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Objectives

- Discuss current trends of STDs and why STD testing is important to patient health.
- Discuss changes in the CDC STD Treatment Guidelines and why the changes were made.
- Explain how these changes will affect the clinical management of STDs and their associated syndromes.

Thanks

- Gail Bolen
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- Christie Mettenbrink
- Mel Mattson

Why Diagnose and Treat STDs?

- > 19 million STDs in US annually
- Health consequences of untreated STDs
  - Women's reproductive health
    - Untreated Chlamydia (CT) or gonorrhea (GC) may lead to pelvic inflammatory disease (PID)
    - Leading infectious cause of infertility in the U.S.
  - Infant mortality/morbidity
    - Neonatal HIV, herpes simplex virus (HSV) and congenital syphilis
  - HIV transmission
- Health care cost
  - $16.4 billion (2009)†

†Estimates incorporate minor corrections noted in Persp Sex Rep Hlth, Dec 2009.

“Life in Lubbock, Texas taught me … that sex is the most awful, filthy thing on earth, and you should save it for someone you love.”

- Butch Hancock

Populations at Greatest Risk for STDs

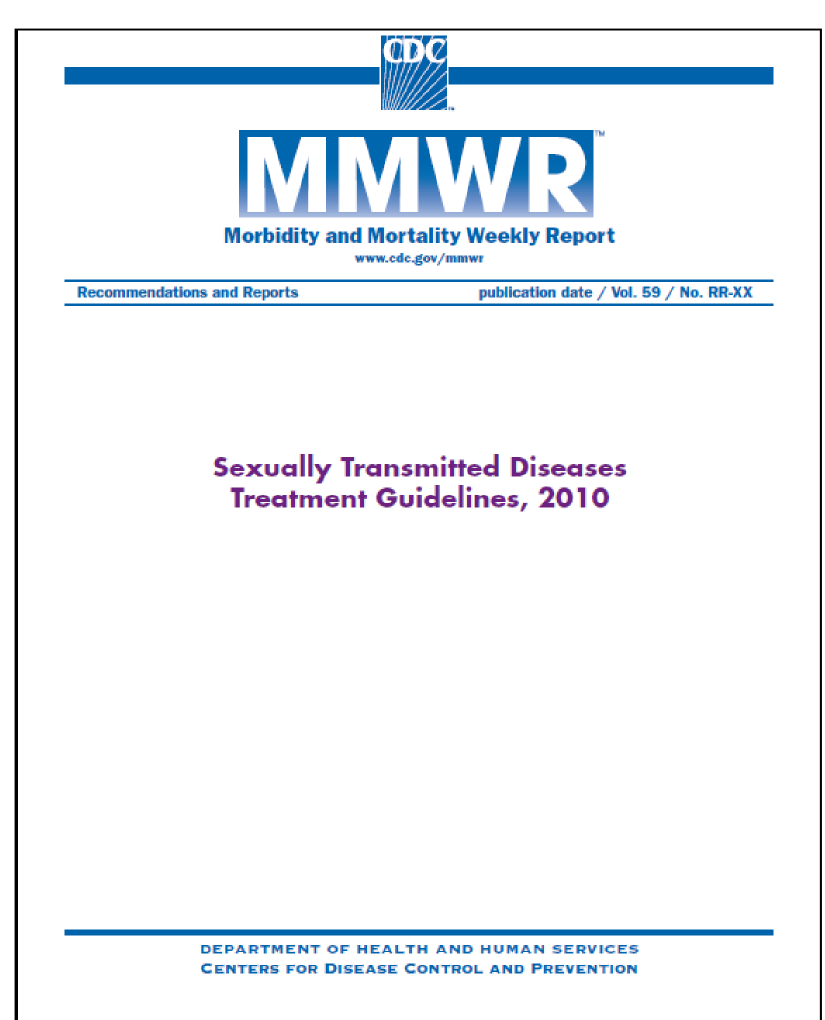
- Youth
  - Nearly 50% of STDs estimated to occur in 15-24 year olds
- Racial/ethnic minorities
  - STDs among highest of all racial/ethnic health disparities
  - African-Americans: 71% of GC, 48% CT, 52% syphilis
  - Over last 5 years syphilis cases increased more than 150% among young African American men
- MSM
  - Account for 62% of syphilis cases in 2009
  - High rates of HIV co-infection

STD Prevention: Clinicians' Role

- Talk to patients about pre-exposure vaccination
- Provide or refer for prevention/risk-reduction counseling
- Talk to patients about testing
- Assess patients' risk and test accordingly
- Diagnose and treat infected patients
- Provide or refer for partner services
- Report STD/HIV and AIDS cases in accordance with state and local statutory requirements
- Keep STD/HIV reports confidential

2010 STD Guidelines

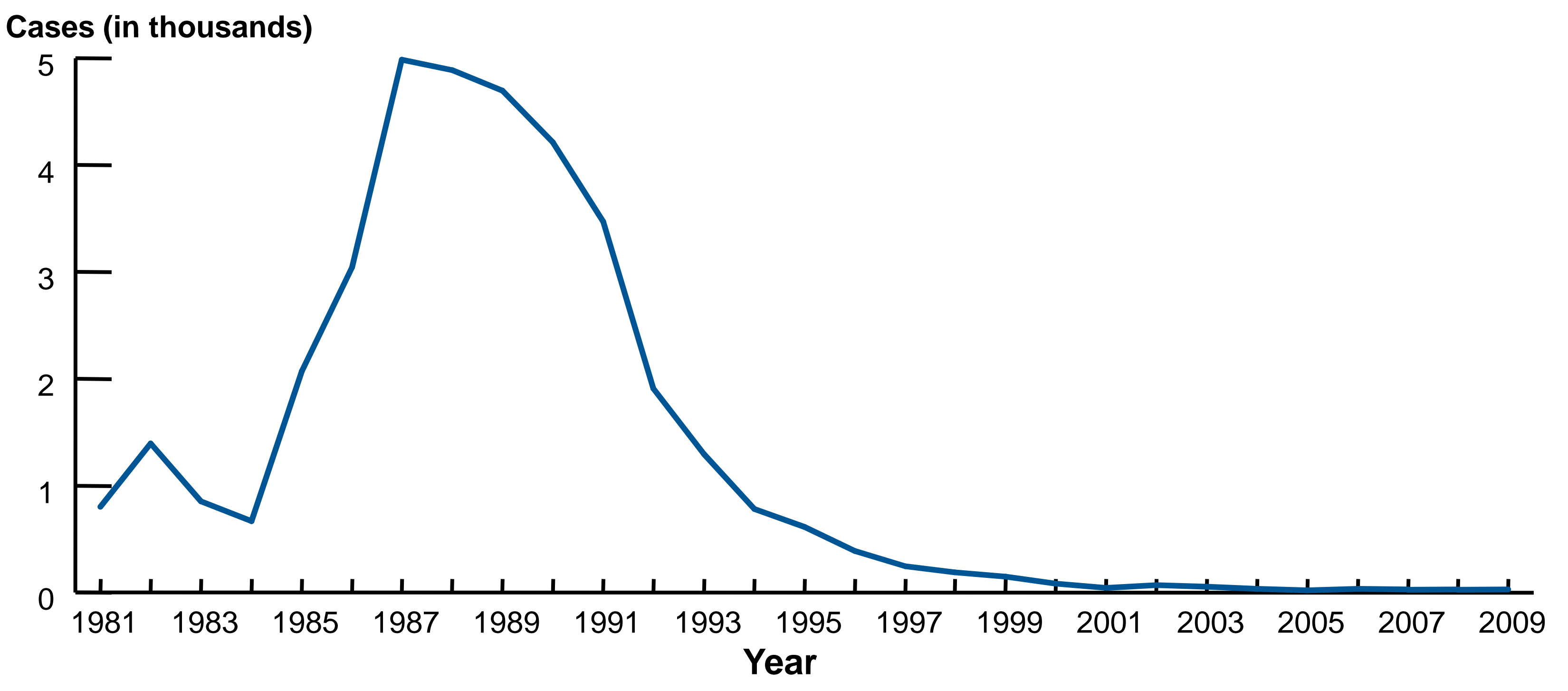
- Authoritative source for STD management
- Diagnostic evaluation, treatment regimens, prevention, and vaccination strategies
- Order hard copies www.cdc.gov/std
- Wall charts, pocket guides


CDC
MMWR
Morbidity and Mortality Weekly Report
www.cdc.gov/mmwr
Recommendations and Reports
publication date / Vol. 59 / No. RR-XX
Sexually Transmitted Diseases
Treatment Guidelines, 2010
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

STD Syndromes

Genital Ulcer Disease	Urethritis/ Cervicitis	Vaginal Discharge
Syphilis (*T. pallidum)* **Genital Herpes** (Herpes simplex virus) **Chancroid** (*H. ducreyi)* **Donovanosis** (*C. granulomatosis)* **LGV** (*C. trachomatis)*	**Gonorrhea** (*N. gonorrhoeae*) **NGU/MPC** (*C. trachomatis, U. urealyticum, M. genitalium*)	**Trichomoniasis** **Bacterial vaginosis** **Vulvovaginal candidiasis**
STD Complications	**Human papillomvirus**	**Ectoparasites**
PID / Epididymitis Proctitis / procto-colitis	Genital Warts	Pediculosis Pubis Scabies

Chancroid—Reported Cases, United States, 1981–2009



Consult expert in STD/ID

Rare

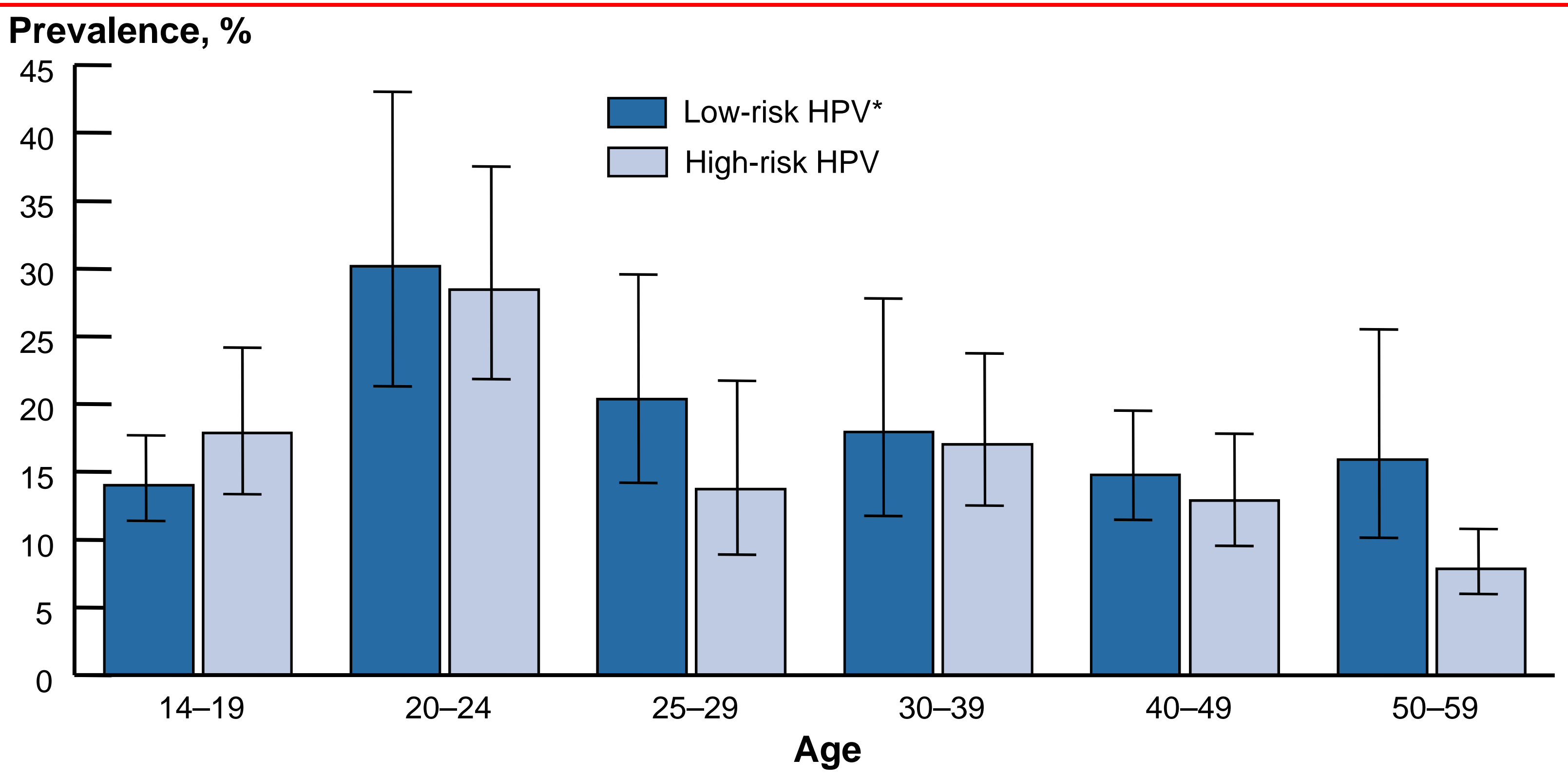
- Chancroid
- LGV
- Donovanosis

May require intervention

- Acute HIV
- Syphilis
- Complicated STDs

Or anytime you have a question

Human Papillomavirus—Prevalence of High-risk and Low-risk Types Among Females Aged 14–59 Years, National Health and Nutrition Examination Survey, 2003–2004



* HPV = human papillomavirus.

NOTE: Error bars indicate 95% confidence intervals. Both high-risk and low-risk HPV types were detected in some females.

SOURCE: Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, et al. Prevalence of HPV infection among females in the United States. JAMA. 2007;297(8):813-9.

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HPV

- New treatment for genital warts:
  - 15% sinecatechins (Veregen)
- More detailed information on:
  - HPV vaccine
  - HPV-associated cancers
  - ACS screening guidelines
  - HPV test indications
- Discussion of use/value of anal Pap in HIV+ MSM

Pelvic Inflammatory Disease—Hospitalizations of Women Aged 15–44 Years, United States, 1998–2007

Hospitalizations (in thousands)

75
60
45
30
15
0

1998 1999 2000 2001 2002 2003 2004 2005 2006 2007

Year

Acute, Unspecified
Chronic

NOTE: The relative standard errors for these estimates of acute unspecified pelvic inflammatory disease (PID) cases are 11.9%–17.2%. The relative standard errors for these estimates of chronic PID cases are 11%–18%. Data only available through 2007.

SOURCE: 2007 National Hospital Discharge Survey [Internet]. Atlanta: Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/nchs/nhds/about/nhds.htm.

Syndromes Associated with STDs- Pelvic Inflammatory Disease Issues

- Quinolones not recommended
  - If cephalosporin or parental treatment is not possible, if NAAT positive then consider quinolone plus azithromycin 2 gm +/- metronidazole
- No oral cephalosporins are recommended
- Azithromycin 2 gm q week x 2 weeks plus ceftriaxone 250 mg IM with short term success mentioned

Syndromes Associated with STDs-Pelvic Inflammatory Disease Issues

- No change in criteria for diagnosis or hospitalization
- Recommendation regarding when to use metronidazole is still unclear
  - Not for parental treatment
  - With or without for outpatient treatment
  - Assess for BV and if present use
    - If no wet mount available, use metronidazole

Syndromes Associated with STDs

- Cervicitis:
  - Research is needed on the etiology of persistent cervicitis including role of *M genitalium*
- NGU:
  - *M genitalium* is emerging as an important etiology but testing for M genitalium is not recommended
  - Doxycycline is less effective than azithromycin in treating *M genitalium*
  - Moxifloxacin for persistent NGU

Syndromes Associated with STDs

- Epididymitis:
  - Ceftriaxone 250 mg + Doxycyline 100 mg PO for 10 days
  - Ceftriaxone and a quinolone if risk for both sexually transmitted and enteric organisms
    - e.g. MSM with insertive anal intercourse
  - Return in 48 hrs if fail to improve

- Proctitis:
  - Ceftriaxone 250 mg IM plus Doxycycline 100 mg po BID x 7 days
  - If rectal CT positive in MSM then doxycycline for 3 weeks if HIV infected or evidence of > 10 WBCs/HPF on anorectal smear for presumptive LGV

Vaginitis: Trichomoniasis

- Screening is recommended in HIV-infected women and may be considered in women at high risk
  - New or multiple partners, Hx of STD, inconsistent condom use, exchange of sex for payment, IDU
- New diagnostic recommendations and issues
  - If trich is suspected and microscopy is negative or if low risk and Pap suggests trich, confirm with culture or NAAT
- Retesting at 3 month should be considered for women

Trichomoniasis Treatment

Recommended regimen:

- Metronidazole 2 g PO x 1
- **Tinidazole 2 g po x 1**

Recommended regimen in HIV infected women:

- Metronidazole 500 mg PO BID x 7d

Alternative regimen:

- Metronidazole 500 mg PO BID x 7d

Recommended regimen in pregnancy:

- Metronidazole 2 g PO x 1

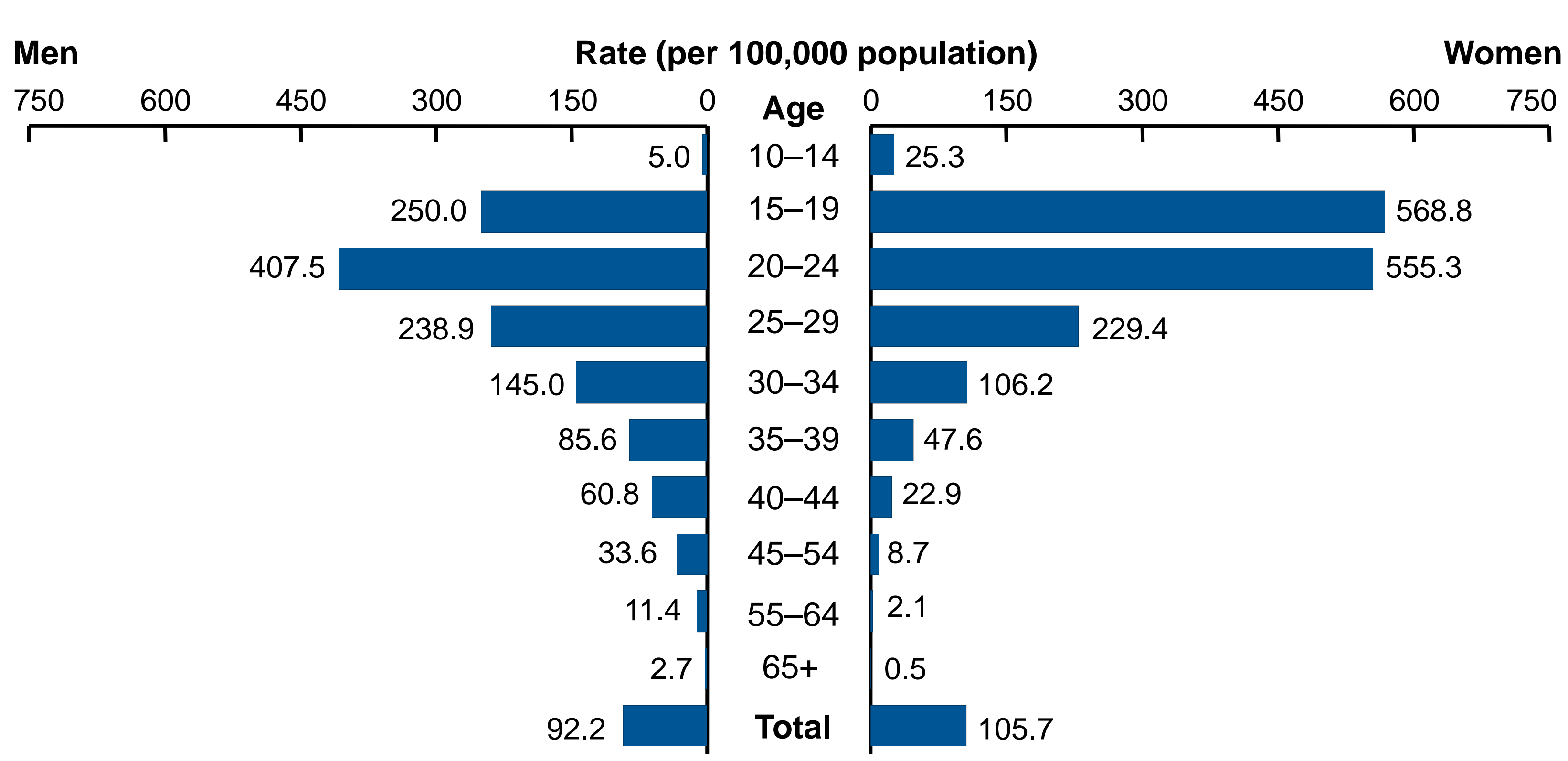
Urethritis

- Bacterial STDs: GC (5-20%), CT (15-40%)
- Nongonoccocal urethritis (NGU)
  - *Mycoplasma genitalium* 5-25%
  - *Ureaplasma* 0-20%; data inconsistent, biovars differ
  - *Trichomonas vaginalis* 5-20% (age, geography)
  - HSV 15-30%; urethritis in primary infection
  - Adenovirus, enterics, Candida, anaerobes

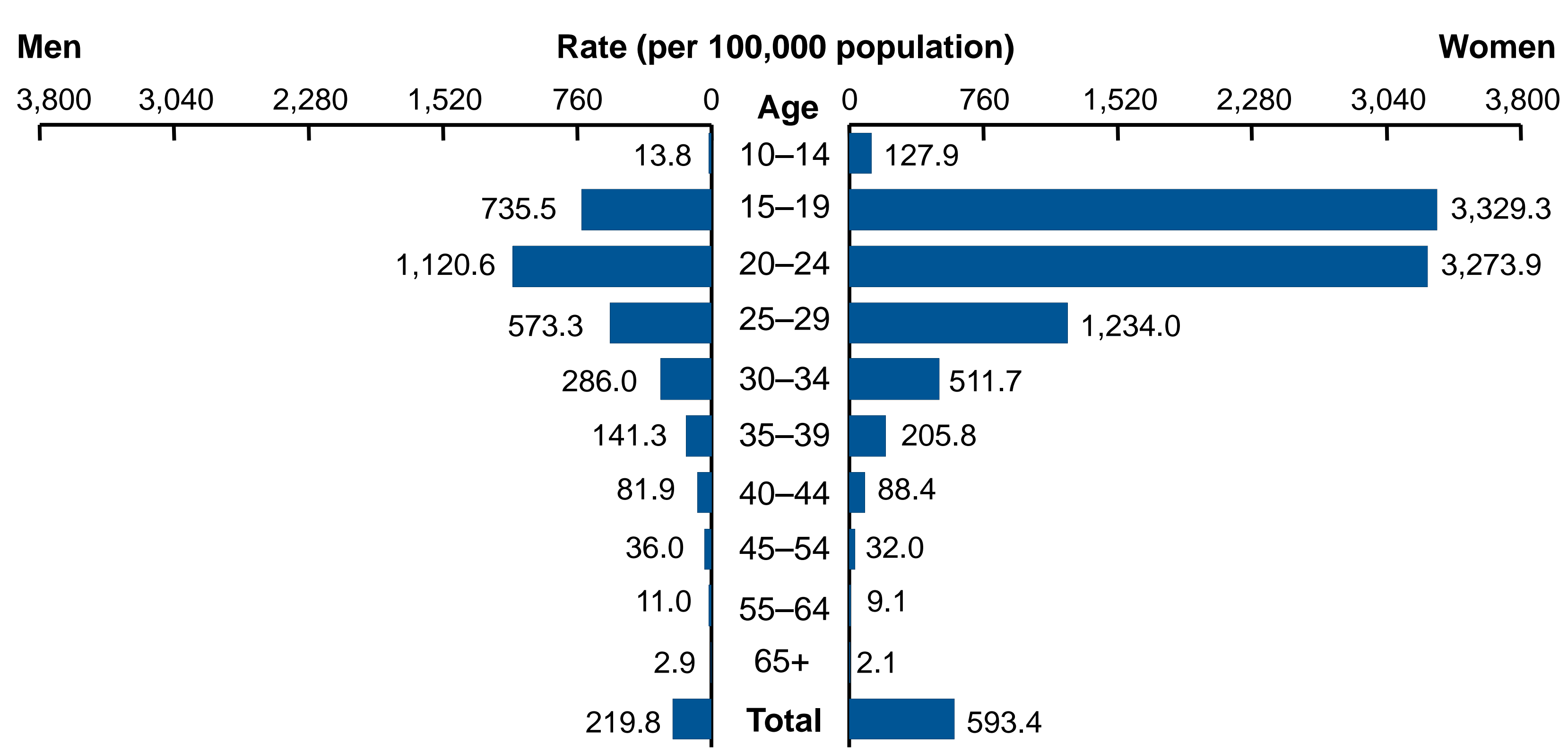
Mycoplasma genitalium

- New info:
  - Association with disease: urethritis, endometritis/PID
  - Association with adverse reproductive health outcomes unclear
  - No current FDA-cleared test
- Treatment
  - Azithromycin 1 g ~ 82% effective
  - Doxycycline ineffective < 40%
  - Moxifloxacin effective in small studies of treatment failure

Gonorrhea—Rates by Age and Sex, United States, 2009



Chlamydia—Rates by Age and Sex, United States, 2009



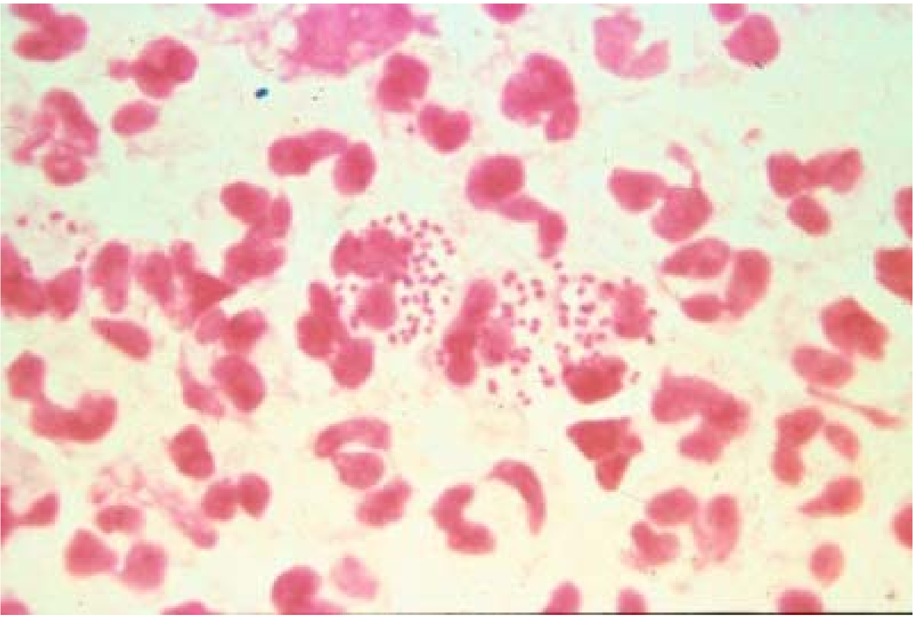
Biology of CT and GC

Chlamydia

- Slow growth
- Obligate intracellular organism
- Biphasic with sporelike form

Gonorrhea

- Rapid growth
  - Multiple generations *per* hour
- Facultative intracellular organism
- Doesn't tolerate drying



Clinical Manifestations of Chlamydia and Gonorrhea

- *Men*: CT and GC both can cause urethritis, epididymitis, proctitis, conjunctivitis, pharyngitis (rare – asymptomatic carriage more common)

- *Women*: CT and GC both can cause cervicitis, urethritis, PID, proctitis, conjunctivitis, pharyngitis (rare – asymptomatic carriage more common)

- CT: men >50%, women >85% asymptomatic
- GC can disseminate (skin lesions, arthritis)
- *Infants*: GC: conjunctivitis; CT: conjunctivitis, pneumonia

Diagnostic Tests for Chlamydia

- Culture
  - Only test that requires viability
  - Used for research but not clinical care
- Antigen – based (less sensitive):
  - EIA or Fluorescent
- DNA – based (more sensitive):
  - Hybridization
  - NAAT: Nucleic Acid Amplification Tests

CT Screening Recommendations

- Annual screening of all sexually active women $\leq$ 25 y.o. and $>$ 25 if risk factors (new or multiple partners)
- Selective male screening (adolescent clinics, corrections, national job training program, $<$ 30 yrs, STD, military)

Chlamydia trachomatis

Azithromycin 1 gm po as a single dose

or

Doxycycline 100 mg po bid x 7d

No change in 2010 Guidelines

Chlamydia trachomatis

Alternative regimens

Erythromycin base 500 mg po qid x 7 days

or

Erythromycin ethylsuccinate 800 mg po qid x 7 days

or

Ofloxacin 300 mg po bid x 7 days

or

Levofloxacin 500 mg po qd x 7 days

Chlamydia trachomatis
Treatment in Pregnancy

Recommended regimens

Azithromycin 1 gm po as a single dose

or

Amoxicillin 500 mg po tid x 7 days

Resistance of *C. trachomatis* to Antimicrobial Agents

- No convincing change in MICs to tetracyclines, macrolides over past 25 years, in contrast to GC
- Treatment failure is most likely due to non-compliance or re-infection
- Test-of-cure not advised routinely, though may consider with pregnancy, atypical treatments
- Rescreen in 3 months both men and women – risk of re-infection, even if patient thinks all sex partners treated

Diagnostic Testing for *N. gonorrhoeae*

- Gram stain & Culture
- DNA probe:
  - Hybridization
  - NAAT (best DNA based tests)
- Non-culture testing doesn't permit susceptibility testing but same sample can be tested for *C. trachomatis*
- NAAT in non – genital sites (pharynx, rectum) is not FDA approved but some labs have validated such testing and samples from those sites can be tested by those labs

GC Screening Recommendations

- Routine screening for GC in all sexually active women at risk for infection:
  - < 25 years
  - Previous GC or other STDs
  - Commercial sex work
  - New or multiple partners
  - Inconsistent condom use
  - Drug use
- Women aged < 25 years are at highest risk.

Neisseria gonorrhoeae

Cervix, Urethra, Rectum

Ceftriaxone 250 mg IM x 1

Or, if not an option:

Cefixime 400 mg po x 1

(2010 Guidelines increased dosage of ceftriaxone from 125 mg to 250 mg)

PLUS Chlamydial therapy if infection not ruled out

N. gonorrhoeae: Cervix, Urethra, Rectum

Alternative regimens

Single dose 3rd generation cephalosporin IM
(ceftizoxime 500 mg, cefotaxime 500 mg)

or

Cefpodoxime 400 mg po x 1

(addition to 2010 Guidelines)

or

Cefuroxime axetil 1 gm po x 1

or

PLUS Chlamydial therapy if infection not ruled out

Neisseria Gonorrhoeae Treatment in Pregnancy

- Azythromycin 2 gr orally can be considered for women who cannot tolerate a cephalosporin
- Either Azithromycin or Amoxicillin is recommended for presumptive or diagnosed CT during pregnancy.

Neisseria gonorrhoeae

Pharynx

Ceftriaxone 250 mg IM in a single dose

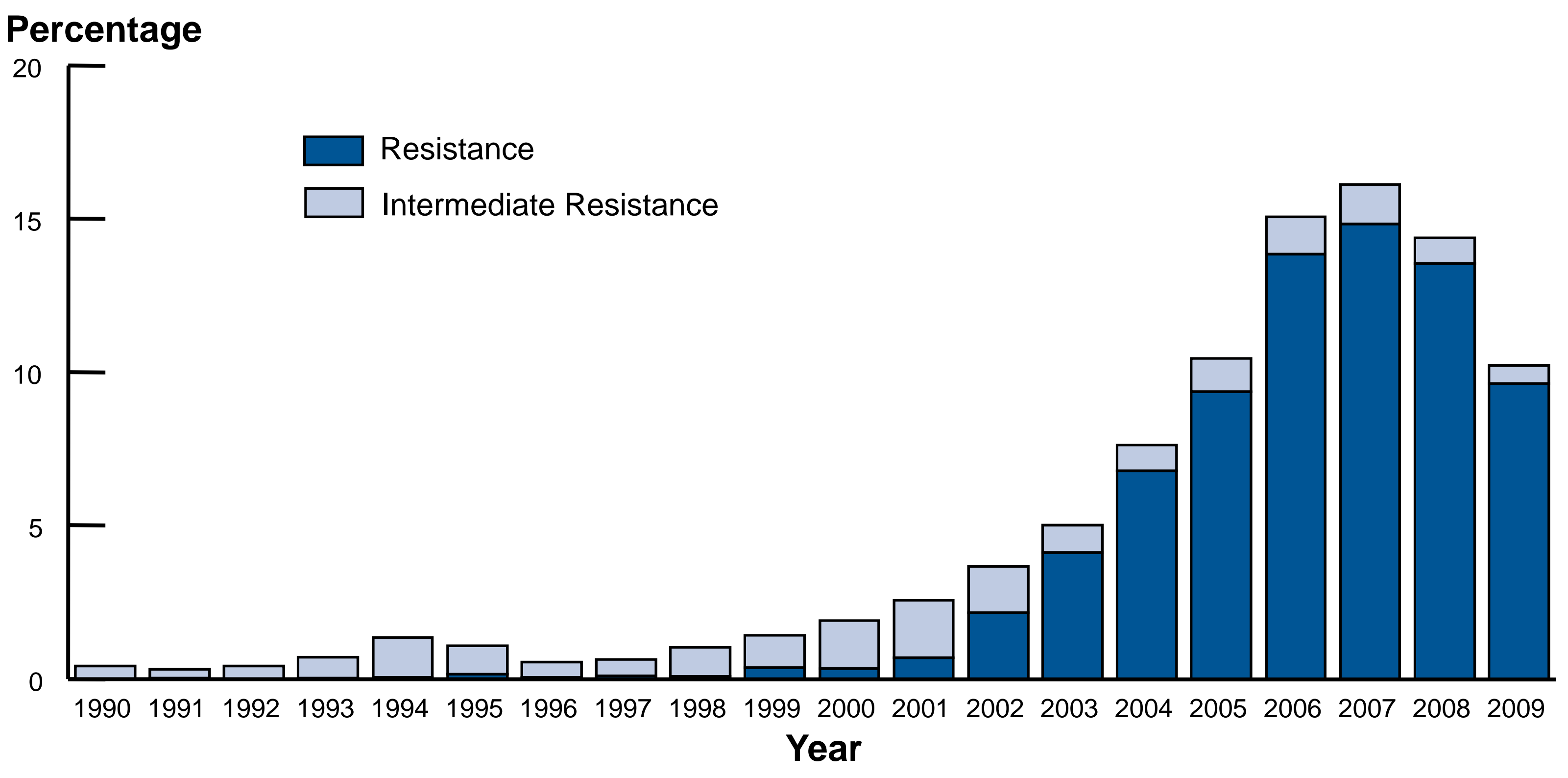
(2010 Guidelines increased dosage from 125 mg to 250 mg)

PLUS Chlamydial therapy if infection not ruled out

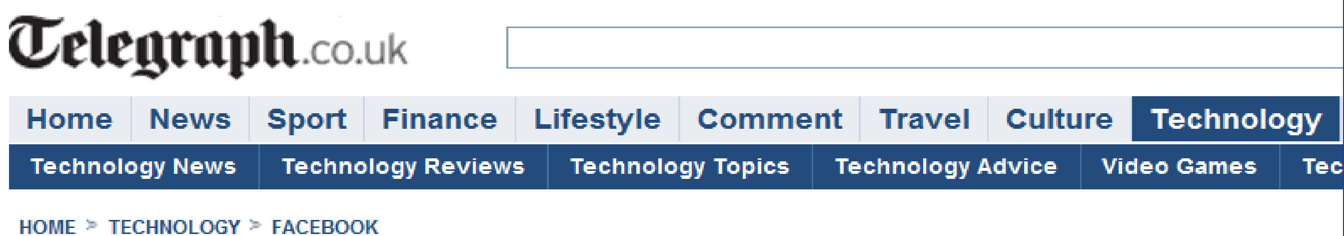
Resistance of *N. gonorrhoeae* to Antimicrobial Agents

- Overall 20% of GC isolates resistant to penicillin, tetracycline, or both
- Increasing resistance to quinolones
  - As of 4/13/07 quinolones no longer recommended for tx of GC in the U.S.
- Increasing resistance to azithromycin
- All isolates susceptible to ceftriaxone
  - Resistance in cefixime and cefpodoxime is rare but beginning to be seen

Gonococcal Isolate Surveillance Project (GISP)—Percentage of *Neisseria gonorrhoeae* Isolates with Resistance or Intermediate Resistance to Ciprofloxacin, 1990–2009



NOTE: Resistant isolates have ciprofloxacin minimum inhibitory concentrations (MICs) >1 µg/ml. Isolates with intermediate resistance have ciprofloxacin MICs of 0.125–0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.



Facebook 'linked to rise in syphilis'

Facebook has contributed to a resurgence in the sexually-transmitted disease syphilis, a health expert has claimed.

Published: 6:30AM GMT 24 Mar 2010

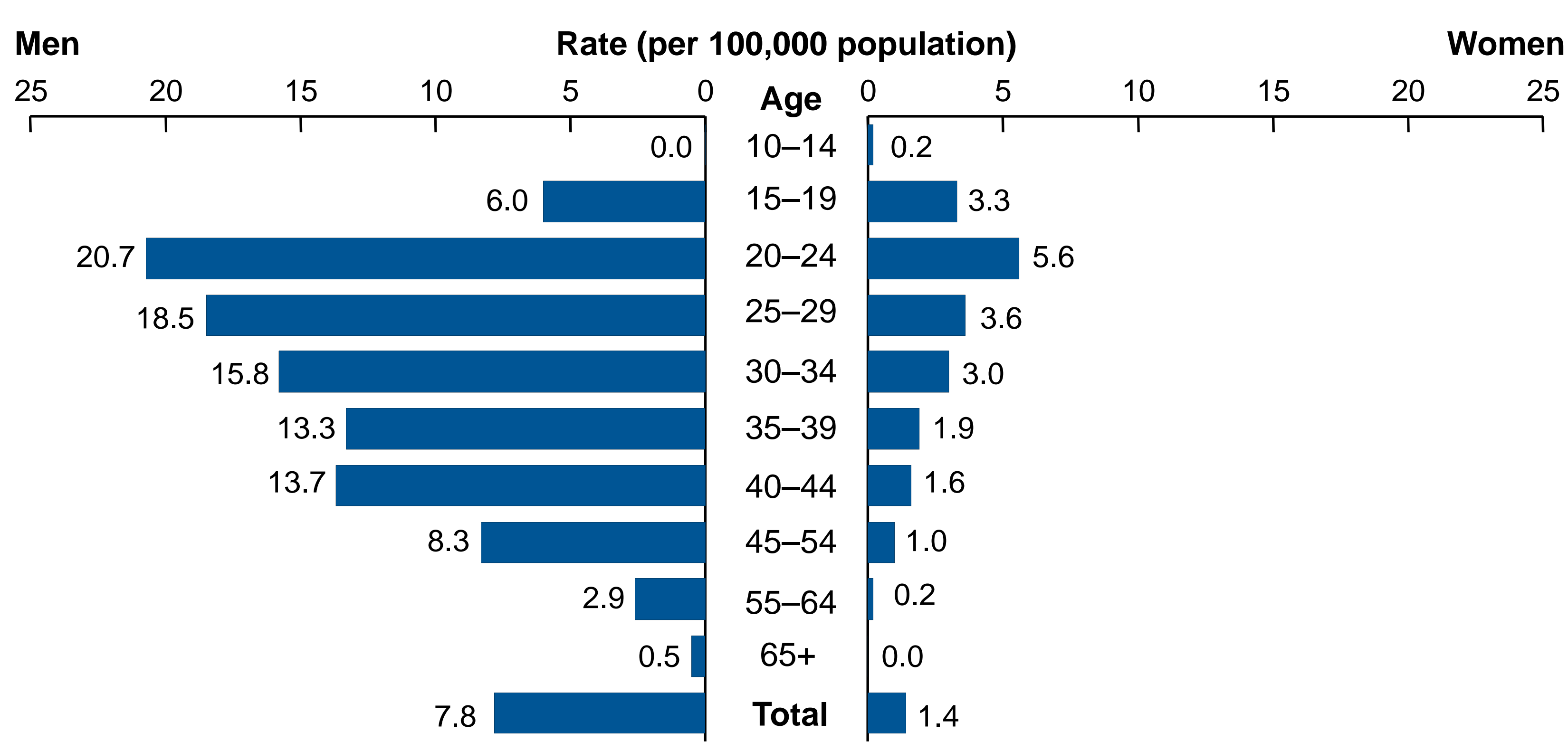
39 Comments

Facebook has been linked to a resurgence in the sexually-transmitted disease syphilis, according to health experts. Photo: BLOOMBERG

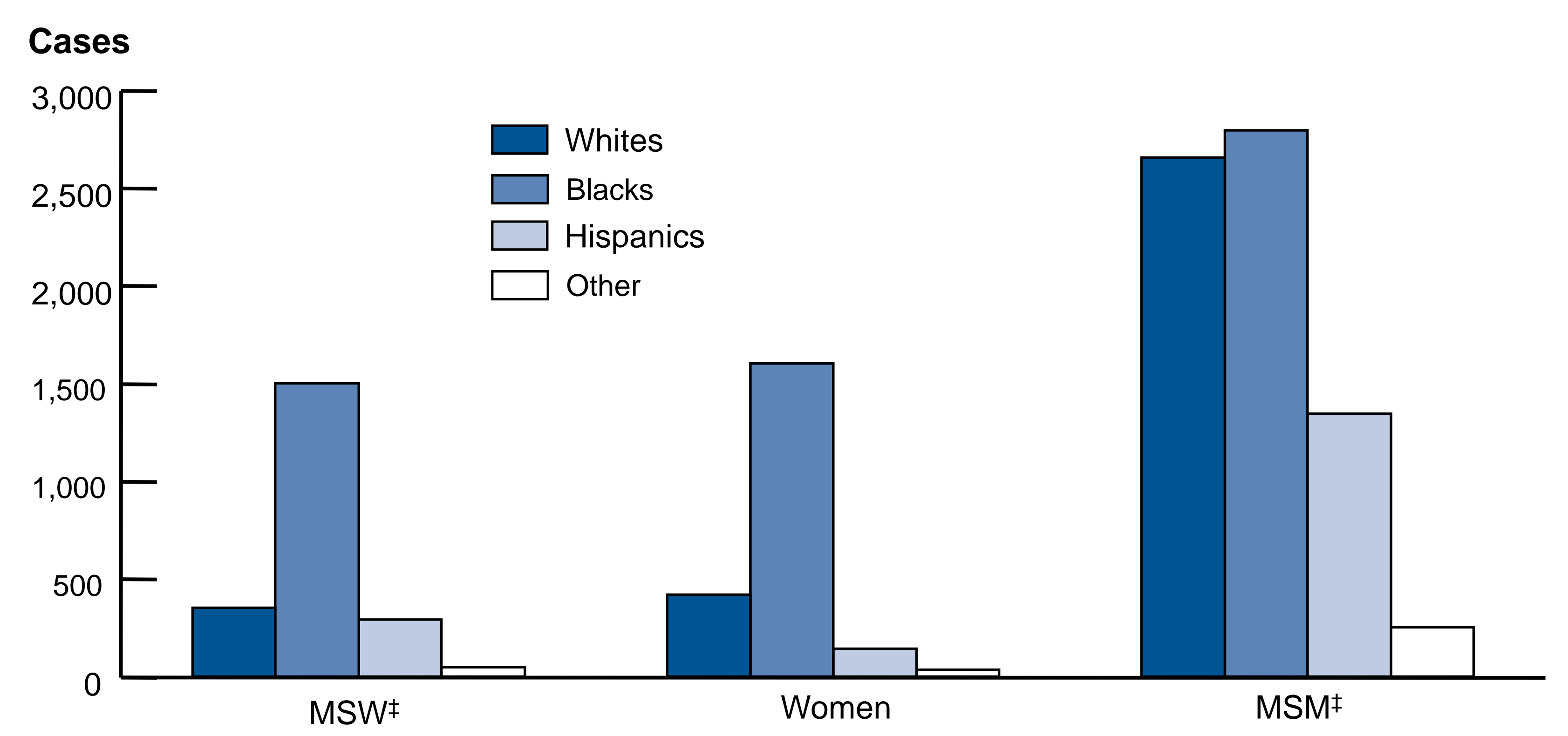
Case have increased fourfold in Sunderland, Durham and Teesside, the areas of Britain where Facebook is most popular.

Professor Peter Kelly, director of public health in Teesside, claimed staff had found a link between social networking sites and the spread of the bacteria, especially among young women.

Primary and Secondary Syphilis—Rates by Age and Sex, United States, 2009



Primary and Secondary Syphilis—Reported Cases* by Sex, Sexual Behavior, and Race/Ethnicity,† United States, 2009

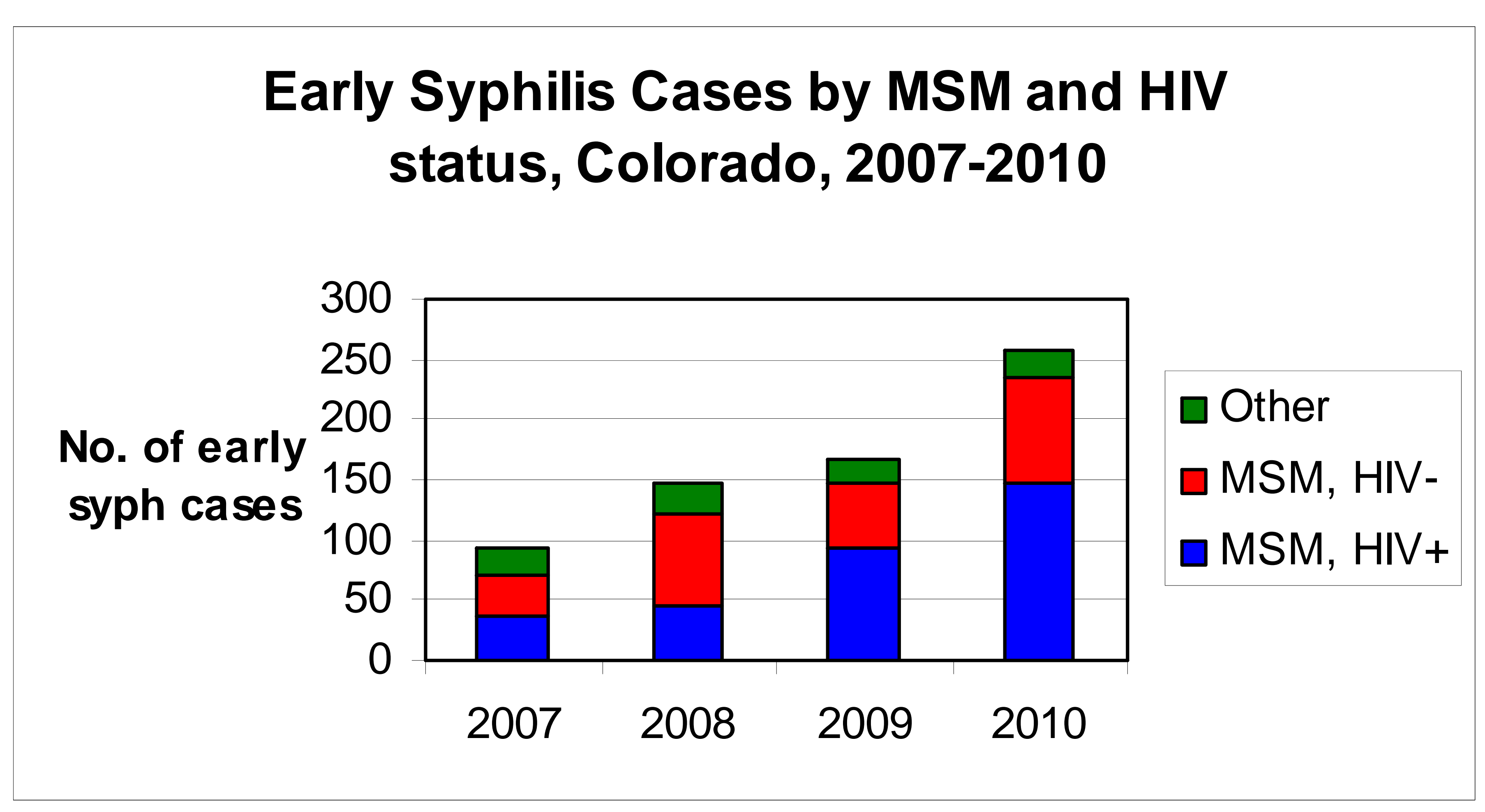


* Of the reported male cases of primary and secondary syphilis, 20% were missing sex of sex partner information; 1.7% of reported male cases with sex of sex partner data were missing race/ethnicity data.

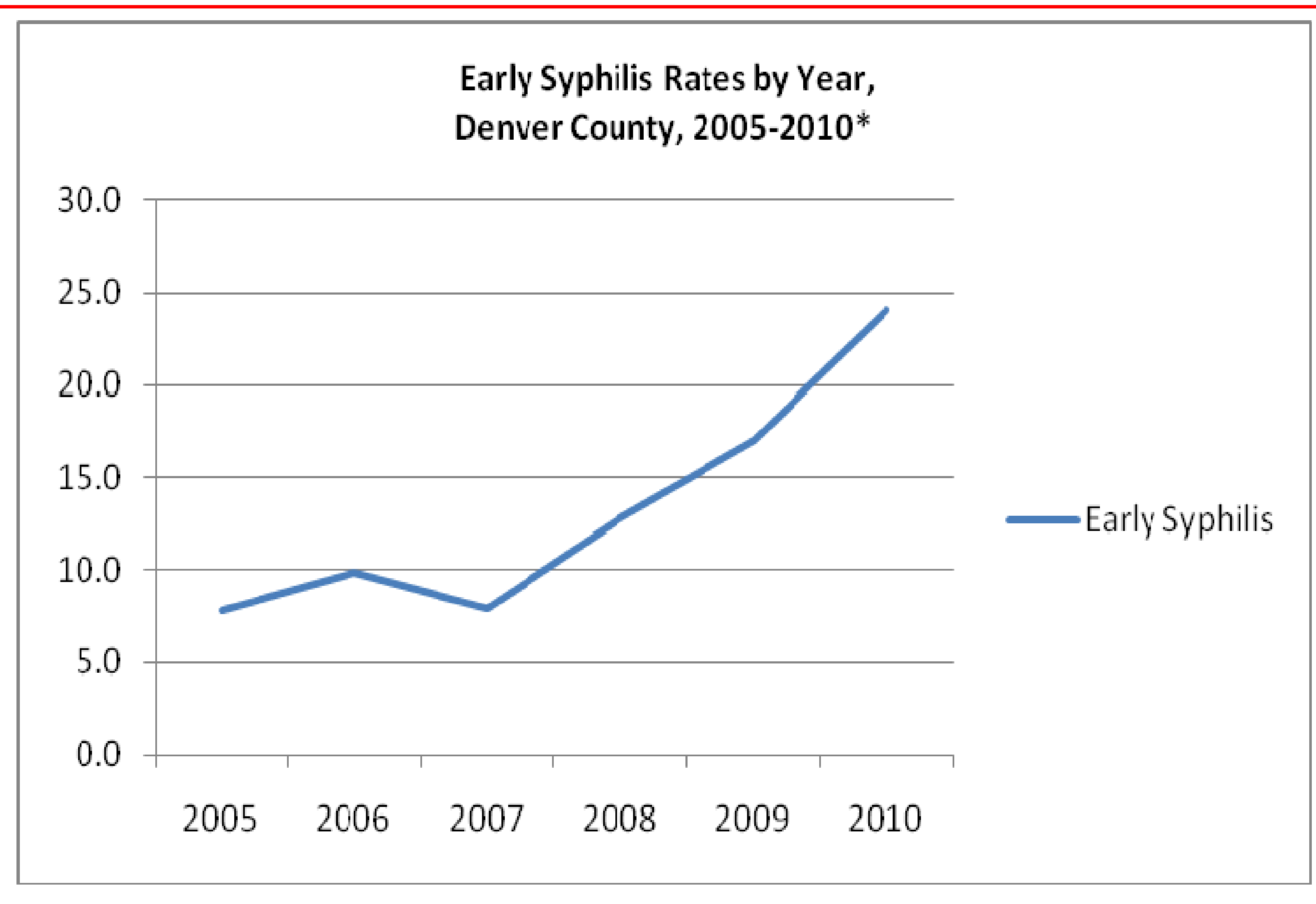
† No imputation was done for race/ethnicity.

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

Colorado Syphilis



Denver Syphilis



Syphilis – Common Lab Tests

- Darkfield microscopy
  - Useful for evaluation of lesions in primary and secondary syphilis
  - Sensitivity decreases with age of lesion and use of topical agents

- Serology – Two Types:
  - Non-treponemal tests (RPR, VDRL)
  - Treponemal tests (TP-PA, FTA, EIA, MHA-TP)

Need both types to make an accurate diagnosis of syphilis!!

Non-Treponemal Tests for Syphilis

VDRL (microscopic) and RPR (macroscopic)

- Detect IgG and IgM antibodies but not ones against the treponeme (not specific for T. pallidum - measures antibodies formed in response to cell damage)
- Sensitive but not specific – false positives occur
- Less expensive, less time-consuming, easy to perform
- Titers correlate with disease activity – quantitative and can be used to follow response to therapy and evaluate possible reinfection
- Biologic false positive reactions (BFPs) and false negative (Prozone phenomenon)

Treponemal Tests for Syphilis

FTA-ABS, TP-PA, MHA-TP, EIA/CIA (New!)

- Specific for *T. pallidum* (detect IgG and IgM antibodies directed against *T. pallidum*)
- More sensitive and specific than non-treponemal tests (fewer false positives)
- Titers correlate poorly with disease activity (levels rise earlier in primary but remain positive for a lifetime despite therapy)

Syphilis Screening Paradigm

TRADITIONAL

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

- **Non-specific to TP**
- **Quantitative**
- **Reactivity declines with time**

Treponemal tests (i.e., TPPA, FTA-Abs)

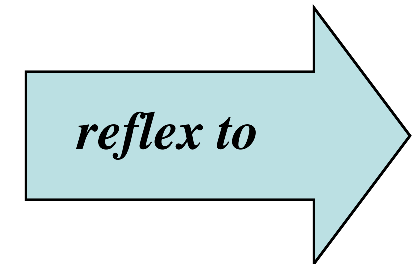
- **Specific to *TP***
- **Qualitative**
- **Reactivity persists over time**

Syphilis Screening Paradigm

EMERGING / NEW…

Treponemal tests (i.e., EIA,CLIA)

- **Specific to *TP***
- **Qualitative**
- **Reactivity persists over time**



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

- **Non-specific to *TP***
- **Quantitative**
- **Reactivity declines with time**

Local syphilis screening recs

- Providers should routinely discuss sexual history with their patients.
- All **men who have sex with men** should be screened for syphilis **every 6 months**.
- All **persons living with HIV** infection should be screened for syphilis **every 3-6 months** in conjunction with routine CD4 count and HIV viral load testing.
- All **pregnant women** should be screened **at least once** for syphilis at their first prenatal visit. Women with multiple sex partners should be re-tested in the third trimester.
- All others should be screened for syphilis according to risk.

Syphilis Treatment
Primary, Secondary & Early Latent

Recommended regimen for adults:

- Benzathine penicillin G 2.4 million units IM in a single dose
- No enhanced efficacy of additional doses of BPG, amoxicillin or other antibiotics even if HIV infected

Alternatives (non-pregnant penicillin-allergic adults):

- Doxycycline 100 mg po bid x 2 weeks
- Tetracycline 500 mg po qid x 2 weeks
- Ceftriaxone 1 g IV or IM qd x 10-14 d
- Azithromycin 2 g po in a single dose should be used with caution and not in MSM or pregnant women

When is an LP indicated?

- Neurologic or ophthalmic/auditory symptoms/signs
- Evidence of tertiary disease (aortitis, gumma)
- Serologic treatment failure

- In HIV infection: unless neurologic symptoms there is no evidence that CSF exam is associated with improved outcomes

Syphilis Management Issues in HIV-Infected Patients

1. Visual complaints (especially unilateral) in HIV infected patients should prompt consideration of ocular syphilis
   - Symptoms: blurred vision, loss of vision, central scotomas
   - Posterior chamber uveitis is typical, but retinitis, retinal detachment, CSF inflammation also possible

Syphilis Management Issues in HIV Infected Patients (continued)

2. Neurologic complaints in HIV infected patients should prompt consideration of neurosyphilis
   - Symptoms: visual changes, hearing loss, facial weakness, stuttering stroke symptoms
   - Early forms of neurosyphilis are most common (months to a few years)
     - Acute syphilitic meningitis (CN VI, VII, VIII)
     - Meningovascular (stuttering stroke)
   - Ocular syphilis
     - CSF inflammation may occur

Syphilis: Treatment Ocular and Neurosyphilis

- Recommended regimen:
  - Aqueous Crystalline Penicillin G 18-24 million units IV daily administered as 3-4 million IV q 4 hr for 10 -14 days
- Alternative regimen:
  - Procaine Penicillin G 2.4 million units IM daily plus Probenecid 500 mg PO q d, both for 10-14 days
- Non-pregnant penicillin-allergic adults
  - Ceftriaxone 2 gm IM or IV x 10-14 d
- ***Additional treatment with benzathine penicillin 2.4 million units IM once per week for up to 3 weeks after completion of 10-14 day course may be considered to provide a comparable total duration of therapy***

Annual STD 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	

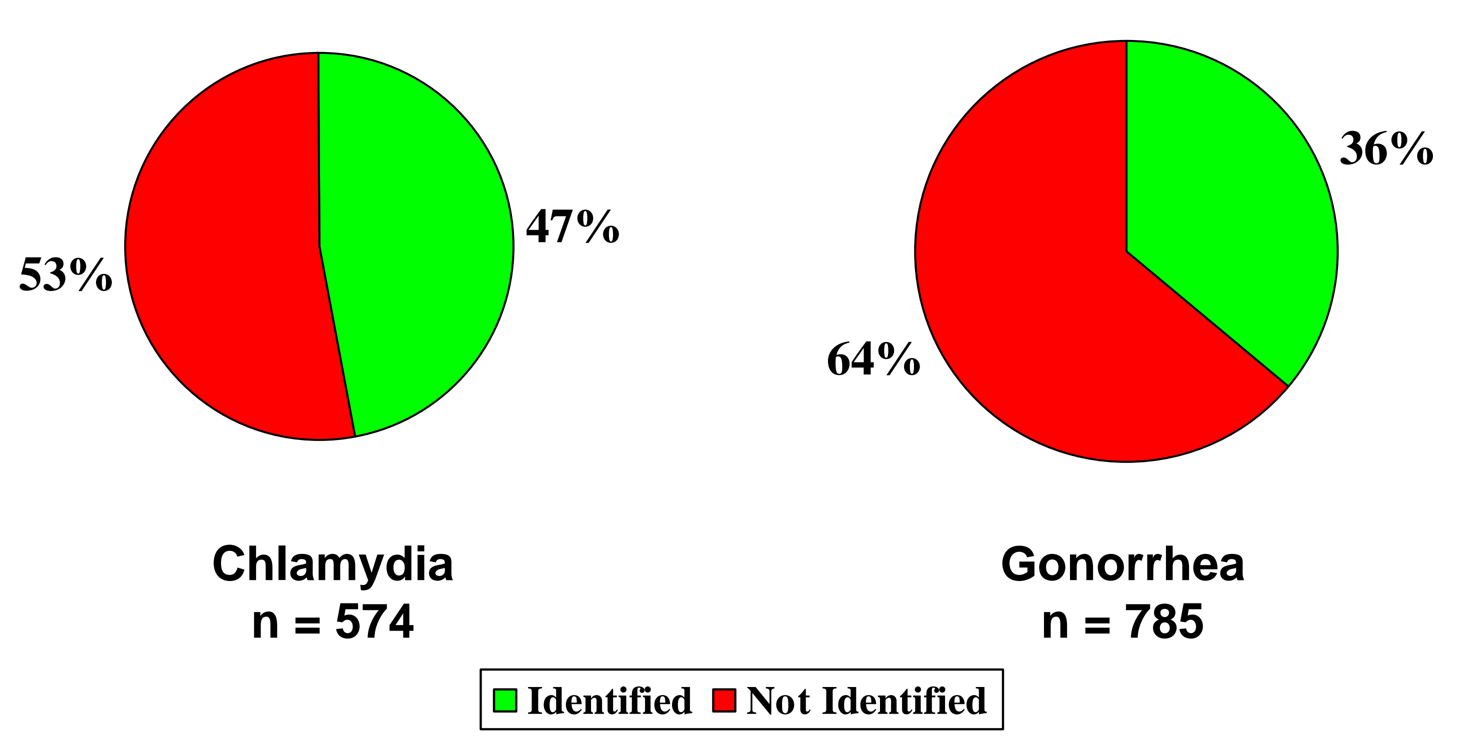
* Some experts recommend

Indications for More Frequent Screening in MSM

- Increased prevalence of STDs in area or patient population
- Symptoms or recent history of any STD in patient or partner
- Risky sexual behavior
  - Multiple or anonymous partners
  - Substance abuse especially methamphetamine
- Risky sexual behavior in partner
- If any of the above, then screen q 3-6 months

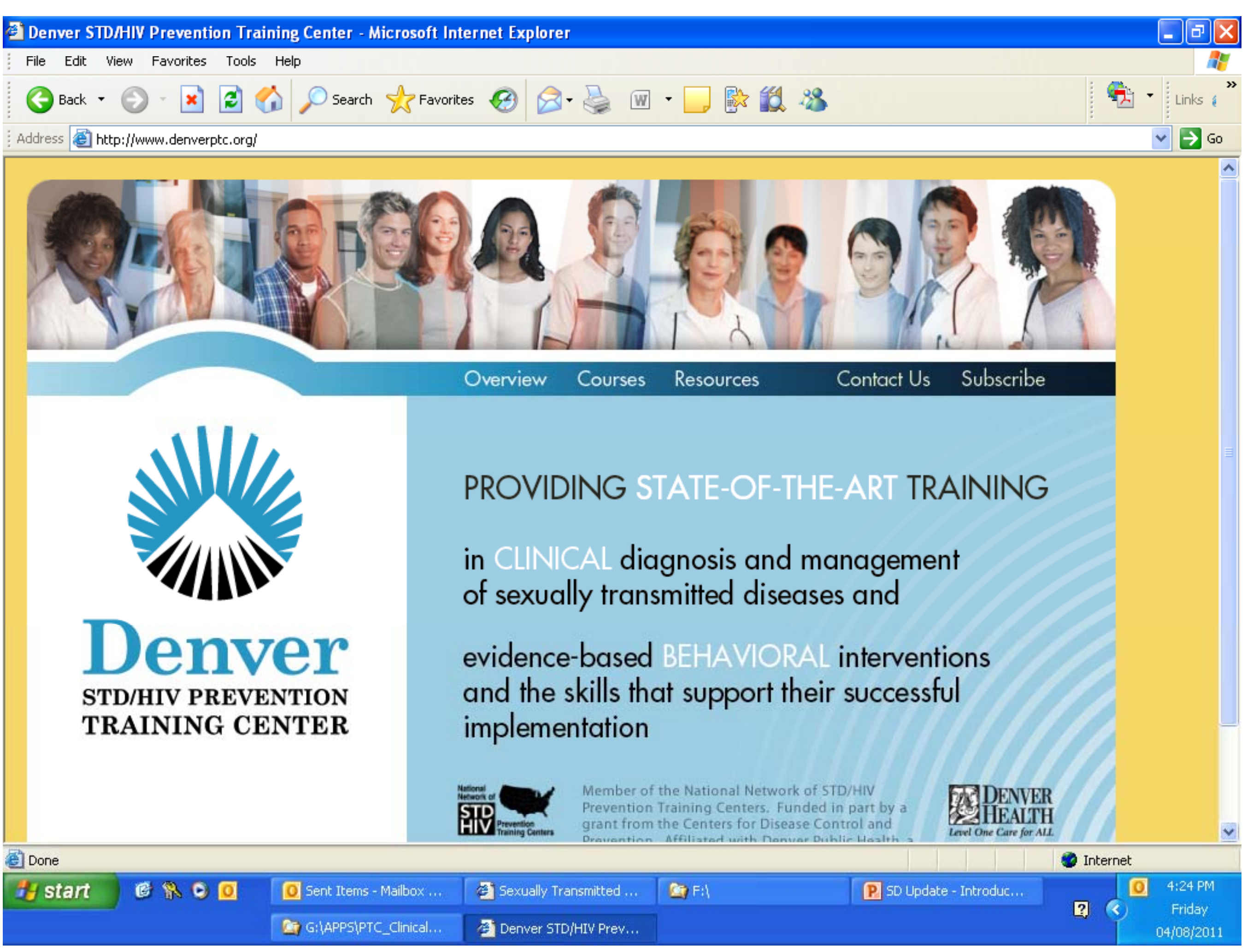
MMWR 2003 52: RR 12

Proportion of unidentified CT and GC infections if only urine/urethral screening performed among MSM: San Francisco – 2003



Kent, CK et al. ISSTDR, July 2005

Denver PTC: www.denverptc.org



“When the authorities warn you of the dangers of having sex, there is an important lesson to be learned. Don’t have sex with the authorities.”

- Matt Groening