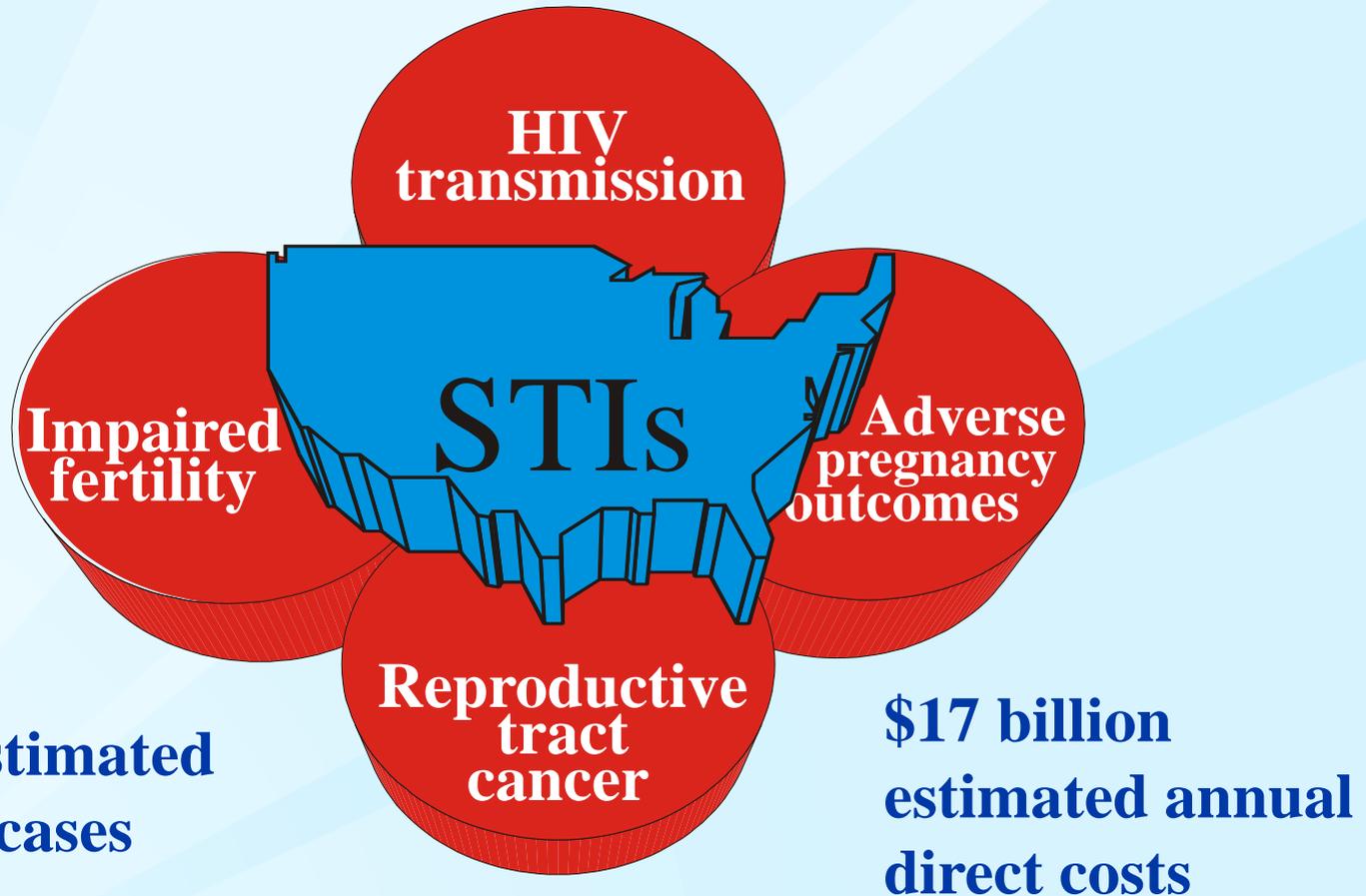


Emerging STIs

Kimberly Workowski, M.D, FACP, FIDSA

Professor of Medicine, Division of Infectious Diseases,
Emory University

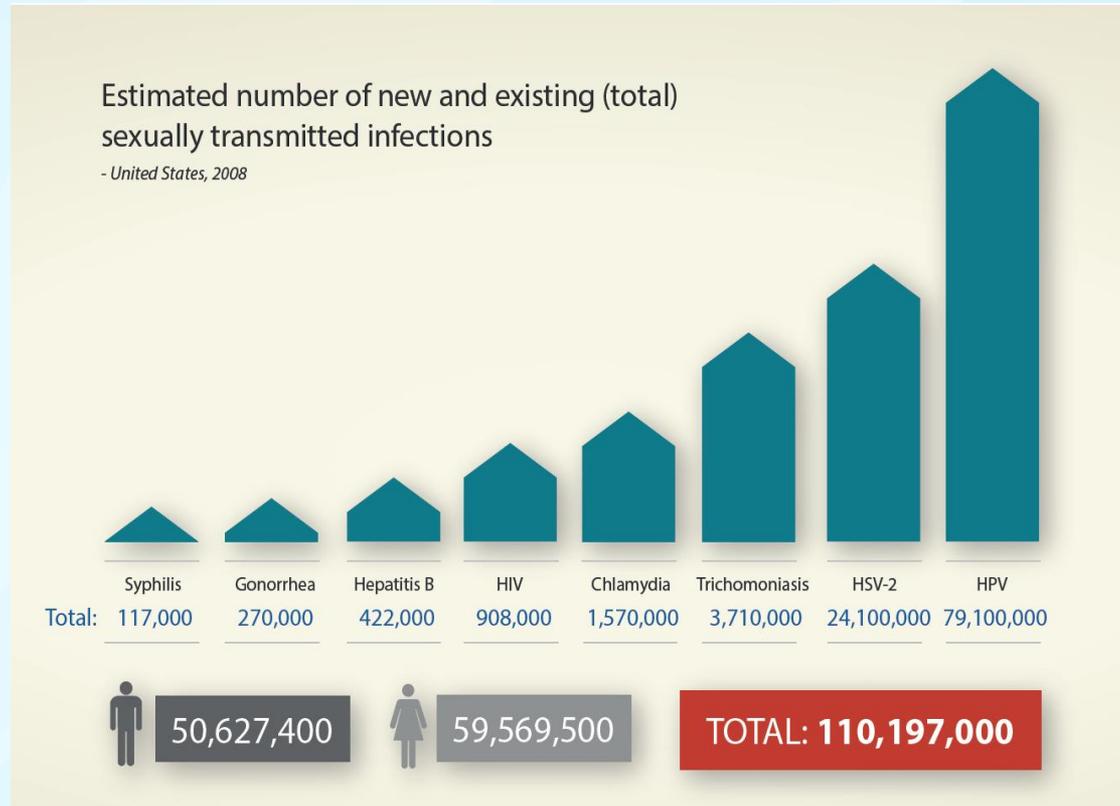
STIs and their Consequences



CDC. *STD Surveillance 2012*. Atlanta: U.S.DHHS; 2012

Chesson HW, et al. *Perspect Sex Reprod Health* 36(1):11–9. 2004

Sexually Transmitted Infections



Satterwhite CL, *STD*. 2013;40:187-193.

Populations at Greatest Risk for STIs

- Youth
 - 50% of STIs estimated to occur in 15-24 yr
- Men who have sex with men (MSM)
 - Account for 66.5% of syphilis cases in 2010
 - High rates of HIV co-infection
- Racial/ethnic minorities
 - STIs among highest racial /ethnic disparity

Prevalence of STIs Among Females, 14 to 19

STI	All ♀ Weighted Prevalence (%)	Sexually Experienced ♀ Weighted Prevalence (%)
Any STI	24.1	37.7
HPV*	18.3	29.5
<i>C trachomatis</i>	3.9	7.1
<i>T vaginalis</i>	2.5	3.6
HSV-2	1.9	3.4
<i>N gonorrhoeae</i>	1.3	2.5

*HPV 6/11 & any of 23 oncogenic types

STI in MSM

- STI risk higher in subgroups of MSM
 - Racial disparity
 - Methamphetamine, internet partnering
 - Syphilis, rectal CT/GC, LGV, hepatitis C
- Changing attitudes
 - Unprotected oral sex perceived as low risk
 - 20% syphilis (MMWR 2004); fellatio only 5% CT/GC (Hourihan, 2004)
 - Serosorting
 - Changes in sexual networks and venues for partners

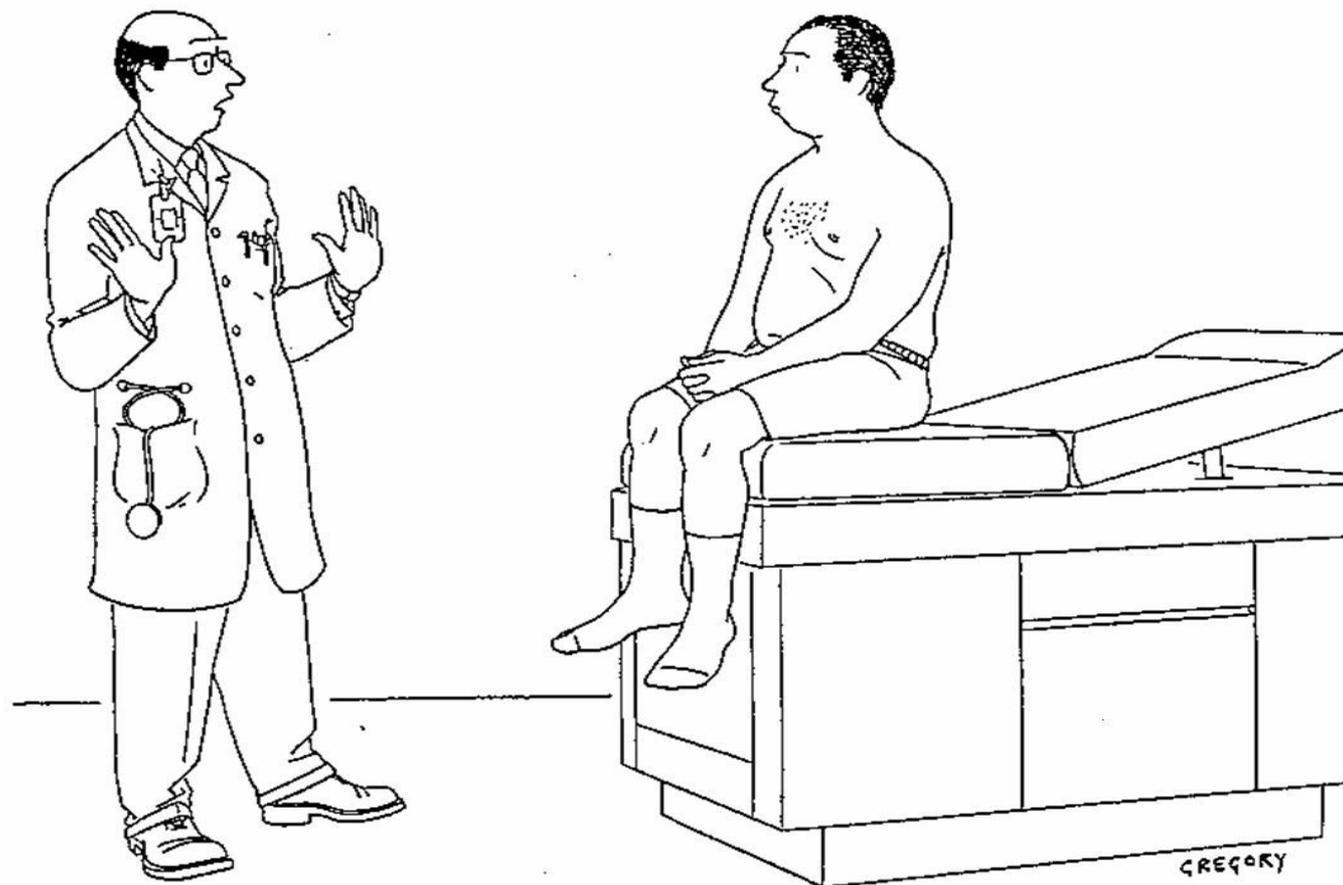
STI Screening for MSM

STD	Site	Type of Sex
HIV	blood	oral, anal
Syphilis	blood	oral, anal
GC/CT	urethra or urine	oral, anal
GC/CT	rectum	receptive anal
GC	pharynx	receptive oral
HSV-2*	blood	

* Consider testing

FREQUENCY: At least at the initial visit then annually or more frequently based on risk

STD Screening: Requires asking



“Whoa—way too much information.”

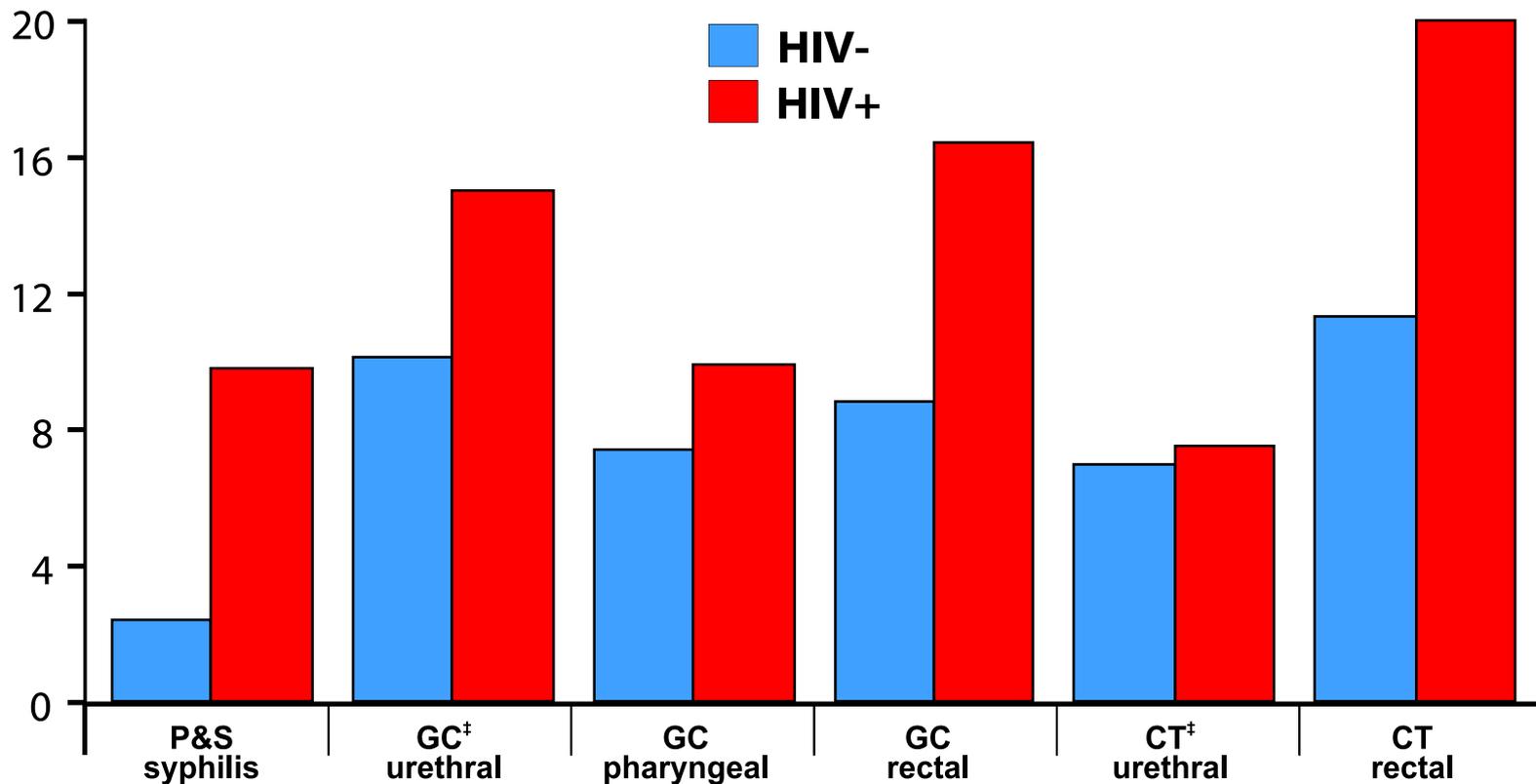
Distribution of GC by anatomical site in MSM attending STI clinics

Site of Infection	% of Subjects
Rectal only	21%
Urethral only	15%
Pharyngeal only	36%
Rectal and urethral	6%
Rectal and pharyngeal	12%
Urethral and pharyngeal	5%
All 3 sites	5%

- 90% of urethral infections were symptomatic
- Only 16% of rectal infections were symptomatic

Proportion of MSM* Attending STD Clinics with Primary and Secondary Syphilis, Gonorrhea or Chlamydia by HIV Status†, STD Surveillance Network (SSuN), 2012

Percentage



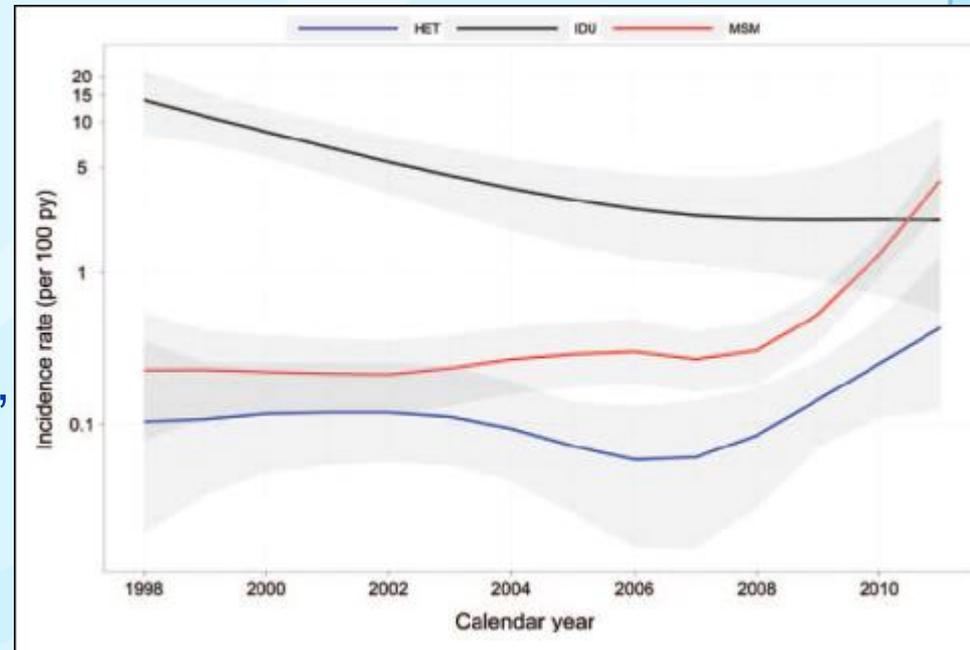
*MSM=men who have sex with men.

†Excludes all persons for whom there was no laboratory documentation or self-report of HIV status.

‡GC urethral and CT urethral include results from both urethral and urine specimens.

Hepatitis C Virus Infection in MSM

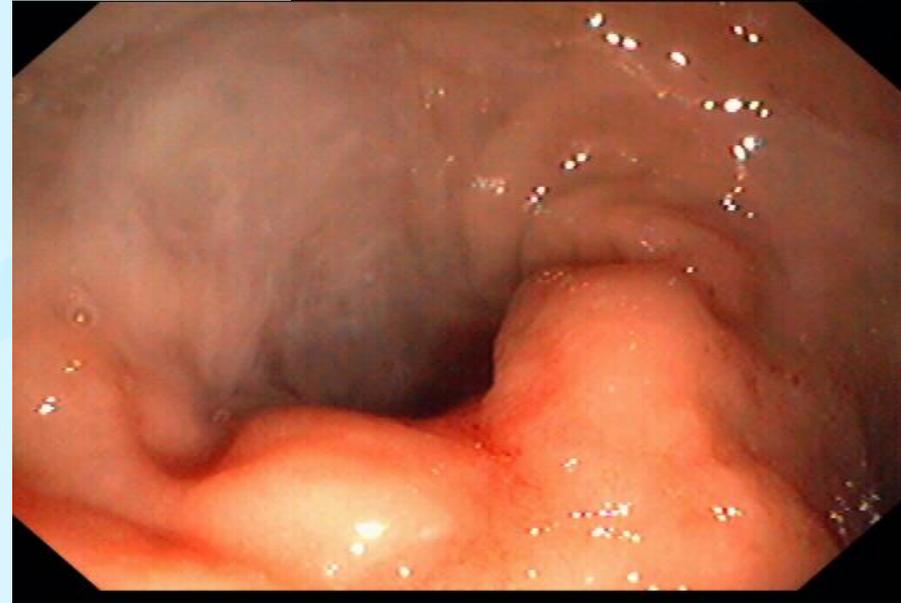
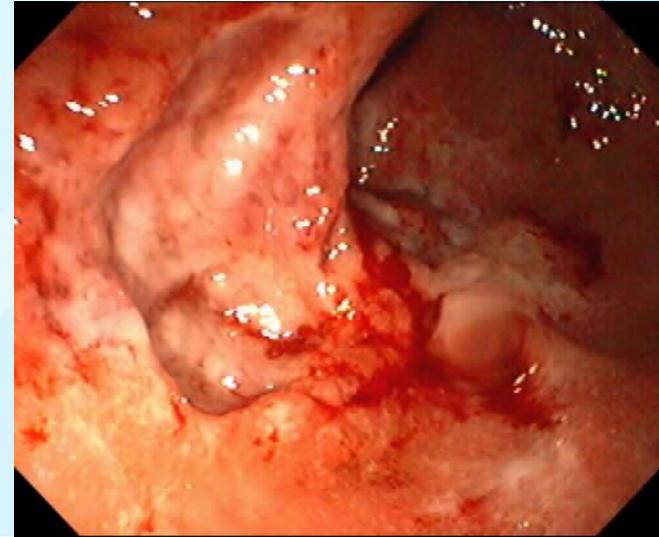
- Increasing incidence of HCV among MSM
- Risks:
 - Unprotected receptive anal intercourse; h/o syphilis
 - Rougher or poorly lubricated unprotected anal penetration, including fisting
- CDC guidelines: screen if HIV+, IDU, and/or born 1945-65
- Acute infection may be HCV antibody negative
 - Check HCV RNA in patients with new, unexplained transaminase elevation



Vandeler, *Clin Infect Dis* 2012

LGV Proctitis

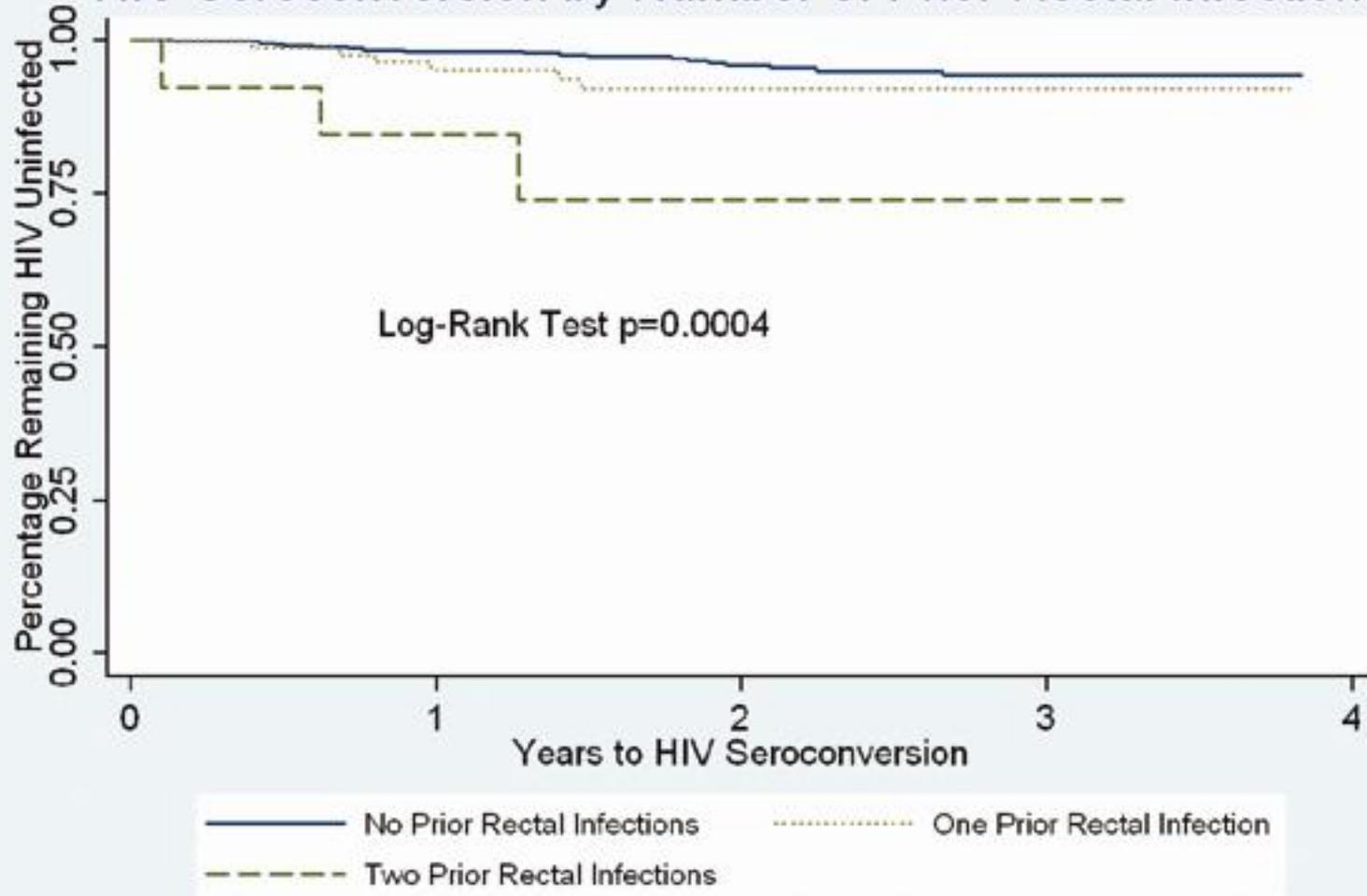
- Rectal exposure in MSM or women
- Rectal ulcers or lesions
- Mucoid anal discharge
- Rectal bleeding
- Tenesmus, constipation
- Rectal scarring/fistulas



STIs are Associated with Increased HIV Acquisition and Transmission

- Mucosal breaks & inflammation
 - Genital ulcers: herpes, syphilis
 - Inflammation: gonorrhea, non-gonococcal urethritis
- Increase amount of HIV shed at genital mucosa
 - Cervix, urethra, rectum
- Increase plasma HIV viral load
- Treatment (gonorrhea, syphilis, and trichomoniasis) can reduce plasma & genital HIV

HIV Seroconversion by Number of Prior Rectal Infections



HIV incidence among MSM with STI

Author, pub. year	Setting	Population	HIV incidence	Other key findings
Pathela ¹ 2013	Population of NYC	2805 MSM w/ P&S syphilis	Annual incidence = 5.6% (95%CI 5.0-6.1)	
Pathela ² 2013	STD clinic (NYC)	276 MSM w/ rectal gonorrhea/chlamydia	Annual incidence = 6.7% (95%CI 4.6-9.4)	Black race associated w/ incident HIV (HR=5, 95%CI 1.8-14.2)
Ackers ³ 2012	47 US cities	450 MSM with <i>hx of STD</i> enrolled in HIV vaccine trial	Incidence 3.8/100 py (95%CI 2.6-4.4)	
Bernstein ⁴ 2010	STD clinic (SF)	541 MSM w/ rectal gonorrhea/chlamydia	Annual incidence = 2.3% (95%CI 1.5-3.3) Annual incidence = 15% (95%CI 3.2-37.9) among those w/ 2 rectal inf. in prior 2y	Annual incidence = 8.3% (95%CI 1.8-22.5) among those also w/ early syphilis dx in prior 2y

¹Pathela, et al. Abs. at ISSTD. Vienna, July 2013, ²Pathela et al. CID. 2013. 57(8): 1203-9. ³Ackers et al. PLoS ONE . 2012.7(4): e34972. ⁴Bernstein et al. JAIDS. 2010. 53(4): 537-543.

Ongoing Sexually Transmitted Disease Acquisition and Risk-Taking Behavior Among US HIV-Infected Patients in Primary Care: Implications for Prevention Interventions

Kenneth H. Mayer, MD, Timothy Bush, BA,† Keith Henry, MD,‡ Edgar T. Overton, MD,§ John Hammer, MD,¶ Jean Richardson, PhD,|| Kathy Wood, RN, BSN,** Lois Conley, MPH,† John Papp, MSc, PhD,†† Angela M. Caliendo, MD, PhD,‡‡ Pragna Patel, MD, MPH,† and John T. Brooks, MD†; the SUN Investigators*

1. -557 HIV-infected adults in primary care (4 cities)
 - -Screened/treated for STI at enrollment and at 6 months
 - -13% with STI at enrollment; 7% incident STI at 6 months
 - Excluding trichomoniasis, 94% of incident STDs were in MSM
 - Most common in men: rectal chlamydia, oropharyngeal gonorrhea
 - Risks: polysubstance use, > 4 partners in 6 months
 - 20% of MSM diagnosed with an STI by 6 mo: most asymptomatic

Prevention Strategies

- Behavioral counseling
 - Partners, pregnancy, protection, practices, past STIs
- Pre-exposure vaccination (hepatitis A, B, HPV)
- Male latex condoms
 - Mucosal fluids (HIV, GC, CT, trichomonias)
- Avoid agents that disrupt anal/vaginal epithelium
 - N9 spermicide, hyperosmolar lubricants
- Male circumcision reduces risk of HPV, genital herpes (African heterosexuals)

HPV Vaccine Recommendations

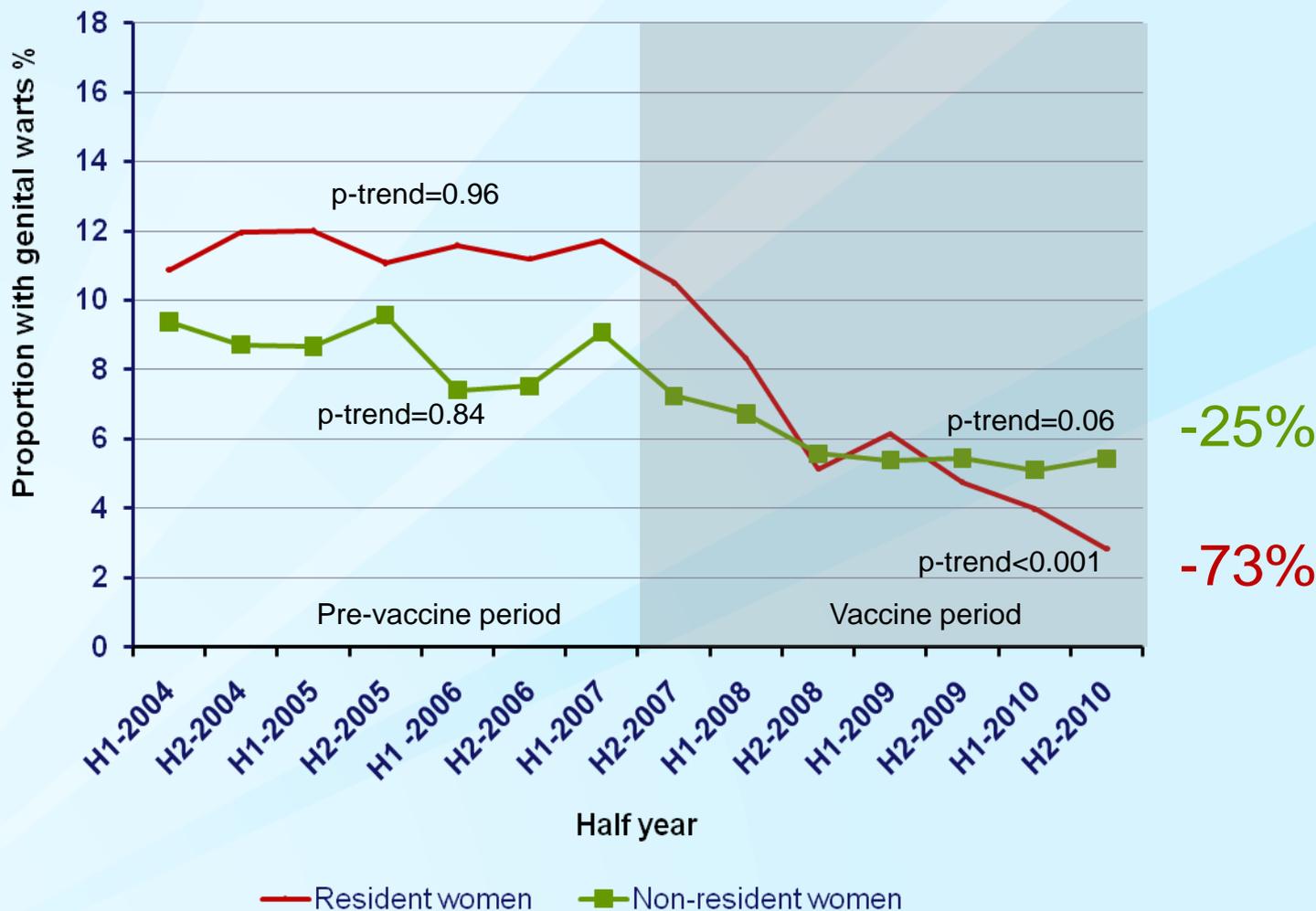
Population		Recommendation
Gender	Age	
All Females	9-26	Routine with HPV4 or HPV2
All Males	9-21	Routine with HPV4
	22-26	Permissive HPV 4
MSM and HIV+ Males	22-26	Routine with HPV 4

* Irrespective of history of abnormal Pap, HPV, genital warts

MMWR, May 28 2010; 59(20):626-629 , 630-632

MMWR , December 23 2011; 60(50);1705-1708

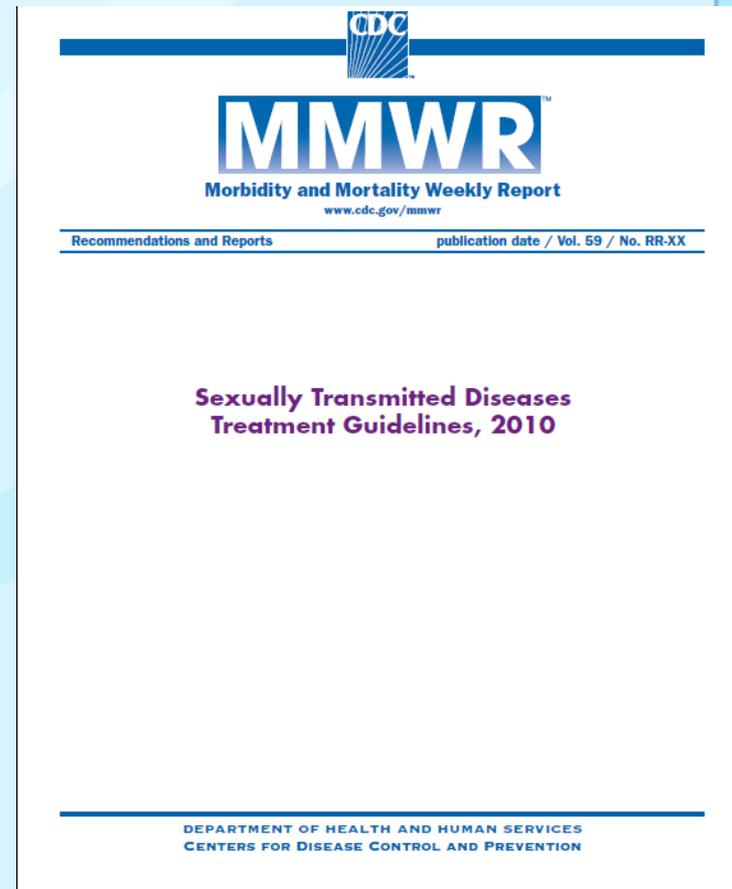
Proportion of eligible age women* with genital warts, by resident status, Australia, 2004-2010



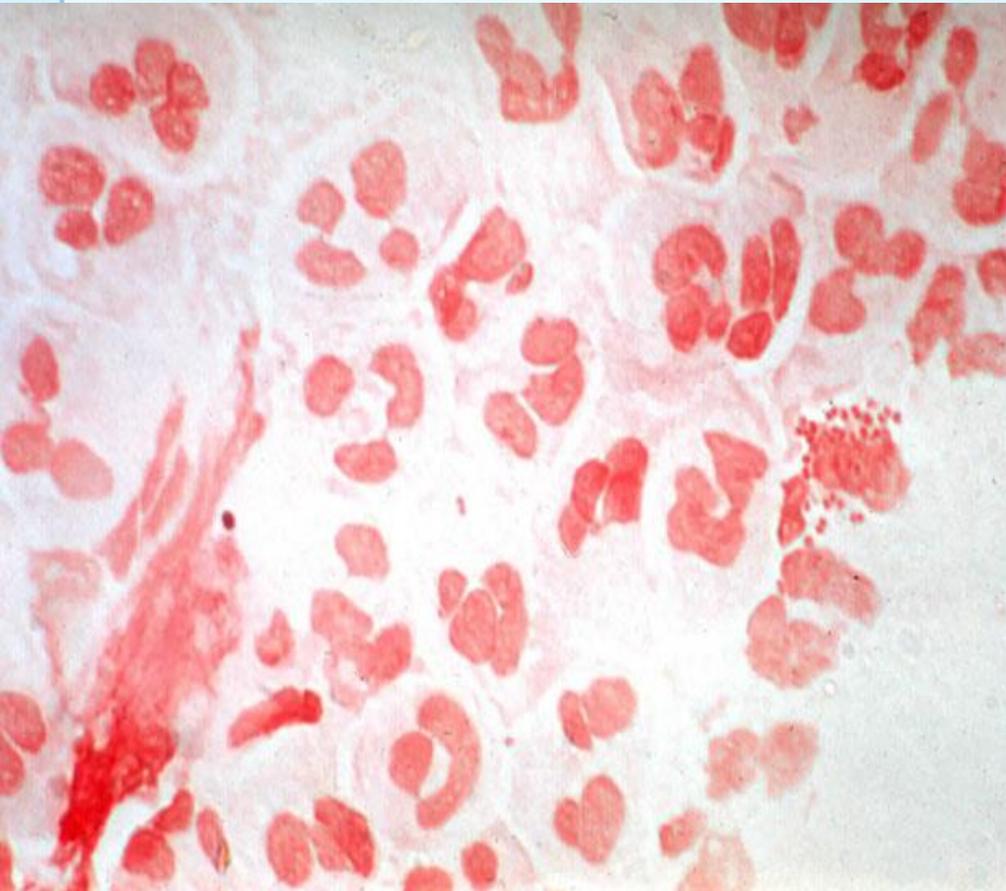
* Eligible age - ≤ 26 years old in July 2007

CDC STD Treatment Guidelines

- ❑ Authoritative, evidence-based source for STD clinical management
- ❑ Available at www.cdc.gov/std
- ❑ Wall charts, pocket guides, eBook
- ❑ Webinars, podcasts
- ❑ STD Treatment Mobile App for Apple devices (iPhone & iPads) and Droid devices (phones & tablets).
- ❑ Currently under revision for release in 2014



Urethritis



GC (5-20%)

Chlamydia 15-40%

M. genitalium 5-25%

Ureaplasma 0-20%

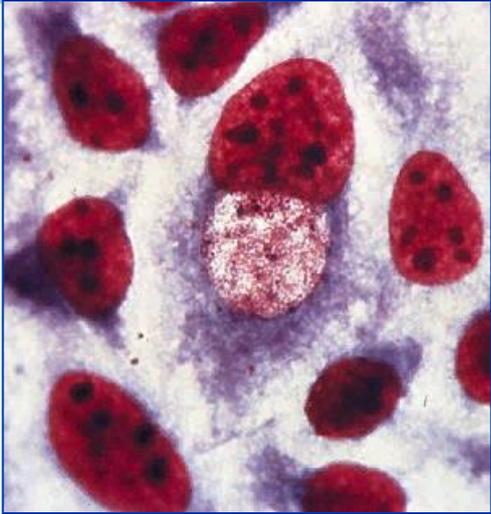
Trichomoniasis 5-20%

HSV 15-30%, adenovirus

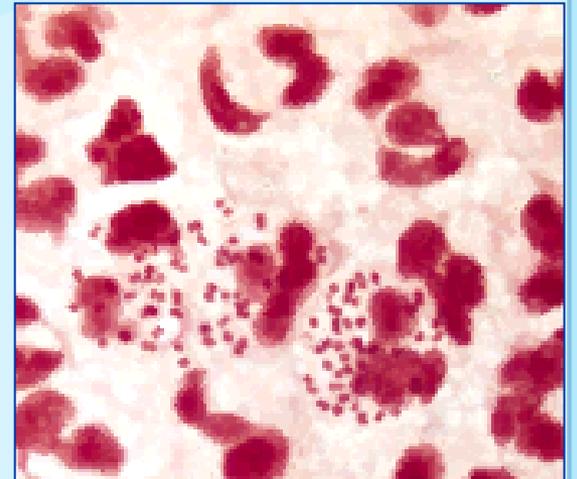
Enterics, *Candida*

Mycoplasma genitalium

- Small bacteria that lacks cell wall (gram stain neg)
- Association with acute or persistent NGU (29 studies)
 - No role in male infertility
- Conflicting evidence in women: cervicitis, PID, infertility, ectopic pregnancy, birth outcomes
- Azithromycin superior to doxycycline for MG urethritis (Mena 2009)
 - Resistance to azithromycin (Jensen 2009)
- Moxifloxacin for persistent NGU
 - 400 mg daily x 7 d

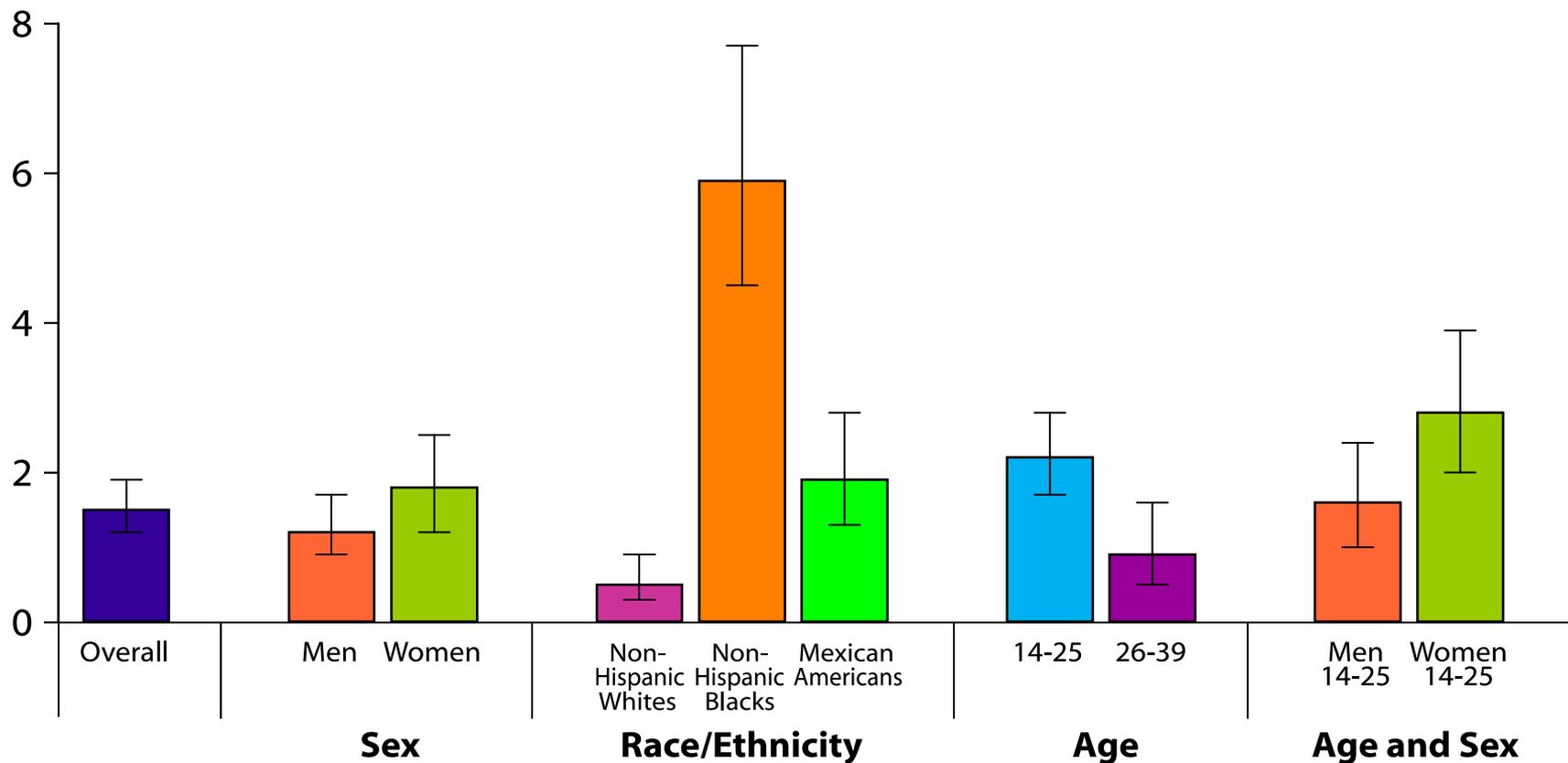


Chlamydia & Gonorrhea



Chlamydia—Prevalence Among Persons Aged 14–39 Years by Sex, Race/Ethnicity, or Age Group, National Health and Nutrition Examination Survey, 2005–2008

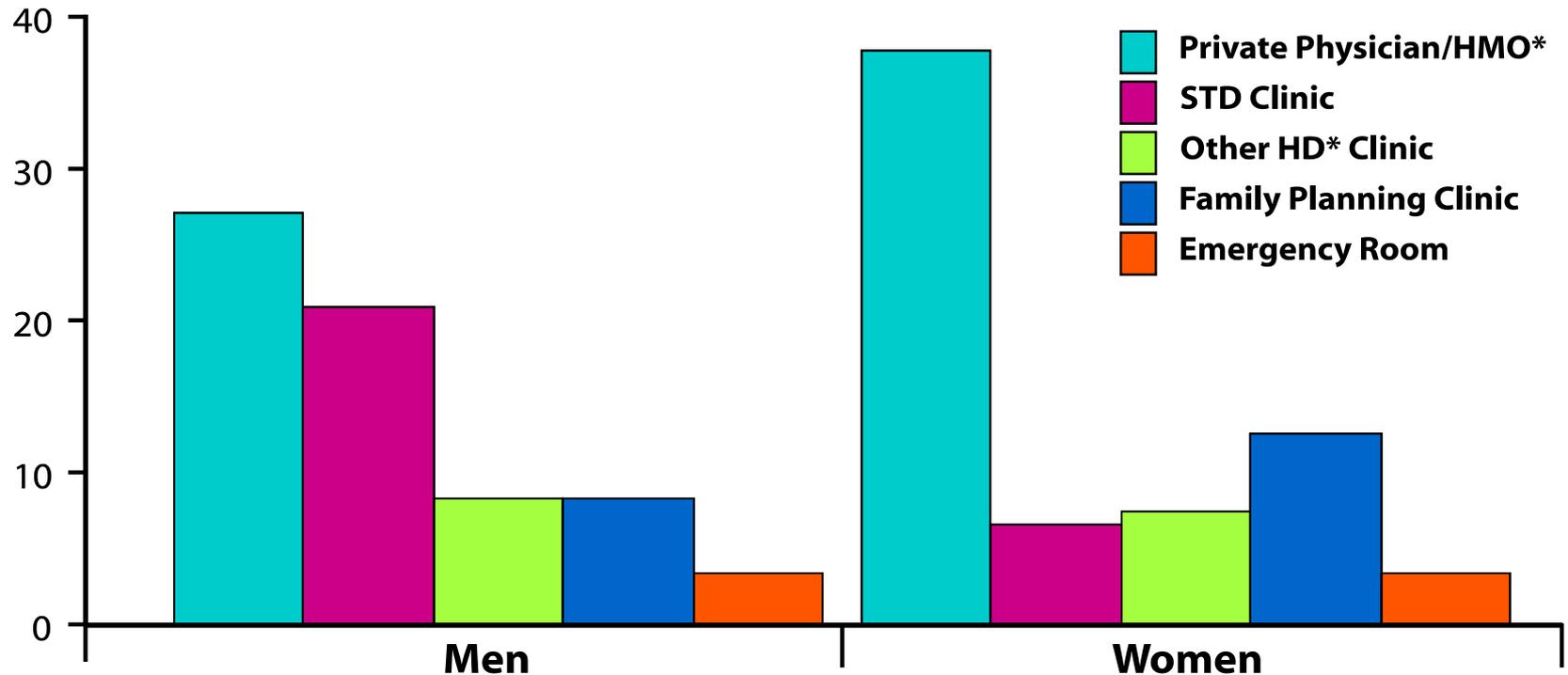
Prevalence, %



NOTE: Error bars indicate 95% confidence intervals.

Chlamydia—Percentage of Reported Cases by Sex and Selected Reporting Sources, United States, 2012

Percentage



*HMO=health maintenance organization; HD=health department

NOTE: Of all cases, 11.4% had a missing or unknown reporting source. Among cases with a known reporting source, the categories presented represent 69.8% of cases; 30.2% were reported from sources other than those shown.

Chlamydia

- Primary focus of screening
 - Sexually active women ≤ 25 (USPSTF, Ann Int Med 2007)
- Selective male screening (adolescent clinics, corrections, national job training program, < 30 yrs, STD, military)
- Retest women/men 3 mo post treatment
 - CT testing in third trimester (reinfection)

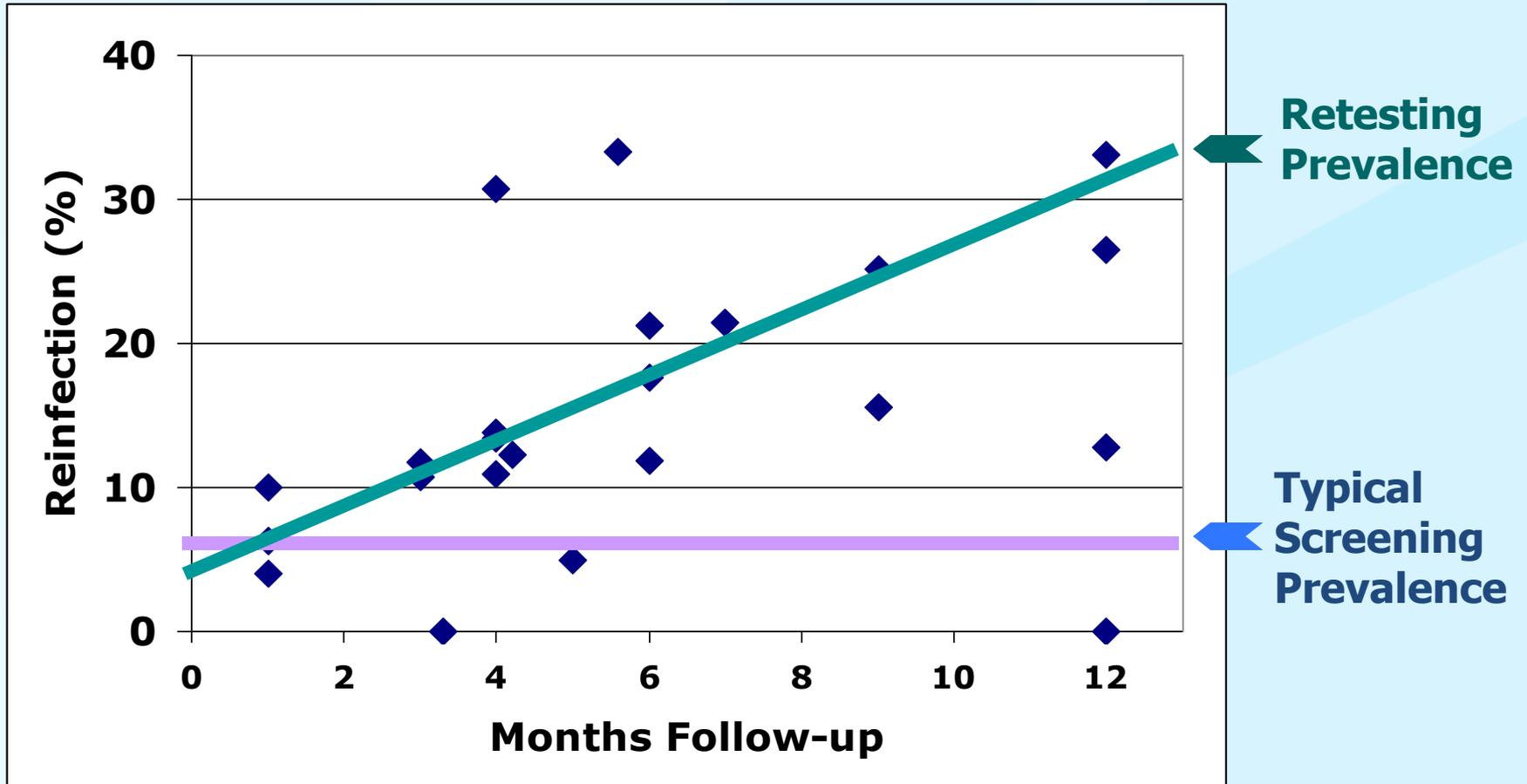
USPSTF Screening Recommendations for Women

	Grade	Age/Special Considerations
USPSTF		
Chlamydia Screening in non-pregnant women	A	Sexually active women ≤ 24 and at-risk women ≥ 25
Chlamydia Screening in pregnant women	B	All women ≤ 24 and at-risk women ≥ 25
Gonorrhea Screening in women	B	All at-risk sexually active women (including pregnant women) - <i>special considerations also include population risk factors</i>
HIV screening in adolescents and adults	A	All adolescents and adults at increased risk
Syphilis Screening	A	All pregnant women and all persons at risk

www.ahrq.gov

www.cdc.gov/vaccine/recs/acip

Repeat Chlamydial Infection is Common in Women



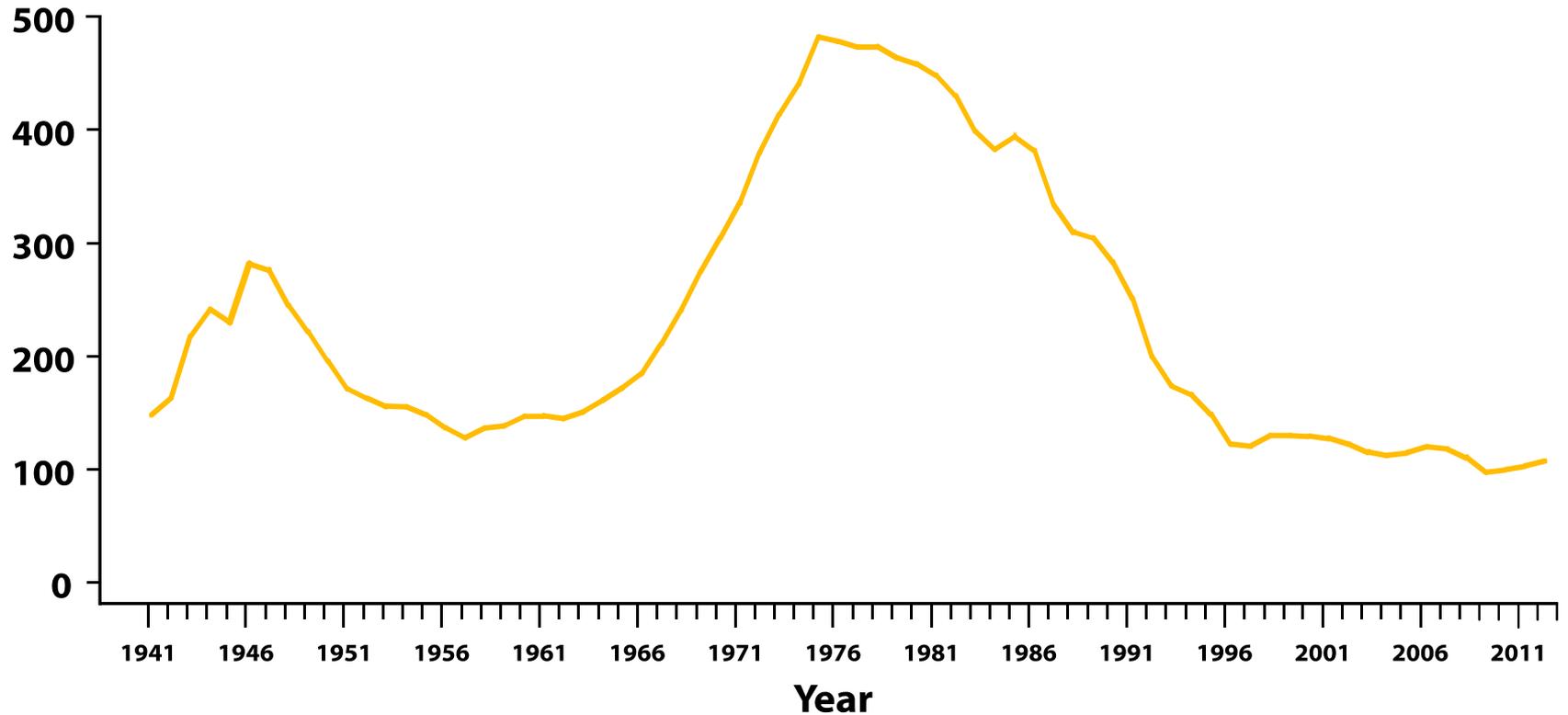
Chlamydia

Emerging Issues

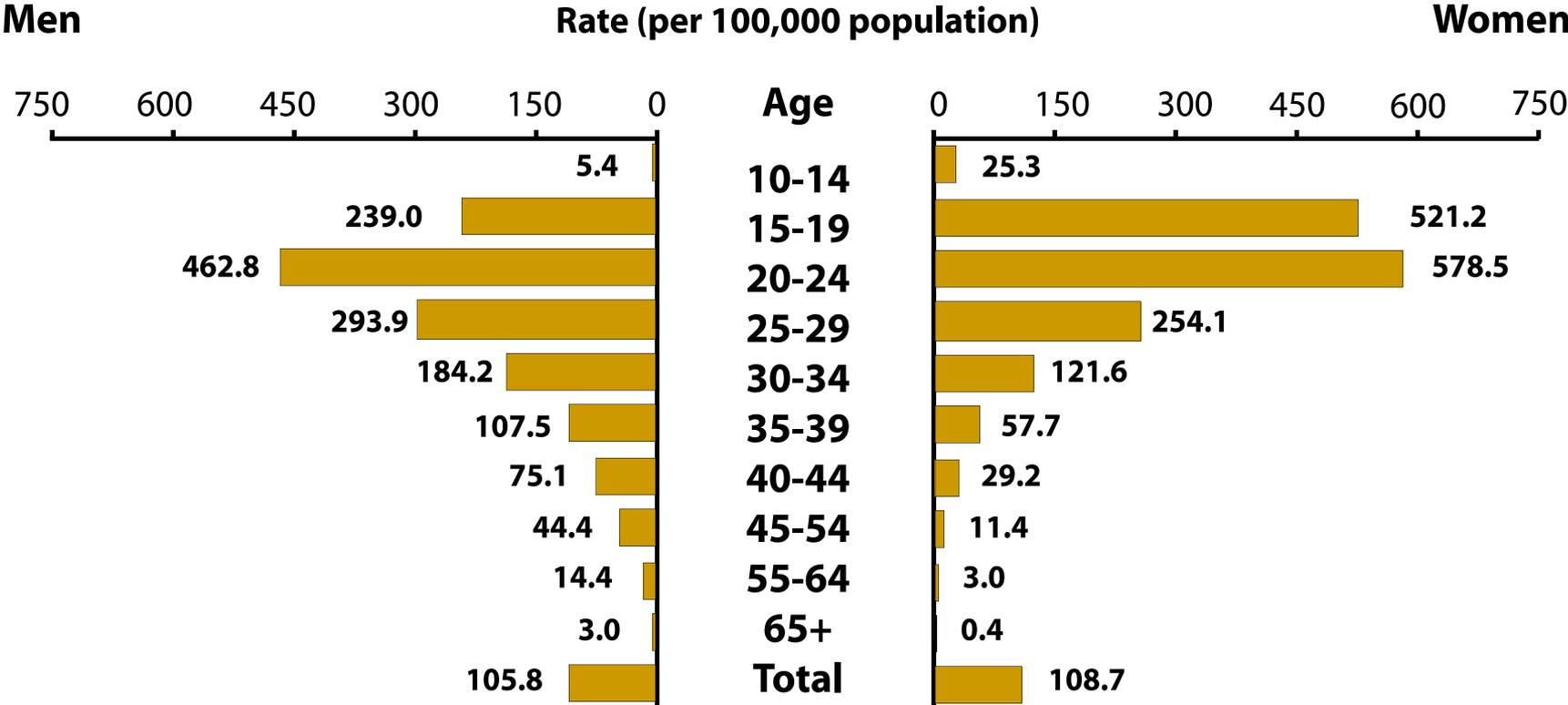
- Effectiveness of azi < doxy for rectal CT
- Doxy delayed release 200 mg d
 - Noninferior to generic doxy
 - Less gi side effect
- Concerns over amoxicillin use in pregnancy (CT persistence *in vitro*)
 - Alternative regimen

Gonorrhea—Rates, United States, 1941–2012

Rate (per 100,000 population)

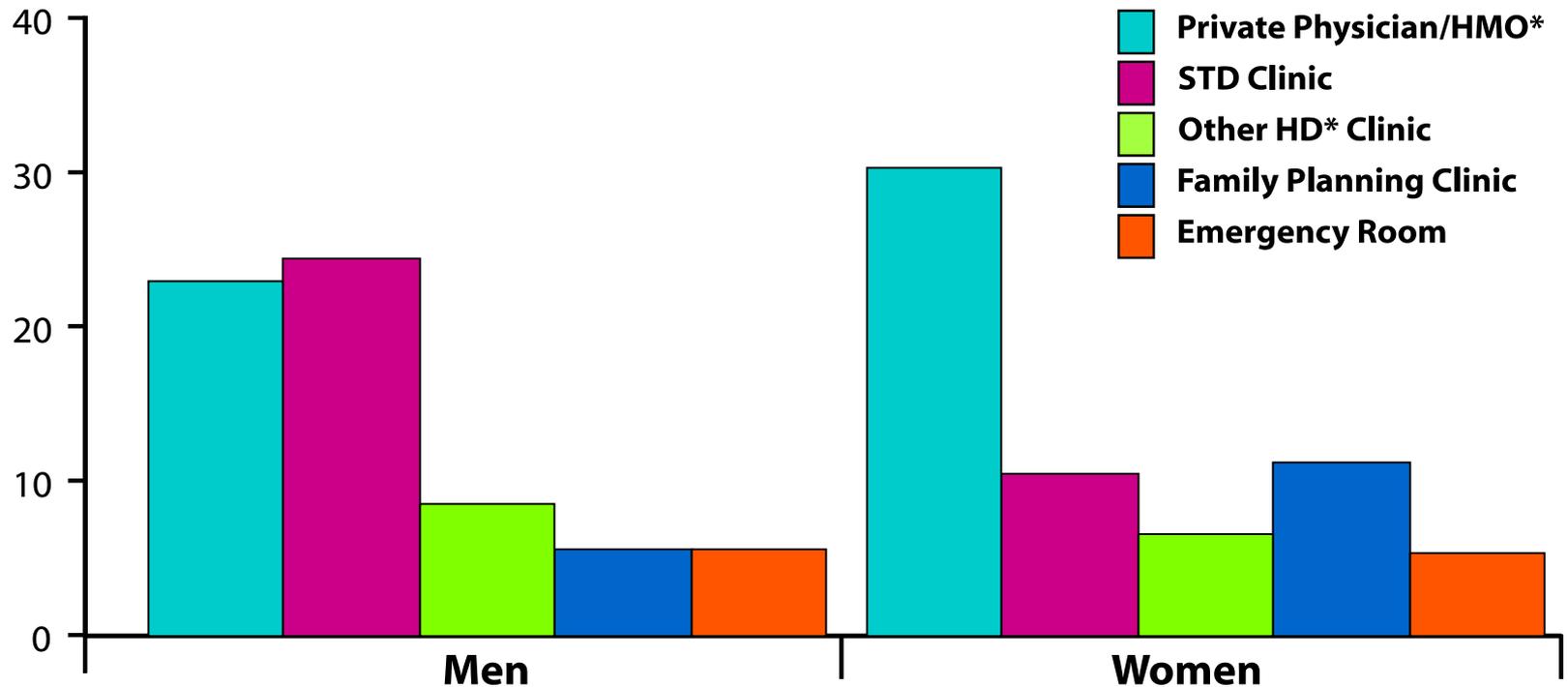


Gonorrhea—Rates by Age and Sex, United States, 2012



Gonorrhea—Percentage of Reported Cases by Sex and Selected Reporting Sources, United States, 2012

Percentage



*HMO=health maintenance organization; HD=health department

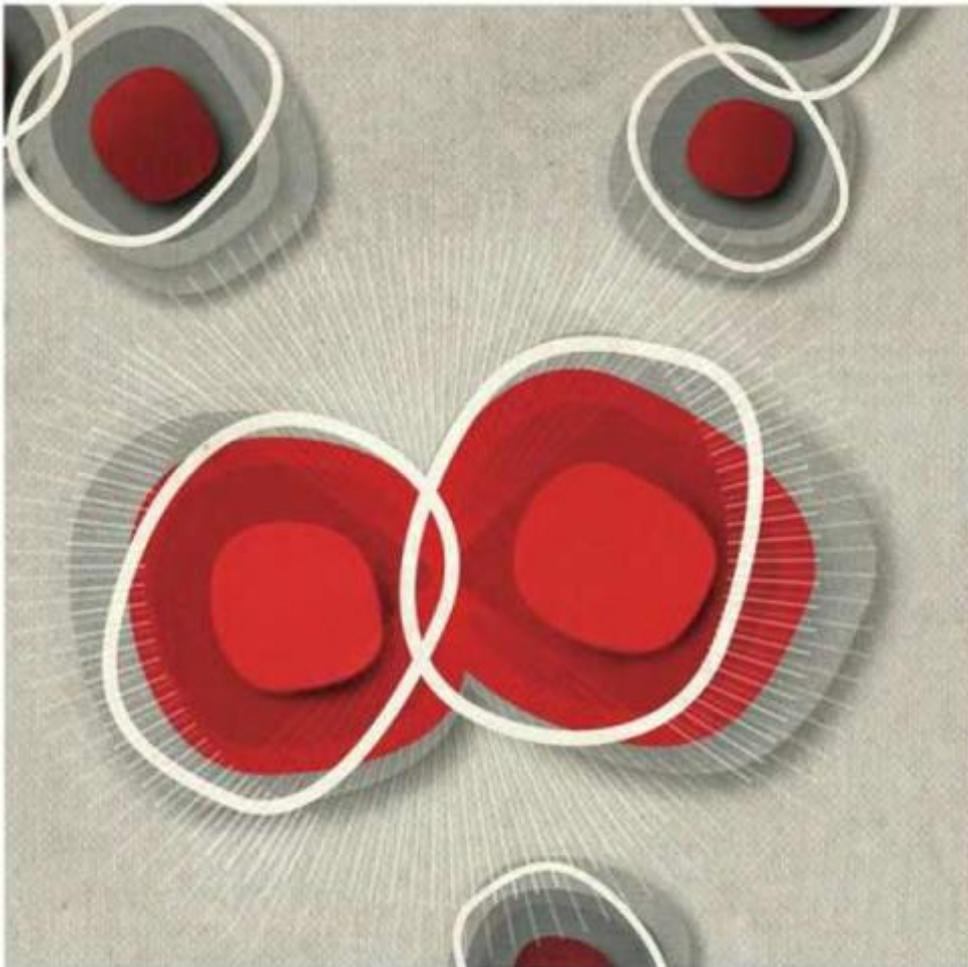
NOTE: Of all cases, 11.7% had a missing or unknown reporting source. Among cases with a known reporting source, the categories presented represent 66.2% of cases; 33.8% were reported from sources other than those shown.

MEDICAL DISPATCHES

SEX AND THE SUPERBUG

The rise of drug-resistant gonorrhea.

BY JEROME GROOPMAN



Gonorrhea mutates in the pharynx, making oral sex far more risky than people think.

*The New Yorker,
October 1, 2012*

“Whatever freedoms were won during the sexual revolution, bacterial evolution promises soon to constrain.”

Neisseria gonorrhoeae Antibiotic Resistance

❑ Antibiotic resistance

- Undermines treatment success
- Heightens risk of complications
- Facilitates transmission

❑ *Neisseria gonorrhoeae* (NG) has demonstrated ability to progressively develop antibiotic resistance

Sulfonamides

Penicillins

Tetracyclines

Fluoroquinolones

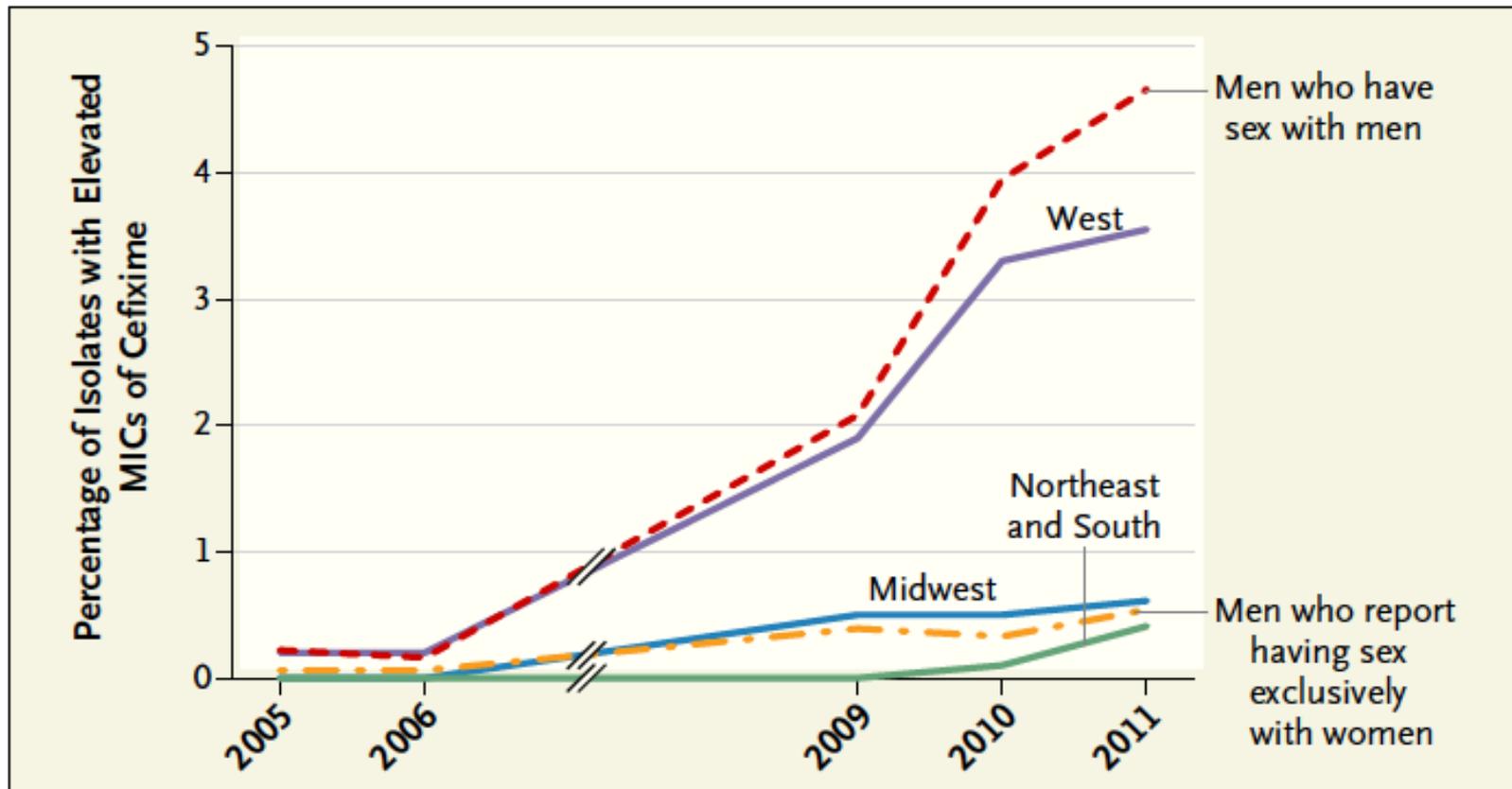
Resistance



The Gonococcal Isolate Surveillance Project (GISP)

- CDC-supported US sentinel surveillance since 1987
- Monitors trends in *N. gonorrhoeae* antibiotic susceptibility in men attending STD clinics
- Methods
 - Urethral isolates obtained from the first 25 men per site each month
 - Susceptibility testing conducted by 5 regional laboratories
 - Minimum inhibitory concentrations (MICs) by agar dilution
 - Confirmatory testing by CDC
 - Limited demographic & clinical data from participating men

N. gonorrhoeae: Isolates with Elevated MICs to Cefixime ($\geq 0.25 \mu\text{g/ml}$), 2005–2011*



Percentage of Isolates in Which Minimal Inhibitory Concentrations (MICs) of Cefixime Were $0.25 \mu\text{g}$ per Milliliter or Higher, 2005–2011.

Susceptibility to cefixime was not tested in 2007 or 2008. From the Gonococcal Isolate Surveillance Project.

Neisseria gonorrhoeae Antimicrobial Resistance Among Men Who Have Sex With Men and Men Who Have Sex Exclusively With Women: The Gonococcal Isolate Surveillance Project, 2005–2010

Robert D. Kirkcaldy, MD, MPH; Akbar Zaidi, PhD; Edward W. Hook III, MD; King H. Holmes, MD, PhD; Olusegun Soge, PhD; Carlos del Rio, MD; Geraldine Hall, PhD; John Papp, PhD; Gail Bolan, MD; and Hillard S. Weinstock, MD, MPH

Percentage of Isolates with Elevated MICs or Resistance by Sex of Sex Partner, 2005-2010

Antibiotic	MSM n=8,117	MSW n=26,483	p
Ceftriaxone*	0.4	0.1	<0.01
Cefixime**	1.7	0.2	<0.01
Azithromycin [†]	0.9	0.2	<0.01
Tetracycline [†]	37.5	13.3	<0.01
Ciprofloxacin [‡]	29.9	6.9	<0.01

* $\geq 0.125 \mu\text{g/ml}$

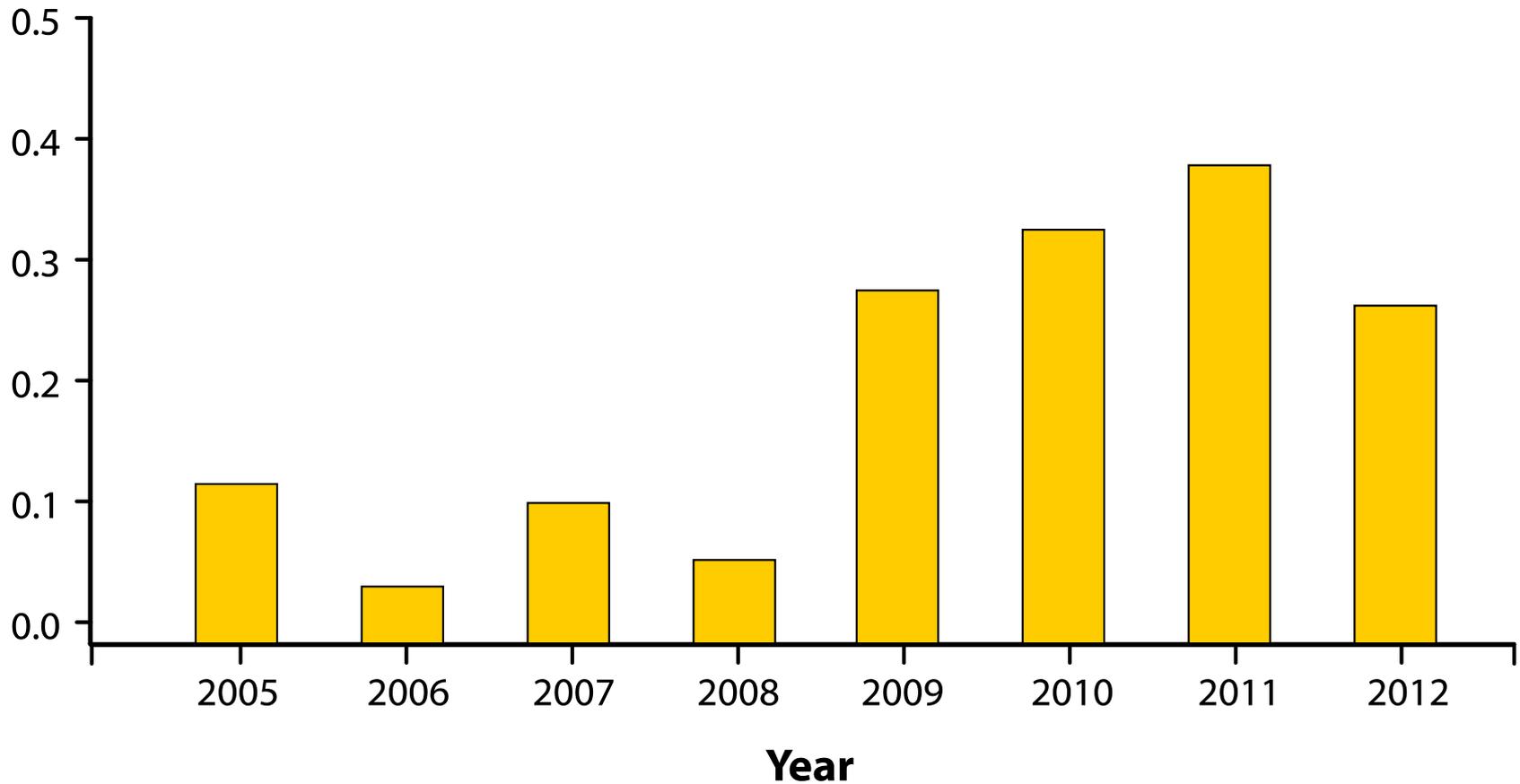
** $\geq 0.25 \mu\text{g/ml}$

† $\geq 2.0 \mu\text{g/ml}$

‡ $\geq 1.0 \mu\text{g/ml}$

Percentage of *Neisseria gonorrhoeae* Isolates with Elevated Ceftriaxone Minimum Inhibitory Concentrations (MICs) ($\geq 0.125 \mu\text{g/ml}$), Gonococcal Isolate Surveillance Project (GISP), 2005 – 2012

Percentage



CDC STD Treatment Guidelines

Uncomplicated Gonococcal Infections of Cervix, Urethra & Rectum

Ceftriaxone 250 mg as a single intramuscular dose

PLUS

**Azithromycin 1 g orally (preferred) or
Doxycycline 100 mg twice daily for 7 days**

New Treatment Options

- NIH sponsored multicenter randomized open-label non-comparative trial (Kirkaldy, ISSTDR 2013)
 - Gentamicin 240 mg IM + azithromycin 2 g PO, OR
 - Gemifloxacin 320 mg PO + azithromycin 2 g PO
- Rationale
 - Additive effect, gentamicin and azithromycin *in vitro*
 - Gemifloxacin more active against GC with known cipro resistance or mutations in GyrA and ParC regions (*in vitro*); possibly stronger inhibition by gemifloxacin of GyrA and ParC
- Primary endpt- culture at 10–17 days



	<u>Gentamicin / Azithromycin</u>		<u>Gemifloxacin / Azithromycin</u>	
	n/N	% (L 95% CI)	n/N	% (L 95% CI)
Urethra/Cervix	202/202	100% (98.5%)	198/199	99.5% (97.6%)
Pharynx	10/10	100%	15/15	100%
Rectum	1/1	100%	5/5	100%

New Agents, New Targets

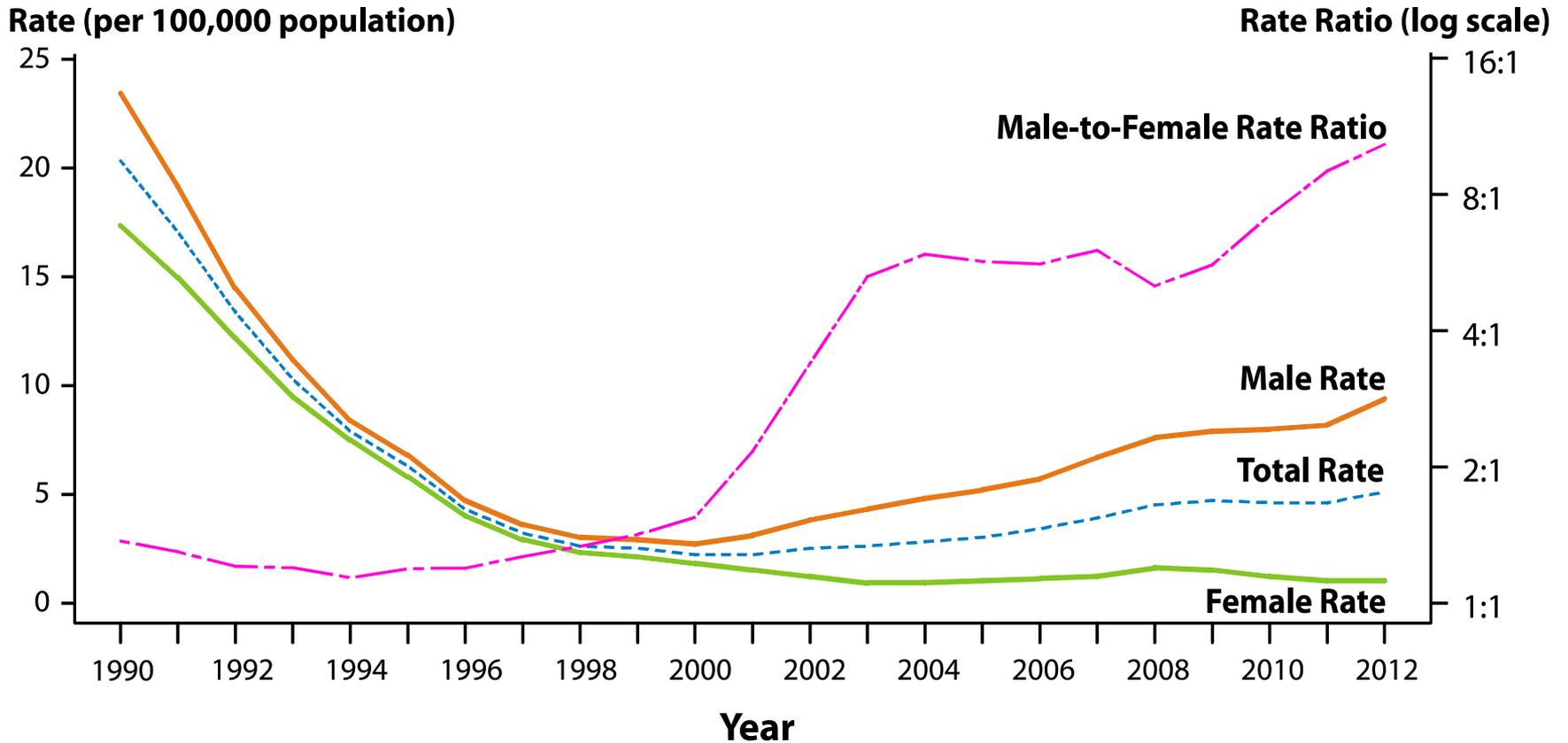
- Solithromycin single dose promising in phase 2, dose ranging study (Hook ISSTDR 2013); 100% clearance by culture at 7 days
- Novel agents
 - MUT056399: inhibitor of fatty acid biosynthesis enzyme
 - Pleuromutilins, bicyclolide, ketolides
 - Non-quinolone topoisomerase inhibitors
 - Host defense peptides (LL-37): direct and indirects antibacterial activity (Bucki, Arch Immunol 2010)
- New targets
 - Gonococcal lipid A: LpxC inhibitors (critical for synthesis)
 - Efflux pumps

Formidable Challenges

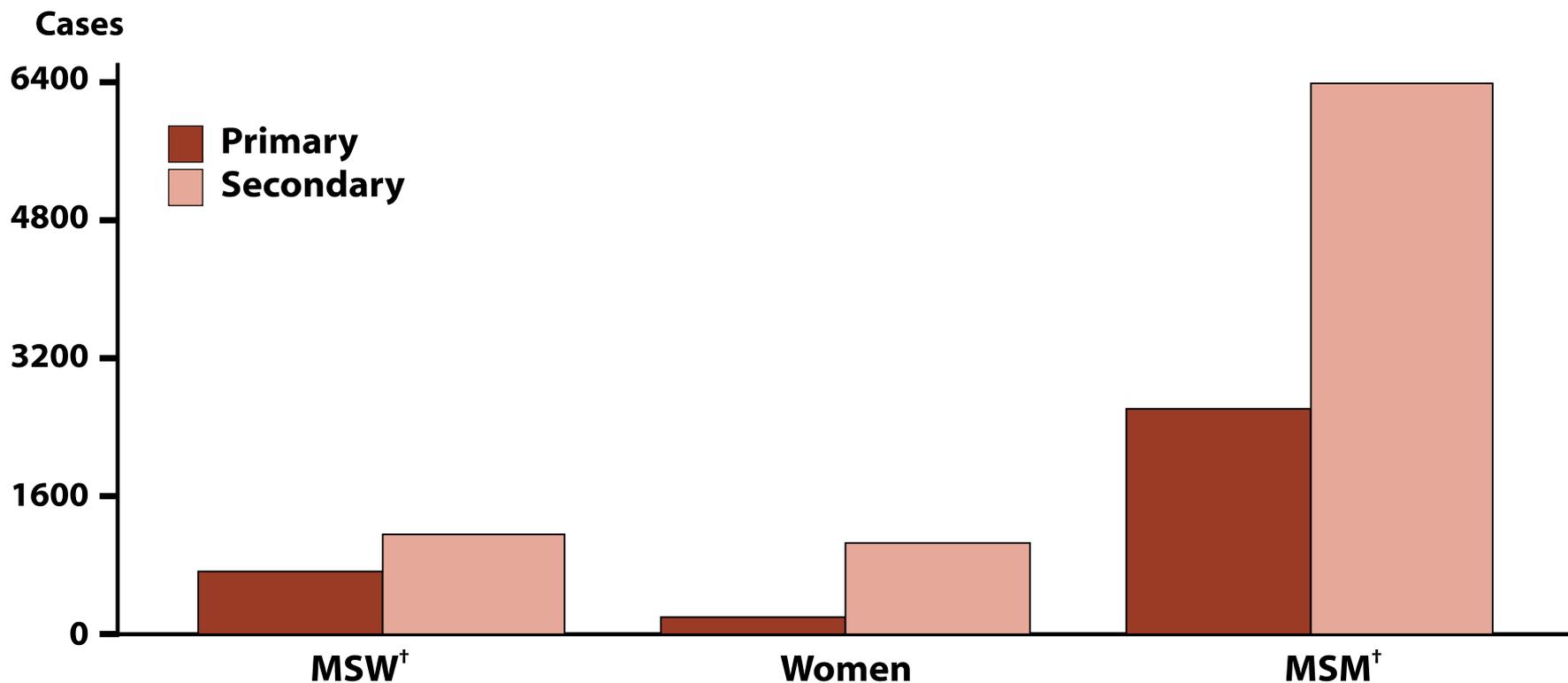
- Surveillance for antimicrobial resistance
 - GISP limitations and selectivity
 - Need to include non-urethral isolates?
 - No consensus on lab criteria for resistance
 - Declining culture & susceptibility capacity
 - Need to define molecular determinants of resistance; however, may not identify emerging mutations in real-time
- Combination of epidemiologic data & molecular typing likely required



Primary and Secondary Syphilis—Rates by Sex and Male-to-Female Rate Ratios, United States, 1990–2012



Primary and Secondary Syphilis—Reported Cases* by Stage, Sex, and Sexual Behavior, 2012

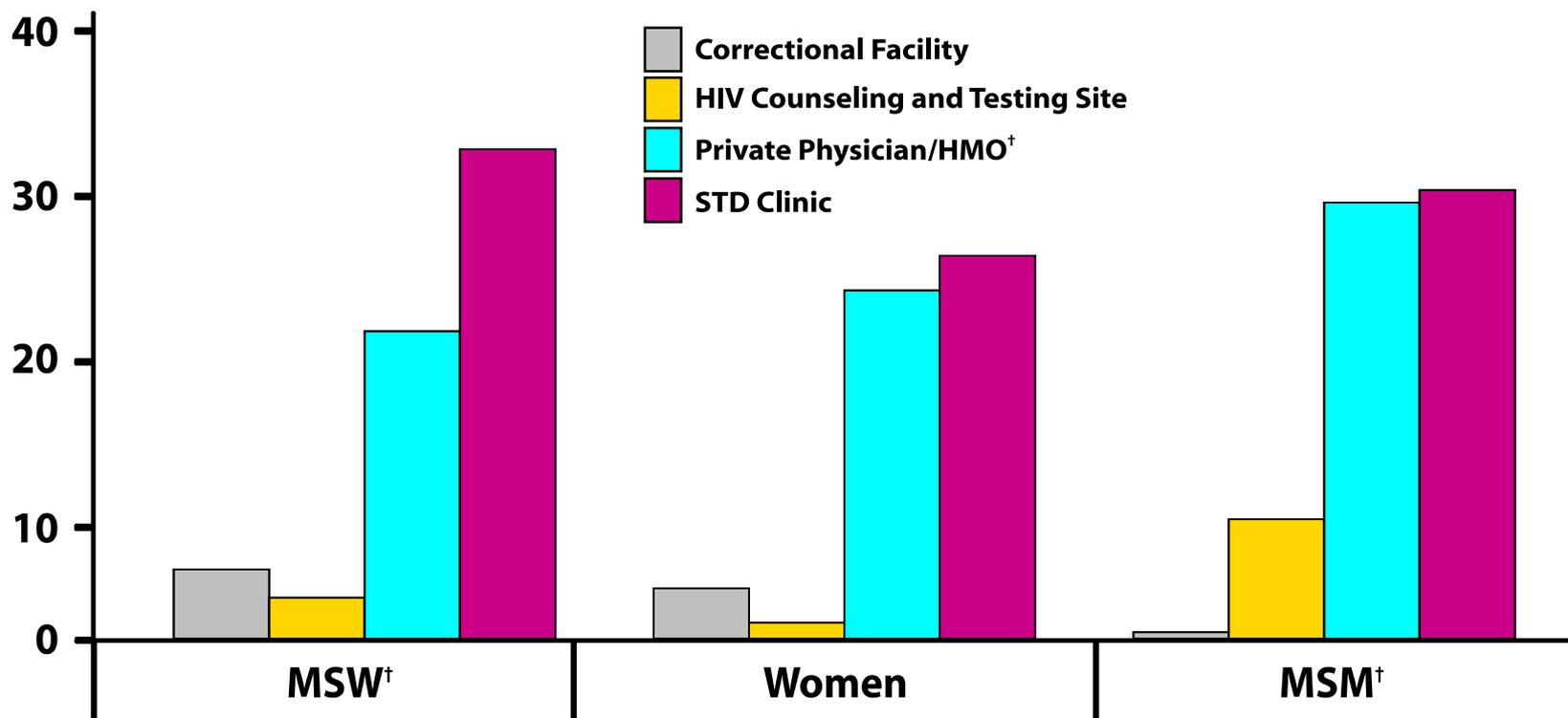


* Of the reported male cases of primary and secondary syphilis, 17.4% were missing sex of sex partner information.

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

Primary and Secondary Syphilis—Percentage of Reported Cases* by Sex, Sexual Behavior, and Selected Reporting Sources, 2012

Percentage, %



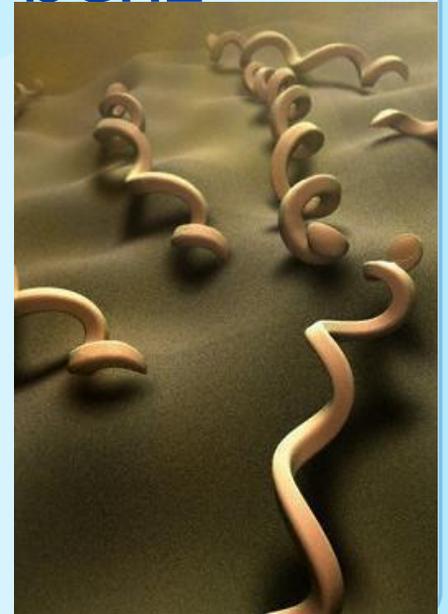
* Of the reported male cases of primary and secondary syphilis, 17.4% were missing sex of sex partner information, and 6.2% of reported male cases with sex of sex partner data were missing source of information data.

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

Syphilis

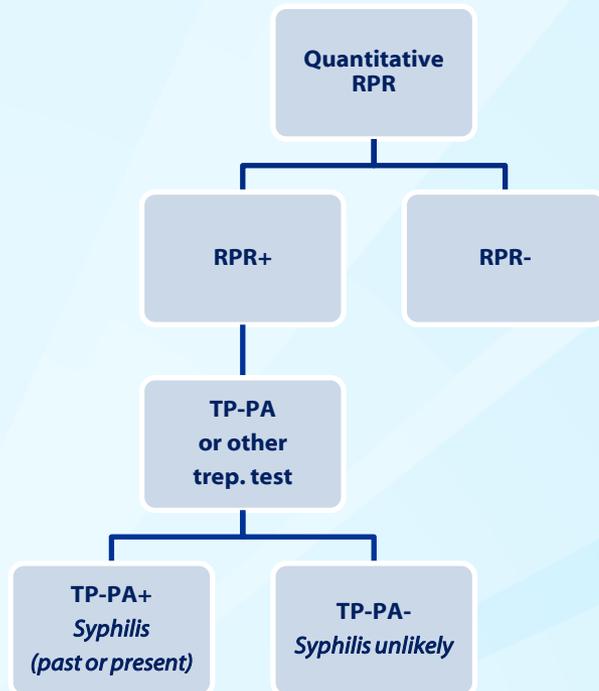
Emerging Issues

- Clarification of neurosyphilis definition
 - VDRL +signs/symptoms
- Pharmacologic interval between benz
pcn doses (7-9 days)
- Serological response to tx
 - Stage and titer (Sena 2011)
- Reverse screening algorithm

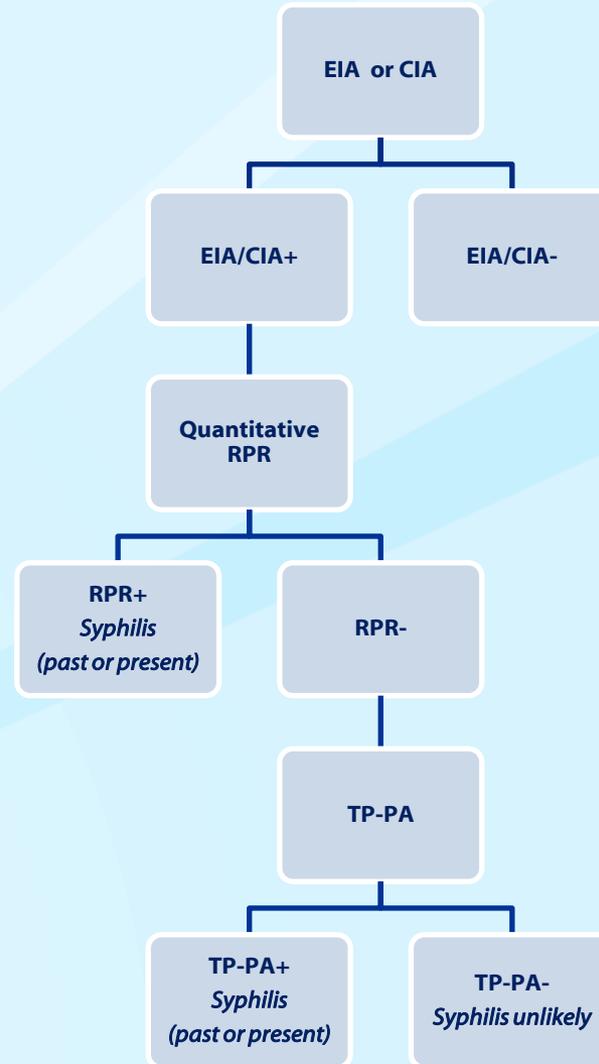


Syphilis serologic screening algorithms

Traditional



Reverse sequence

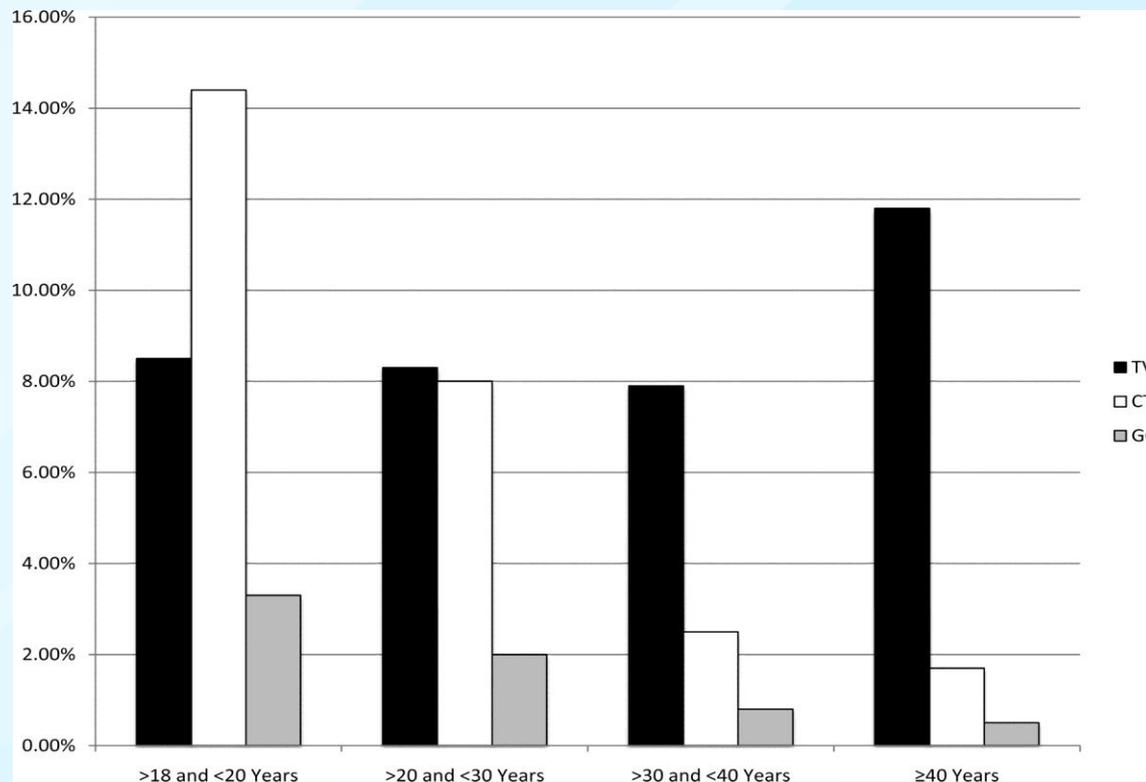


**Discordant Results from Reverse Sequence Syphilis Screening —
 Five Laboratories, United States, 2006–2010**

Population	Test	Total N	Reactive EIA/CIA		Nonreactive RPR		Nonreactive confirmatory treponemal test*	
			n	% total	n	% EIA/CIA+	n	% RPR–
Overall	Various	140,176	4,834	3.4	2,743	56.7	866	31.6
Low prevalence (Kaiser x 3)	<i>Trep-Chek, LIAISON, Trep-Sure</i>	127,402	2,984	2.3	1,807	60.6	737	40.8
High prevalence (New York, Chicago)	Trep-Chek Trep-Sure	12,774	1,850	14.5	936	50.6	129	14.1

Trichomoniasis: disparities by age

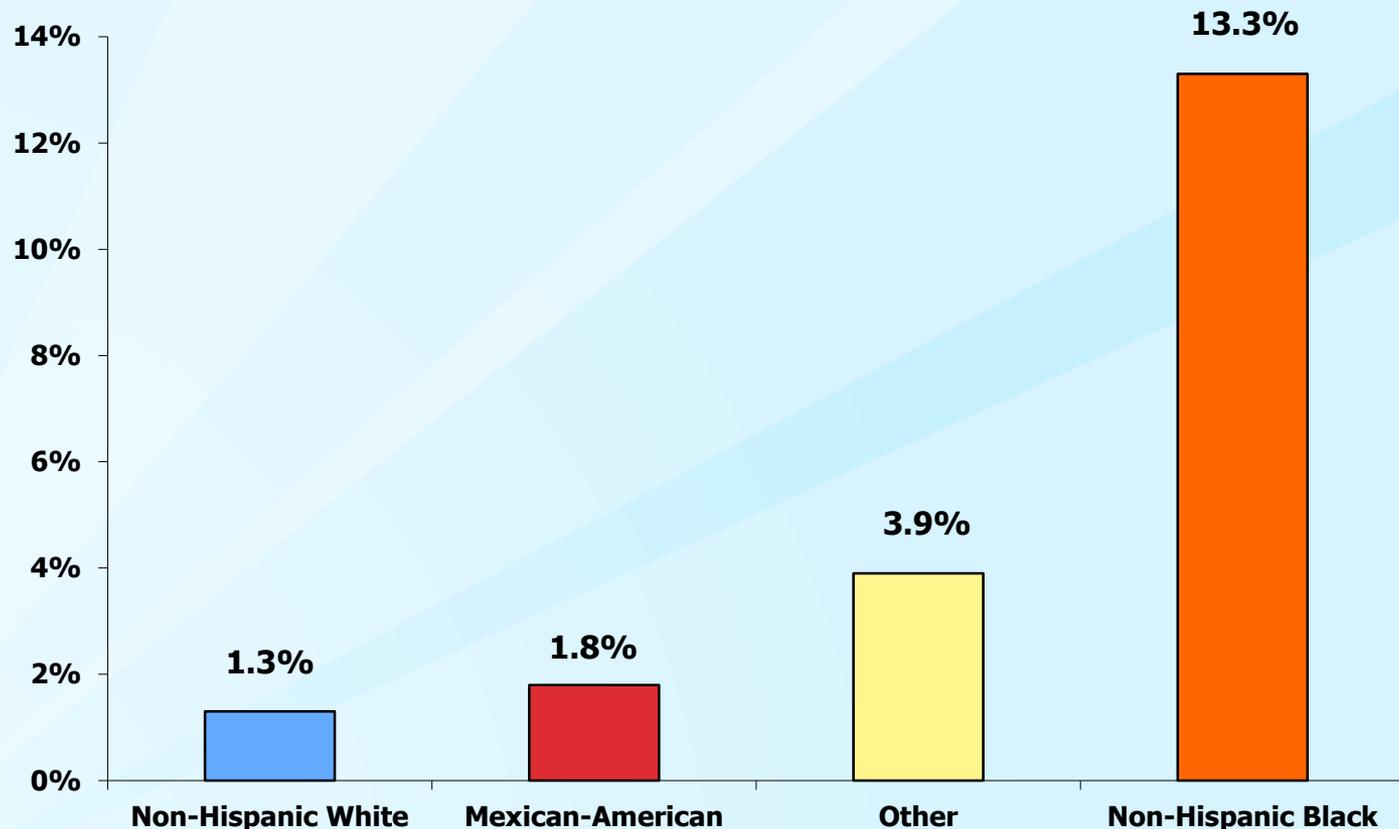
NAAT prevalence of TV, CT, and GC infections among 7593 U.S. women age 18–89, by age group (Ginocchio, 2012)



Changes to 2010 guidance: while feasible to test specimens collected for GC/CT screening, TV should not be overlooked in older adults

Epidemiology: disparities by race/ethnicity

Prevalence of TV infection among women age 14–49 years, by self-reported race — NHANES, 2001–2004 (Sutton, 2007)



Trichomoniasis

- Screening in high risk women
 - HIV+, incarcerated, STD clinic
- Rescreening at 3 mo
- Prevalence increases with age
- FDA cleared NAATs
 - Aptima
 - BD Probe Tec TV Qx

U.S. STD Clinics: A Surveillance System & Safety Net at Risk?

Jersey City's Free STD Clinic Closures Are Postponed for Now

By Matt Hunger • May 26th, 2011 • Category: [Blog](#), [News](#), [Politics](#)



STD programs not sexy enough to avoid funding cuts

Posted by [The Pump Handle](#) on August 22, 2011

(9) Like 0 Tweet 1 +1 0 More »

By Kim Krisberg

Public health director Kerran Vigroux sounds almost matter-of-fact when she talks about having to shut down her department's screening services for sexually transmitted diseases. As she talks about the prevention and education opportunities that packed up and left along with the testing services, there's that familiar, barely audible public health tone to her voice — the one that says "this makes no sense at all."

Sunday, July 24, 2011

STD/HIV clinic closure leaves questions

By ALBERT McKEON
Staff Writer

Print 0 Comments Share

Recommend 26 Tweet 2 +1 0

NASHUA — Health officials hope the closure of the city's STD/HIV clinical services doesn't have severe consequences for people who have contracted or are at risk of acquiring a sexual disease.

City STD Clinics to Close Mondays to Cut Costs Amid Meningitis Outbreak



By Jeff Mays on April 16, 2013 10:03am | Updated on April 16, 2013 10:03am

@JeffCMays

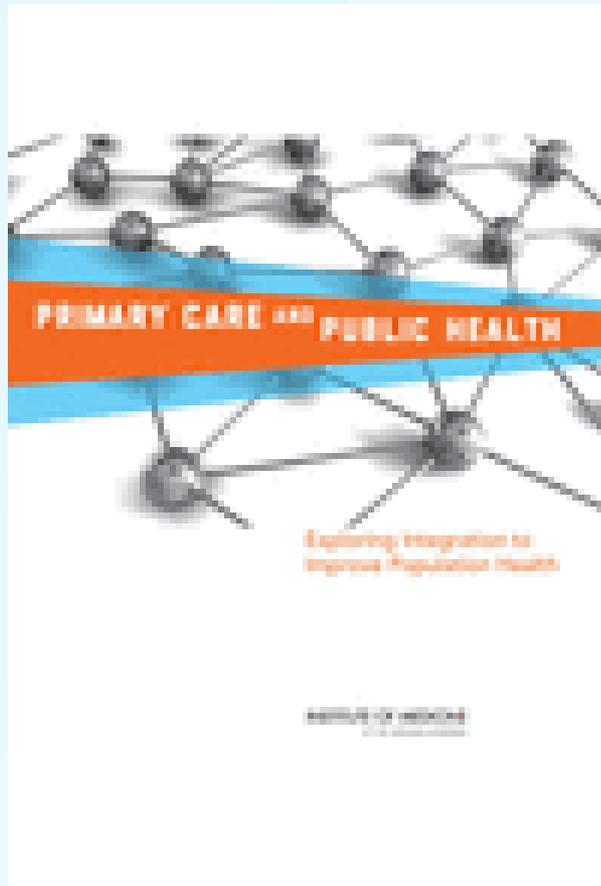
HARLEM — Four city clinics that treat sexually transmitted diseases are cutting hours on

busiest days —
New York struggles to control a deadly meningitis outbreak that has killed seven people in 2010.

proposal the New
Department of



Integration of Primary Care and Public Health: STD as a case study



- Clinical preventative services through population health approach
- High impact services that protect the community (STD, TB, immunization)
- Screening/timely treatment core prevention strategy (asx)
- Most reported cases (CT, GC syphilis) from private sector
- Workforce capacity
 - Primary care
 - Public health

Prevention Guidance

- Education/counseling to reduce risk of STI acquisition
- Detection of asymptomatic infection
- Effective diagnosis and treatment
- Evaluation, treatment, counseling of sexual partners
- Pre-exposure vaccination-hepatitis A, B, HPV



STD Treatment Guidelines Meeting

CDC Atlanta | April 30–May 2, 2013

