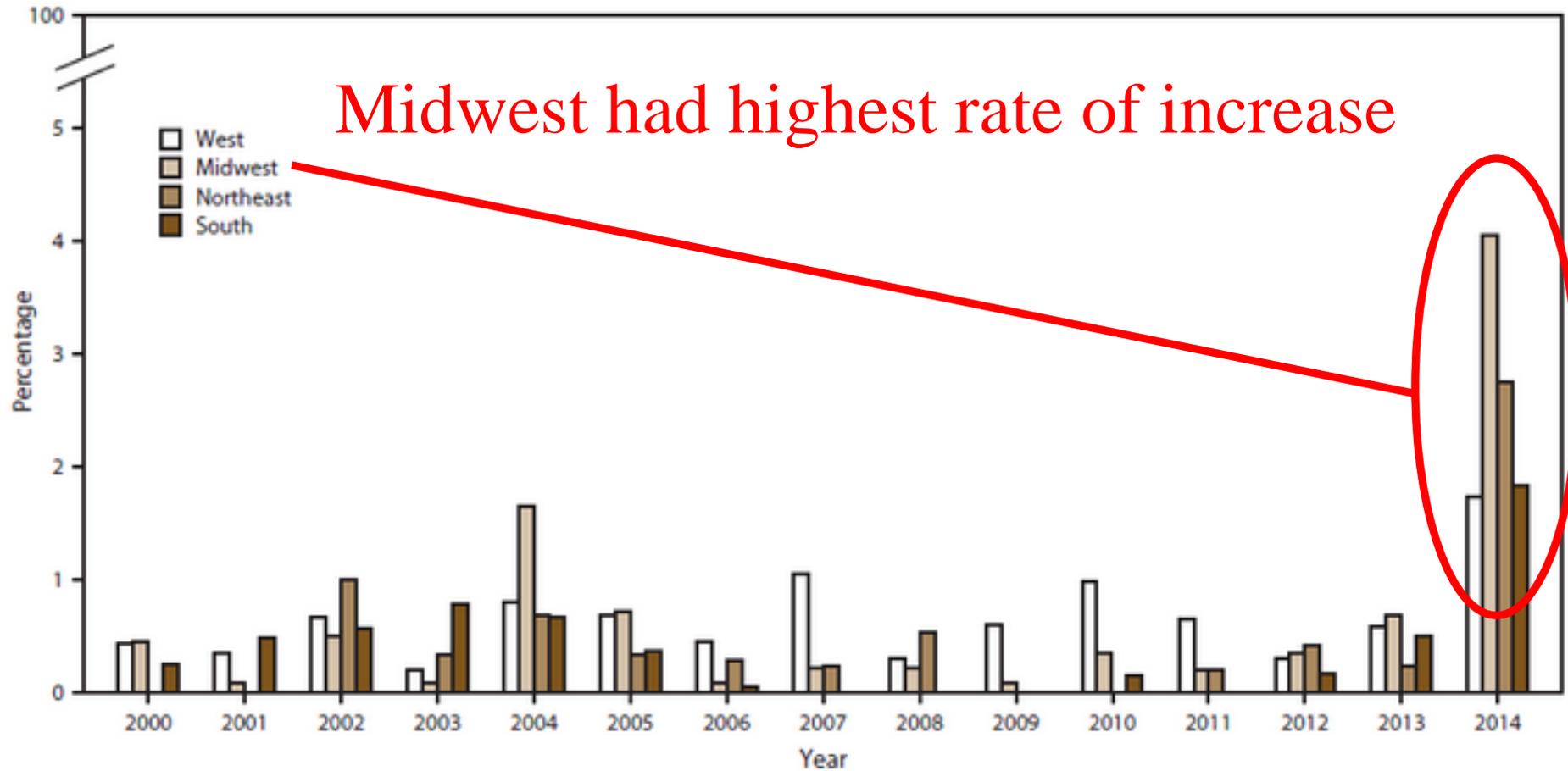
FIGURE 4. Percentage of urethral *Neisseria gonorrhoeae* isolates with reduced azithromycin susceptibility,* by sex of sex partner
Gonococcal Isolate Surveillance Project, United States, 2000–2014



Abbreviations: MSM = men who have sex with men; MSMW = men who have sex with men and women; MSW = men who have sex with women.

* Minimum inhibitory concentration (MIC) $\geq 1.0 \mu\text{g/mL}$ (2000–2004); MIC $\geq 2.0 \mu\text{g/mL}$ (2005–2014).

FIGURE 3. Percentage of urethral *Neisseria gonorrhoeae* isolates with reduced azithromycin susceptibility,* by region and year Surveillance Project, United States, 2000–2014



* Minimum inhibitory concentration (MIC) $\geq 1.0 \mu\text{g/mL}$ (2000–2004); MIC $\geq 2.0 \mu\text{g/mL}$ (2005–2014).

Antibiotic-Resistant Gonorrhea



Gonorrhea is developing resistance to the antibiotics we use to treat it.



There are about **820,000** new gonorrhea infections each year in the U.S.



Gonorrhea is the **2nd** most commonly reported infectious disease



We are down to **1** recommended effective class of antibiotics to treat it

The public health and medical communities must work together to:



Monitor antibiotic resistance



Develop new treatment options

With only one recommended treatment option remaining, **it's time to take action.**

Learn more at www.cdc.gov/std/gonorrhea/arg



Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Gonorrhoea – recommended treatment (cervix, urethra, rectum, pharynx)

◆ Ceftriaxone 250 mg IM

PLUS

◆ Azithromycin 1.0 gram PO

Gonorrhoea – alternative treatment

◆ If ceftriaxone not available:

*Cefixime 400 mg PO

PLUS

Azithromycin 1.0 PO

*limited efficacy for pharyngeal infections – obtain test of cure at 14 days

Gonorrhea –severe PCN or ceph allergy

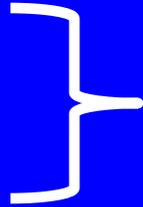
- ◆ Gemifloxacin 320 mg PO + azithromycin 2 gm PO
- ◆ Gentamicin 240 mg IM + azithromycin 2 gm PO

On the horizon: STD testing innovations

- ◆ Self-collected swabs

- clinic-based

- home-based



effective and acceptable

- ◆ Point-of-care testing

- ◆ High-throughput STD clinical services

Dean Street Clinic - London

Welcome to 56 Dean Street



Dean Street is an award winning HIV and sexual health NHS clinic in the heart of Soho. Our 56 Dean Street clinic offers emergency appointments and our convenient online services allow you to book a check-up in your own time or order a HIV home test. We also offer talking therapies and exciting community engagement events to enhance your wellbeing. We're proud to be connected to the people of London, supplying care that, regardless of sex, gender, sexuality or lifestyle meets the needs of all patients.

THANK YOU !