Sexually Transmitted Infections in the HIV Care Setting

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January 2017

Rene P, 20 yo man, referred by a partner “who had syphilis”

- Considers himself healthy, no symptoms
- HIV Ag-Ab test negative today; syphilis serology pending
- Two episodes of rectal gonorrhea last year
- Moved here from Mexico a year ago; limited English, works in fast food place
- Sometimes uses meth on weekends
- 6 partners in last 3 months, some anonymous. Last unprotected sex 12 h ago

Rene P, 21 yo man, referred by a partner “who had syphilis”

What do you do?

A. Send confirmatory syphilis test (EIA, TPPA) before treating for syphilis

B. Treat him with BZN PCN 2.4 x 10-6 mu IM immediately

C. Perform LP

D. Check plasma HIV viral load

E. Offer him TDF-FTC as PrEP and see him in 3 months

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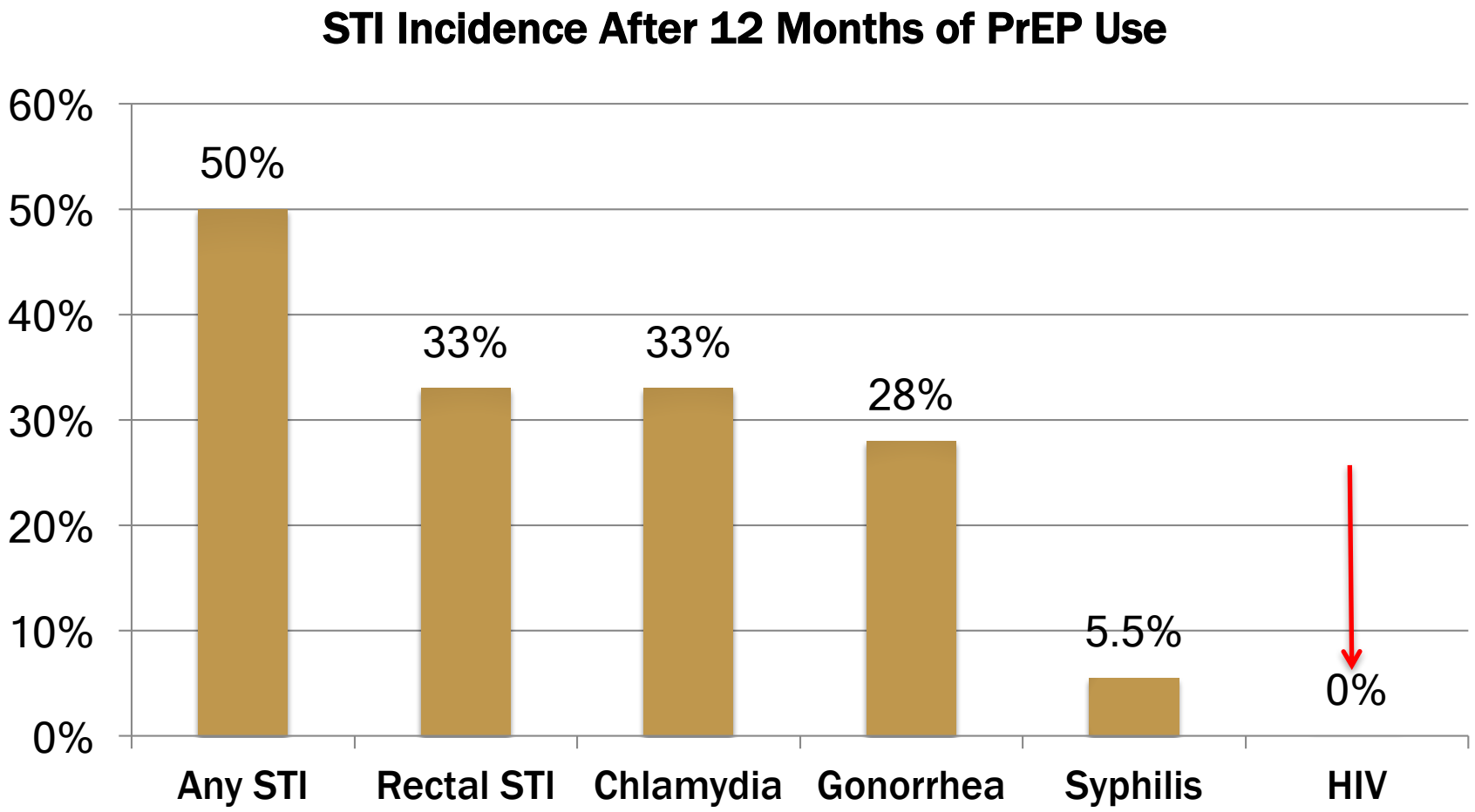
STI in the “Real World”

PrEP and STIs in >600 MSM Kaiser Permanente San Francisco



Volk et al. CID 2015;

Slide courtesy J. Volk

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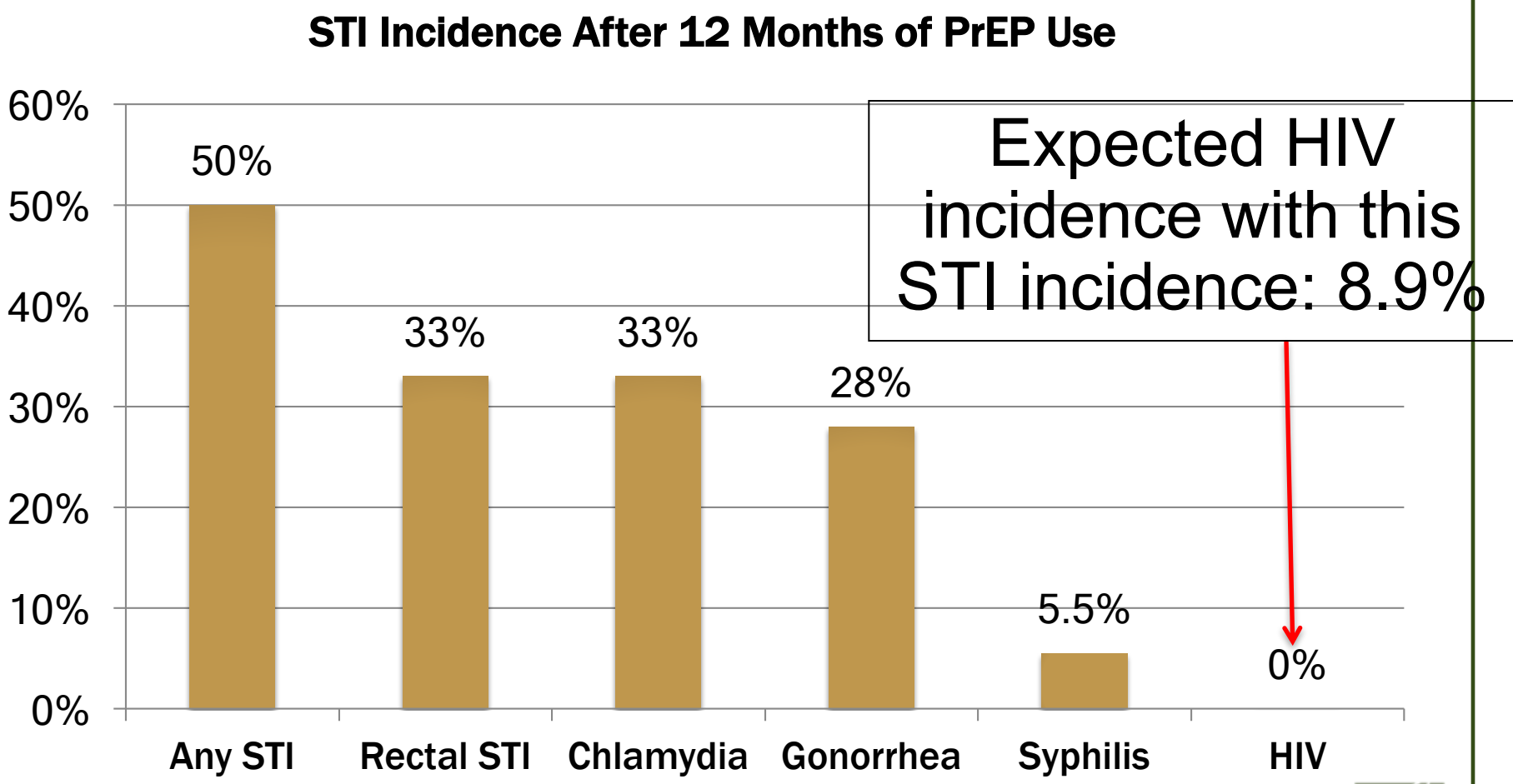
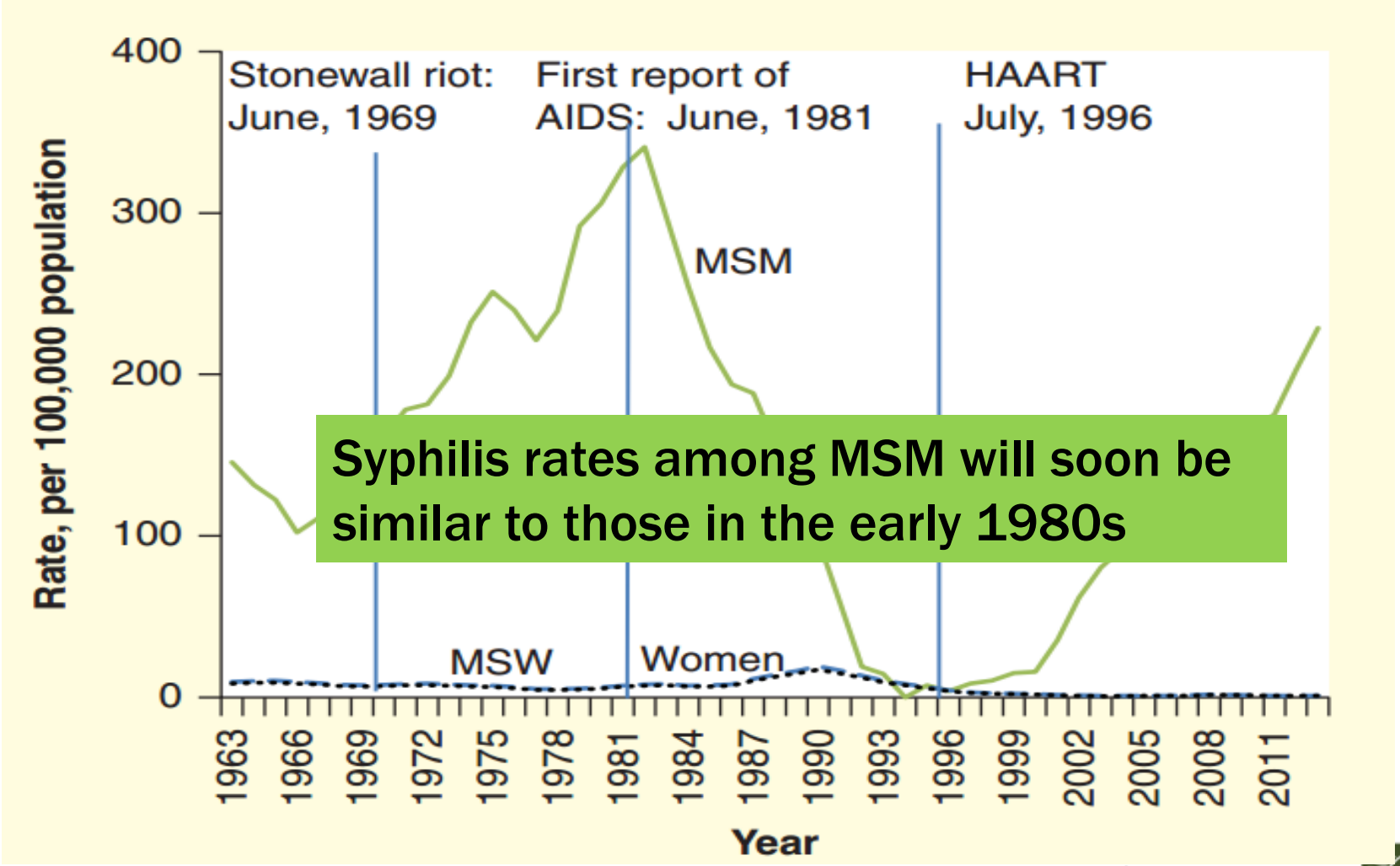


Volk et al. CID 2015;

Slide courtesy J. Volk

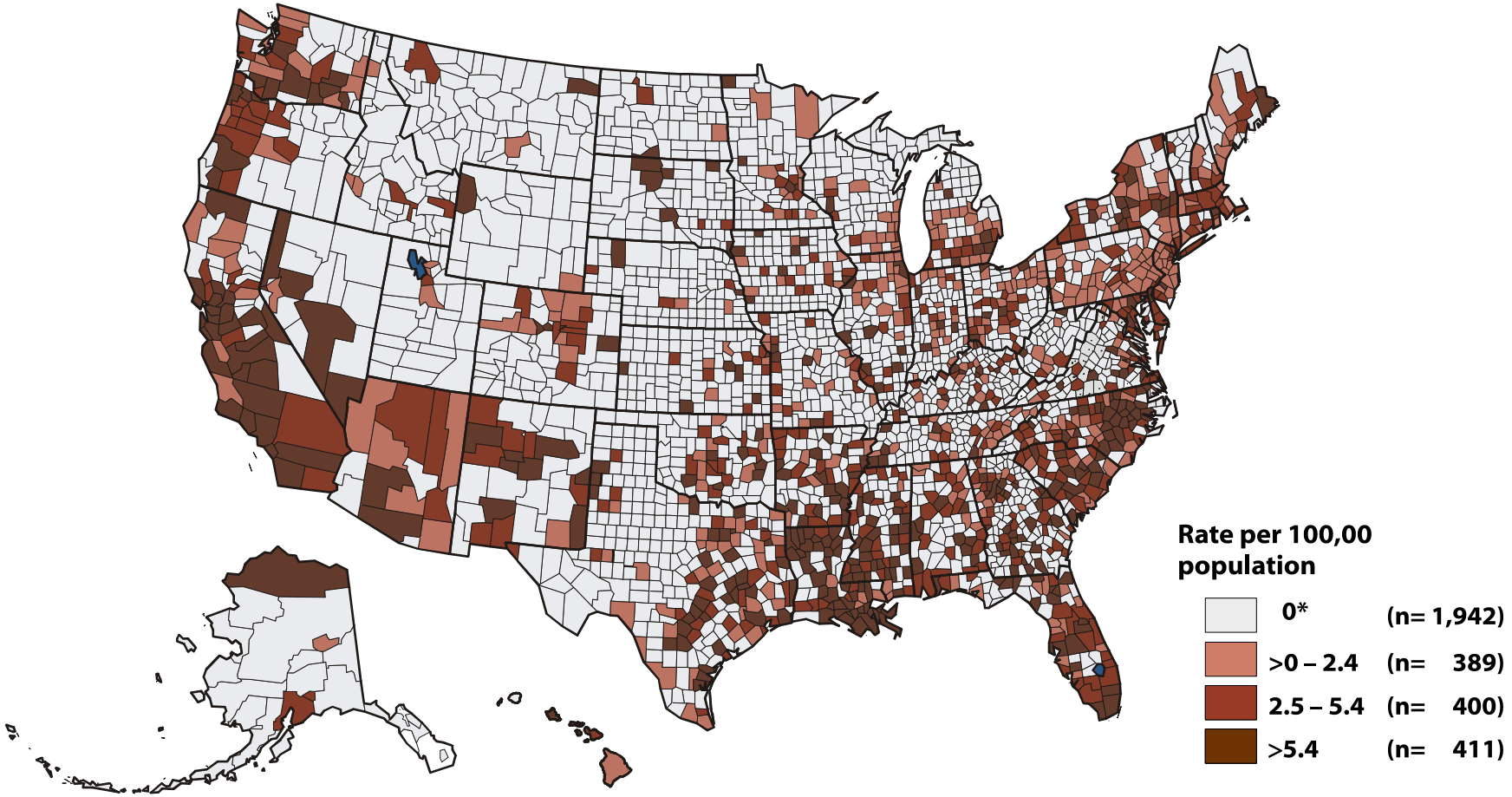
Syphilis rates among MSM: a timeline



Syphilis rates among MSM will soon be similar to those in the early 1980s

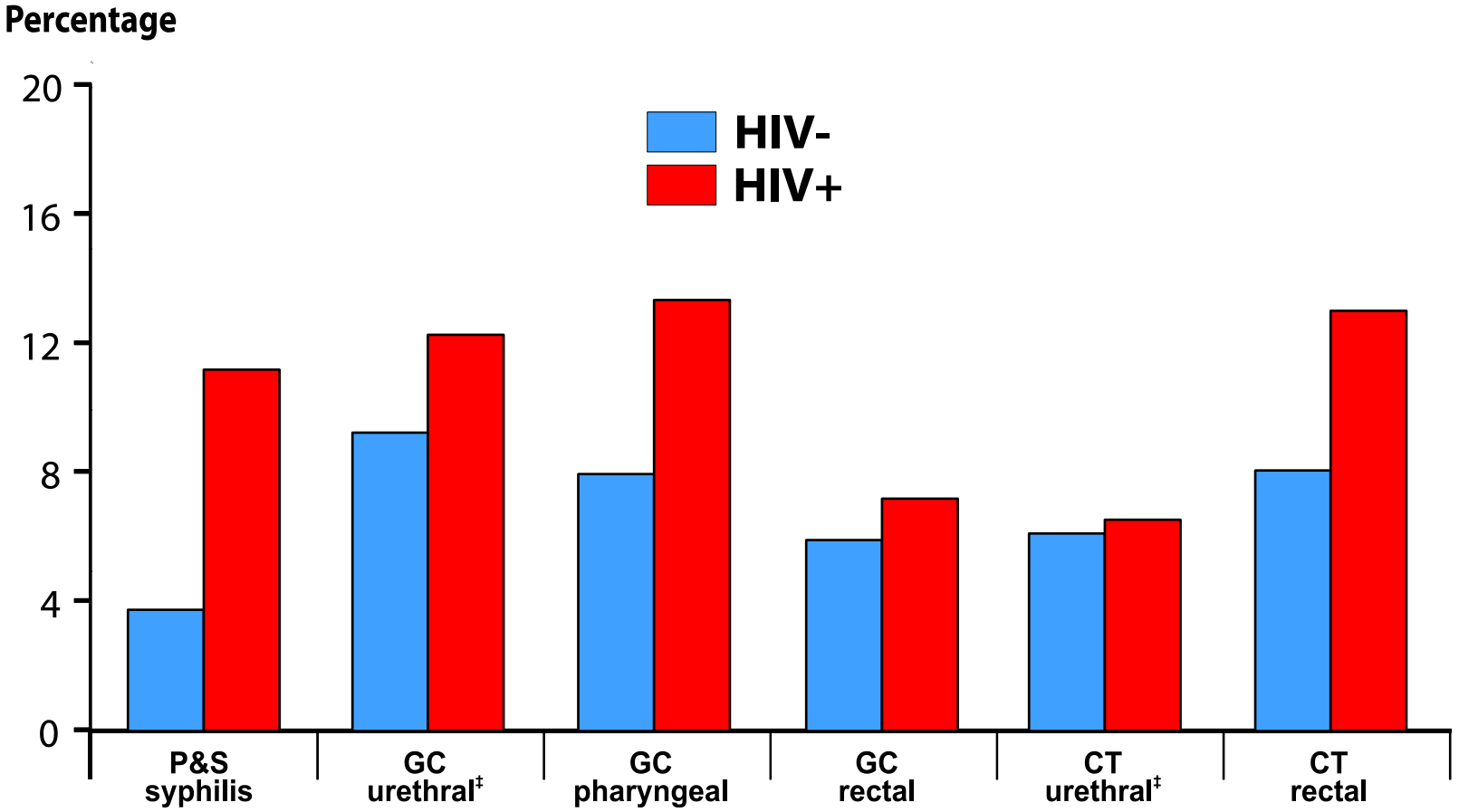
Peterman, 2015, *Expert Rev Anti Infect Ther*

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



* In 2014, 1,942 (61.8%) of 3,142 counties in the United States reported no cases of primary and secondary syphilis.

Proportion of MSM* Attending STD Clinics with Primary and Secondary Syphilis, Gonorrhea or Chlamydia by HIV Status†, STD Surveillance Network (SSuN), 2014



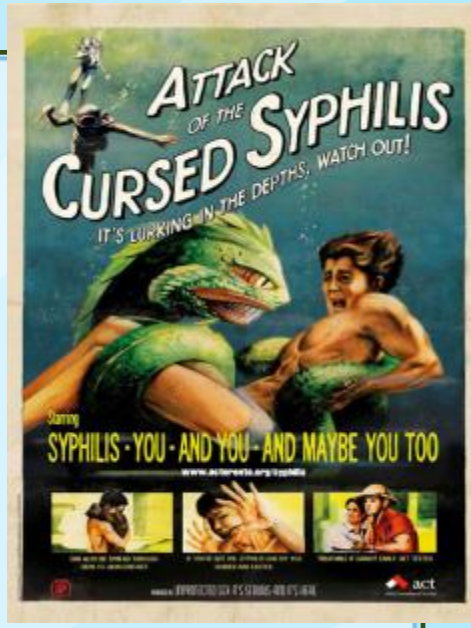
*MSM=men who have sex with men; **P&S** = primary and secondary syphilis; **GC** = gonorrhea; **CT** = chlamydia..

† 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.

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

2014-Fig X. SR. Pg. 76.



- Key points
  - We are in the middle of an impressive resurgent epidemic of STI, especially syphilis, in MSM
  - Among these infected MSM, at least half are co-infected
  - Early syphilis PREDICTS HIV acquisition in those not already infected with HIV
  - Infection is occurring nationwide, across race/ethnicities
  - Congenital syphilis events are still occurring

Rene P, 21 yo man, referred by a partner “who had syphilis”

- What other STDs would you screen for, and where?

STD Screening for MSM

- HIV
- Syphilis
- Urethral GC and CT
- Rectal GC and CT (if RAI)
- Pharyngeal GC (if oral sex)

*

- HSV-2 serology (consider)
- Hepatitis B (HBsAg, freq not specified)
- **Hepatitis C (HIV+MSM, at least annually)**

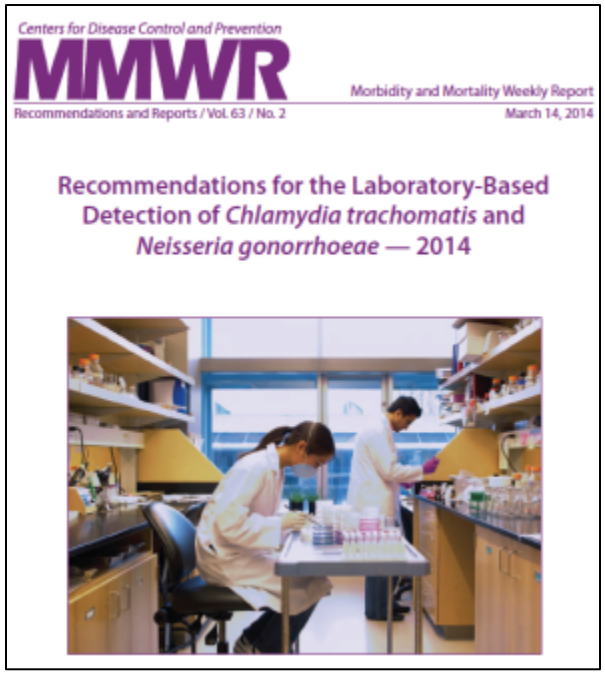
Anal Cancer in HIV+ MSM: Data insufficient to recommend routine screening, some centers perform anal Pap and HRA

* **At least annually, more frequent (3-6 months) if at high risk (multiple/anonymous partners, drug use, high risk partners) & at relevant anatomic sites**

CDC 2015 STD Treatment Guidelines

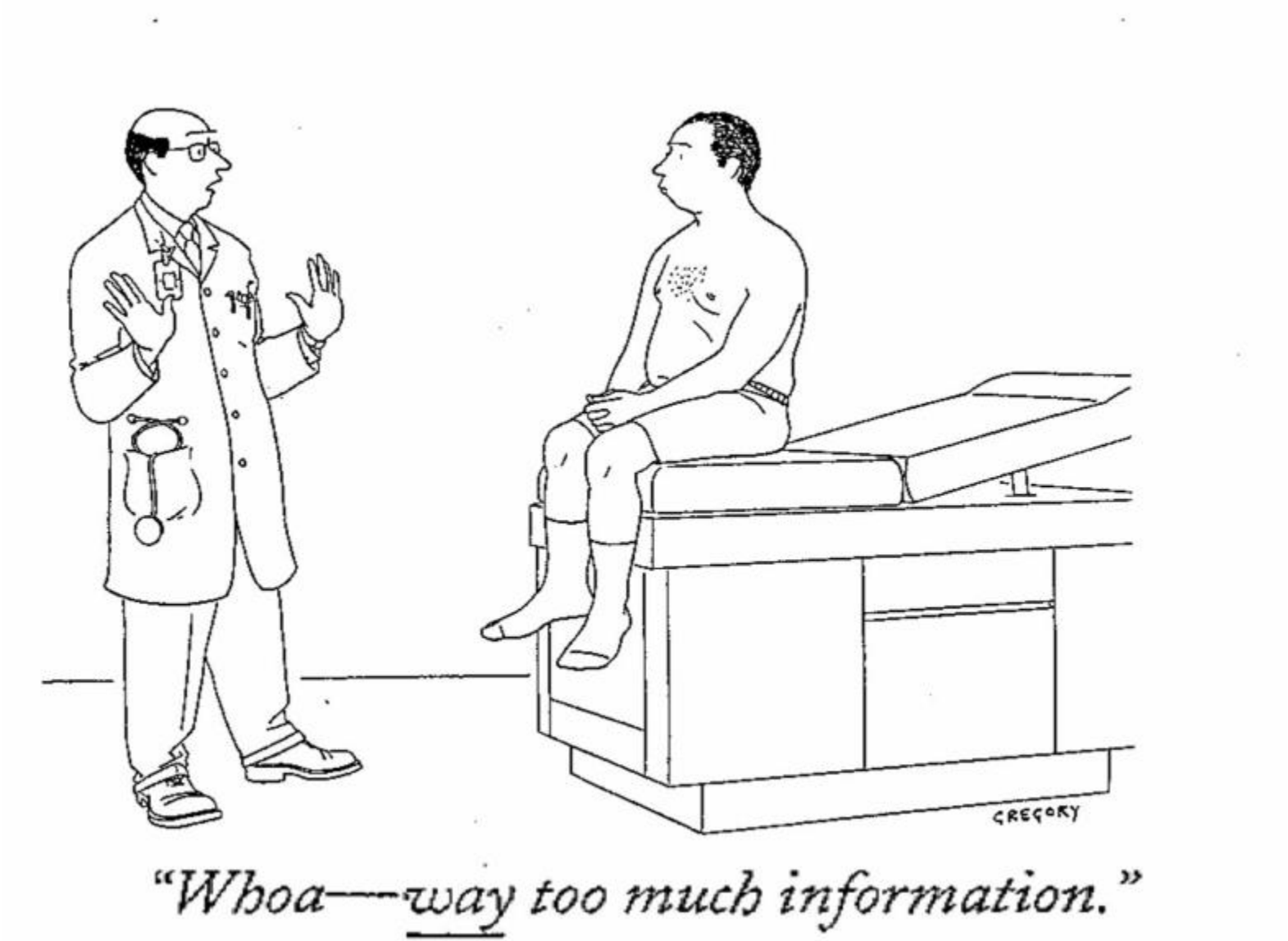
Chlamydia & Gonorrhea: Diagnostic Testing

- Nucleic acid amplification tests (NAAT) recommended for men & women
- Optimal specimen: first-catch urine in men and vaginal swabs in women
- NAAT optimal for rectal and pharyngeal testing; not FDA approved but commercially available & validation protocols available for local labs
- Limitations: no antibiotic resistance testing with NAAT (need culture)



http://www.cdc.gov/mmwr

Targeted Prevention: Requires Asking!



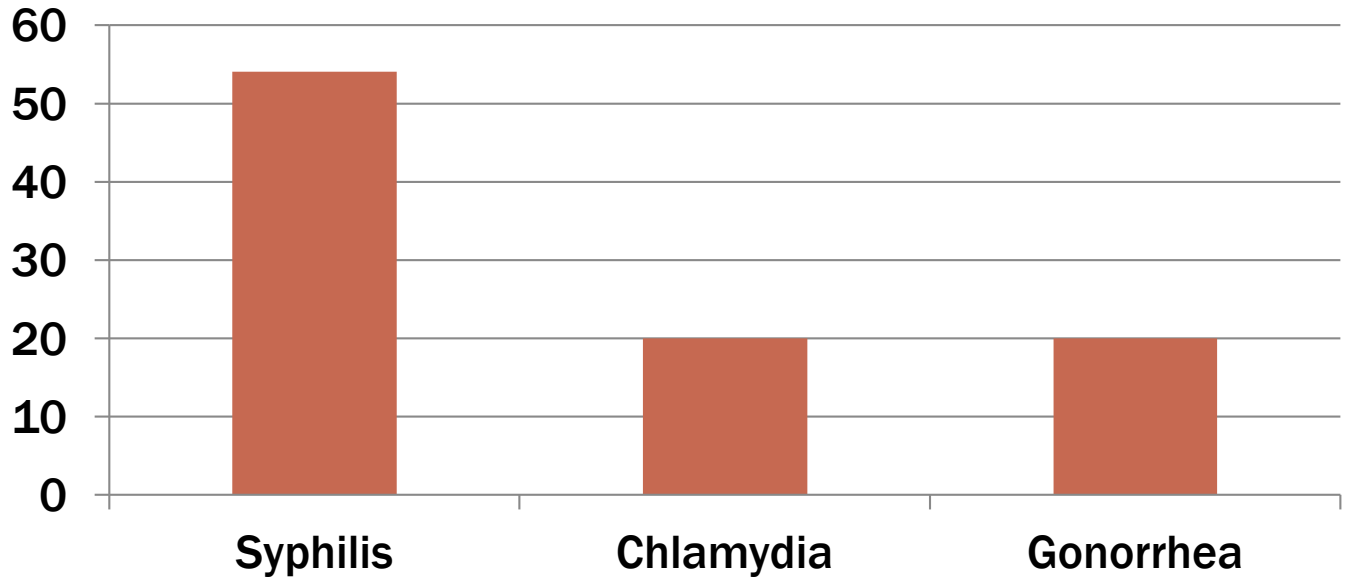
Ask Screen Intervene

www.nnptc.org/online_training/asi

Suboptimal STD Screening among MSM in HIV Care

- N=4217 interviews and chart reviews from Medical Monitoring Project, nationally representative sample of adults in HIV care

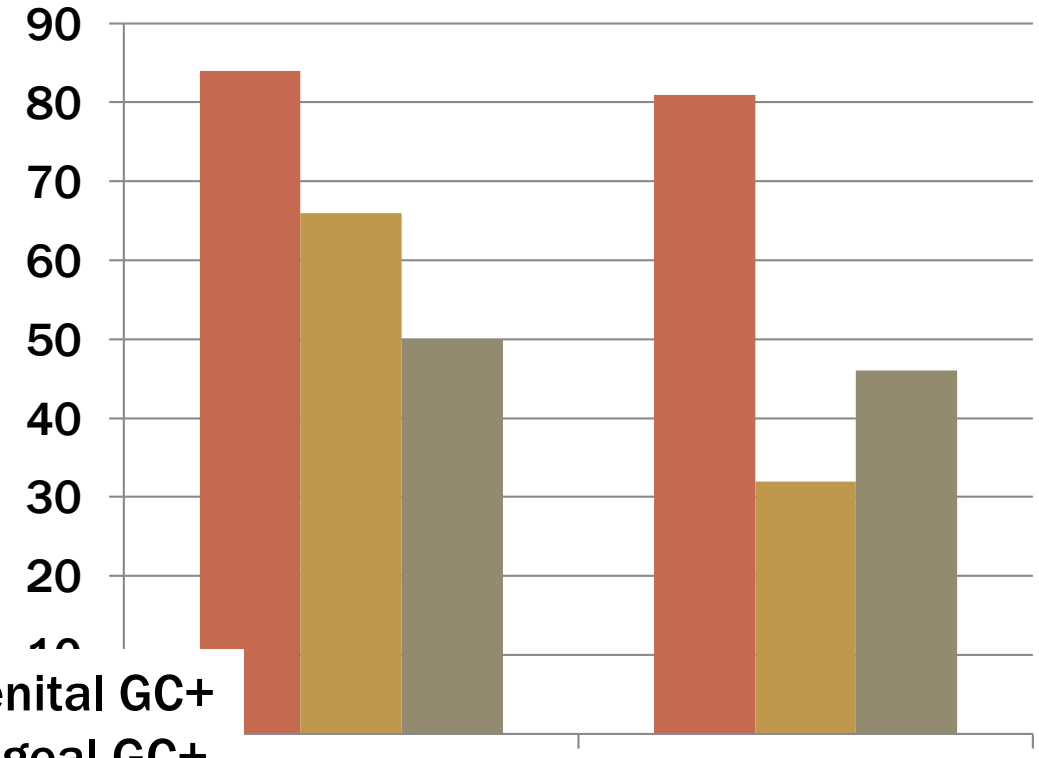
% of sexually active HIV+ MSM screened for STIs, N=1411



Flagg EW, 2015, STD

STD screening among MSM in STD Clinics

- N=21994 MSM in the STD Surveillance Network (SSUN)

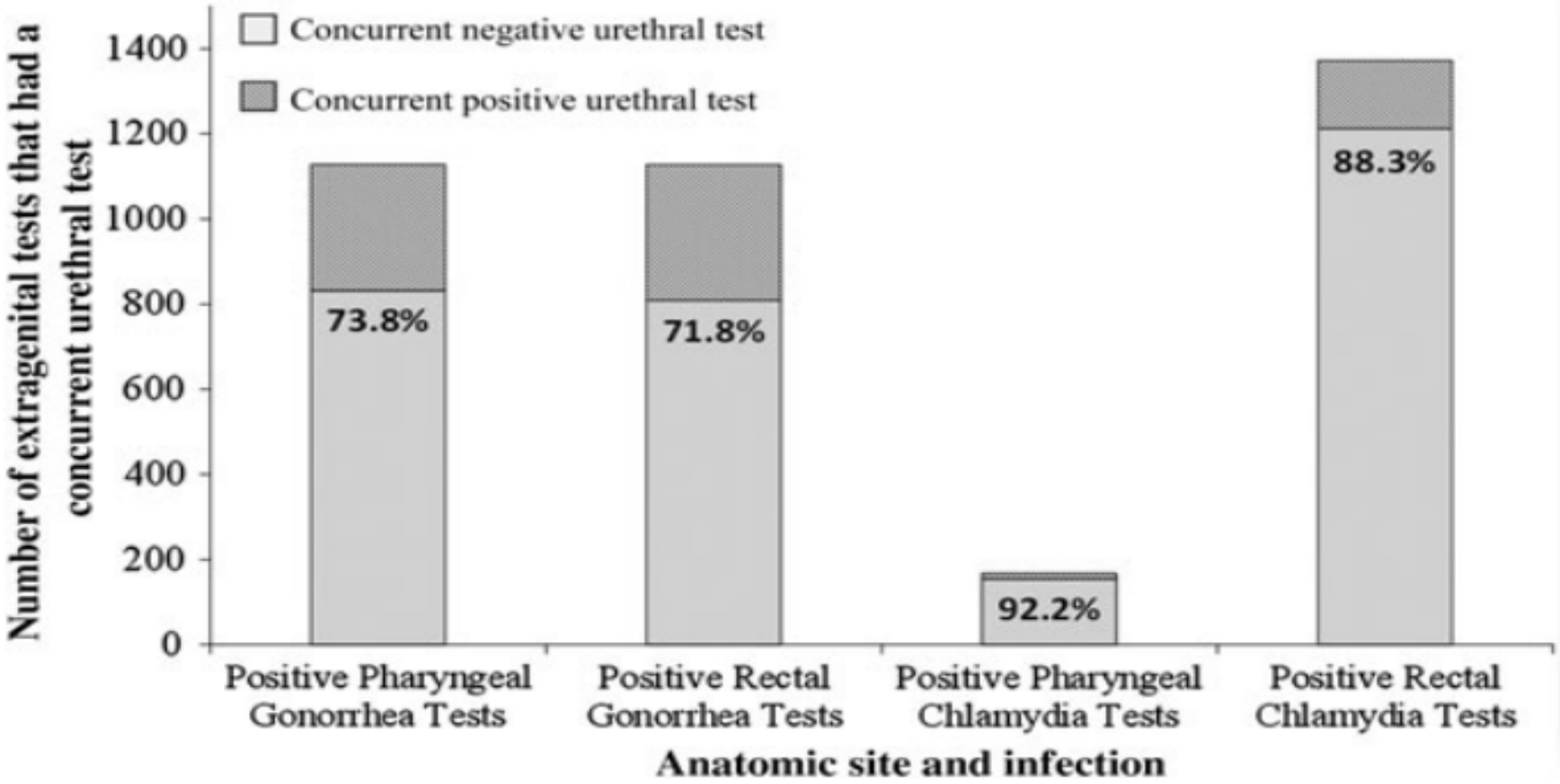


11% Urogenital GC+
8% Pharyngeal GC+
10% Rectal GC+

8% Urogenital CT+
3% Pharyngeal CT+
14% Rectal CT+

Patton et al CID 2014

High Proportion of Extragenital CT/GC associated with negative urine test, STD Surveillance Network (n=21994)



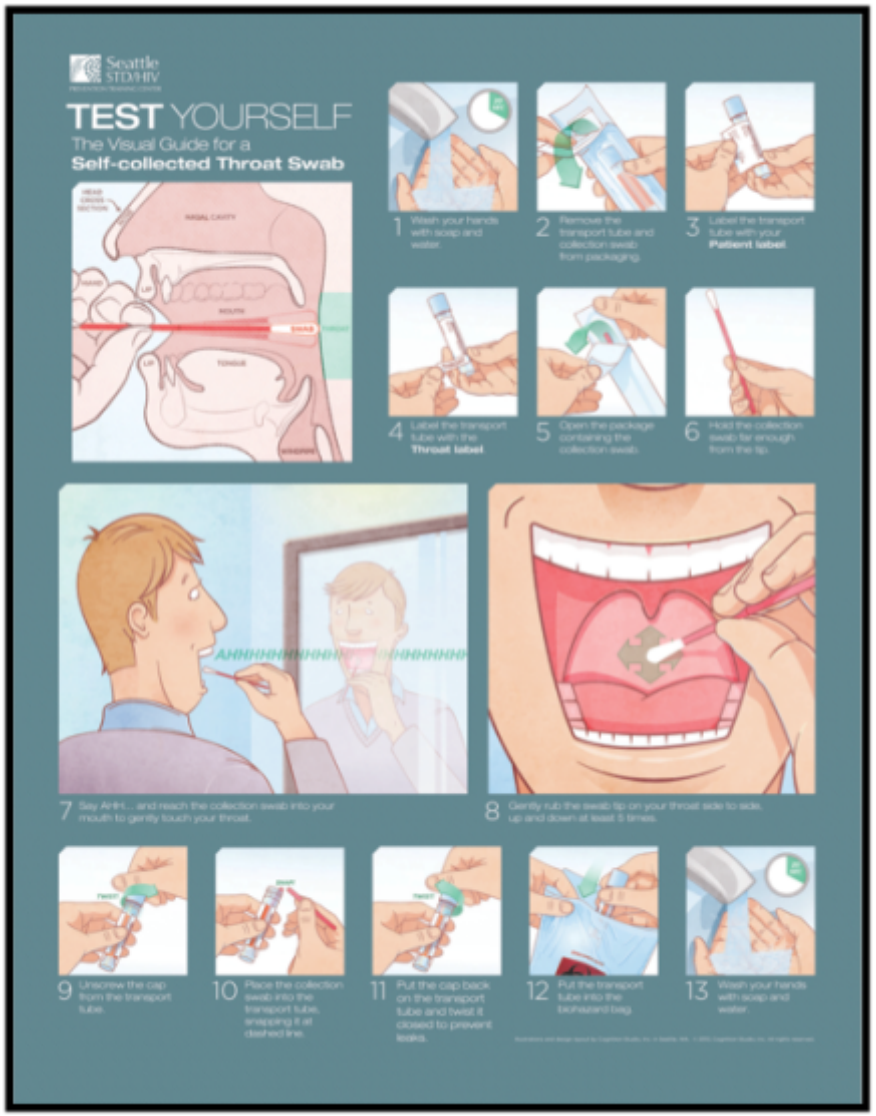
Patton et al CID 2014

Self-collected rectal/pharyngeal STI testing

- Highly acceptable, similar performance compared to clinician-collected specimens
- Self-collection can be performed at laboratory along with blood draw/urine collection or in the exam room before/after the provider visit
- May save patient an office visit
- May save the provider time

Van der helm, 2009, STD; Sexton, 2013 J Fam Pract; Dodge, 2012 Sex Health Freeman 2011, STD; Alexander 2008, STI; Moncada 2009, STD

UW PTC STI Self-Testing Program



A Vexing Problem

- 33 yo man with well-controlled HIV diagnosed with rash of secondary syphilis, confirmed by serology; no indication for LP
- Treated with appropriate BZN PCN therapy
- Serum RPR 1:1024 (day of treatment)
- Two recent sex partners; both treated in same clinic

A Vexing Problem

- Returned in 3 months
- Serum RPR 1:512

A Vexing Problem

- Returned in 6 months
- Serum RPR 1:64

A Vexing Problem

- Returned in 9 months
- Serum RPR 1:32

A Vexing Problem

- Returned in 1 year
- Serum RPR 1:8
- No new partners or known exposures to syphilis
- No intercurrent STD
- What now?

Seña et al. BMC Infectious Diseases (2015) 15:479
DOI 10.1186/s12879-015-1209-0

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

A systematic review of syphilis serological treatment outcomes in HIV-infected and HIV-uninfected persons: rethinking the significance of serological non-responsiveness and the serofast state after therapy

Arlene C. Seña[1*†], Xiao-Hui Zhang[2†], Trudy Li[3], He-Ping Zheng[2], Bin Yang[2], Li-Gang Yang[2], Juan C. Salazar[4], Myron S. Cohen[1], M. Anthony Moody[5,6], Justin D. Radolf[4,7] and Joseph D. Tucker[1]

- Identified 1693 reports in the literature, reviewed 20 studies that met selection criteria.
- Median proportion of patients withserological non-response was 12.1% overall (interquartile range, 4.9–25.6)
- Serofast proportion estimated from 2 studies, which ranged from 35.2–44.4 %. Serological cure was primarily associated with younger age, higher baseline nontreponemal titers, and earlier syphilis stage.
- Relationship between serological cure and HIV status inconsistent; among HIV-infected patients, CD4 count and HIV viral load was not associated with serological cure

Justin, 38 yo man, blurry vision

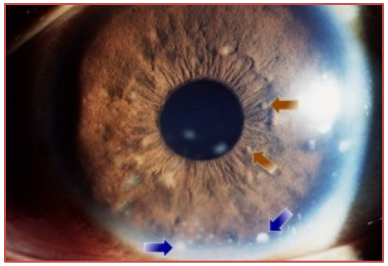
- Well-controlled HIV, CD4 488 (22%)
- Has had a week or so of increasingly blurry vision in R eye
- No other complaints
- 1 primary male partner, also HIV+, no condoms; occasional outside male partners
- Prior h/o of rectal GC; syphilis EIA negative 6 mo ago
- Normal neuro exam; your ophthalmalogic exam is unrevealing (undilated pupils)

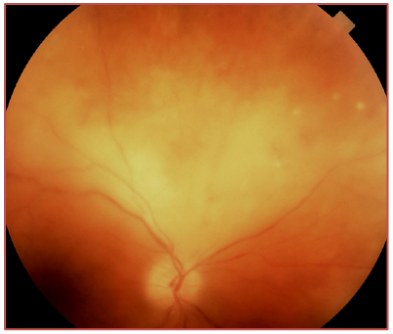
Justin, 38 yo man, blurry vision
What do you do now?

- Send him to ophthalmology clinic for examination (next available appointment)
- Perform a lumbar puncture
- Check routine labs and add syphilis serology before defining management
- Refer for urgent eye examination and initiate presumptive treatment with IV Penicillin (PCN G)

CDC Clinical Advisory: Ocular Syphilis Outbreak April 3, 2015

- 15 cases of ocular syphilis since December 2014 from WA and CA
  - 5 other states with cases under investigation
- Most cases among MSM with HIV
  - A few among HIV-negative persons, including heterosexual men and women
- Several have resulted in significant sequelae including blindness
- Can comprise panuveitis, retinitis
- Treat with parenteral PCN (neurosyphilis regimen)





CDC
HIV/AIDS, Viral Hepatitis, STD and TB Prevention


BUY BONDS
PENICILLIN
CURES
GONORRHEA
IN 4 HOURS
SEE YOUR DOCTOR TODAY

John, 40 yo man, has a positive screening test

- Healthy HIV+ man sexually active with men, receptive/insertive anal/oral sex “usually” with condoms if receptive anal only
- Screening last week at all sites revealed +NAAT for *N. gonorrhoeae* at the pharynx. Though not ordered, the test is also reported positive for *Chlamydia trachomatis.*
- He reports a rash when he received “some penicillin—I think amoxicillin” in his 30s.

John, 40 yo man, has a positive pharyngeal NAAT for GC/CT
What do you do?

- Treat with IM ceftriaxone, 250 mg, now
- Document negative skin testing for PCN allergy prior to treatment with ceftriaxone
- Treat with oral azithromycin, 2 gram, now
- Treat with oral gemifloxacin (320 mg) and oral azithromycin (2 gram) now

2015 CDC STD Treatment Guidelines: Uncomplicated Gonorrhea Infection

Recommended:

- **Ceftriaxone 250 mg injection x 1**

PLUS:

- **Azithromycin 1 g orally x 1**

Doxycycline removed as second agent

Alternatives:

- Cefixime 400 mg orally plus Azithromycin

2015 Updated Gonorrhea Treatment Guidelines

Uncomplicated Gonococcal Infection of Cervix, Urethra, or Rectum
Alternative Therapy (Only if Ceftriaxone not an option)

Cefixime
400 mg PO x 1

+

Azithromycin
1 g PO x 1

NOTES:
- Alternative regimens for use only when ceftriaxone not available
- Doxycycline changed to alternative because of high rate of tetracycline resistance
- NOT RECOMMENDED FOR USE IN PHARYNGEAL INFECTION
- If treatment failure, need culture and sensitivity, notify Public Health

Source: CDC and Prevention. MMWR. 2015.64(3).

2015 Updated Gonorrhea Treatment Guidelines

Uncomplicated Gonococcal Infection of Pharynx
Recommended Therapy

Ceftriaxone
250 mg IM x 1

+

Azithromycin
1 g PO x 1

NOTES:
- No alternatives listed
- Test of cure for any other regimen after 14 days

Source: CDC and Prevention. MMWR. 2015.64(3).

2015 Updated Gonorrhea Treatment Guidelines

PENICILLIN ALLERGY
RECOMMENDED THERAPY

Gentamicin
240 mg IM x 1

OR

Gemifloxacin
320 mg PO x 1

+

Azithromycin
2 g PO x 1

NOTES:
- Urogenital infections only
- Nausea is a common side effect of these regimens

Source: CDC and Prevention. MMWR. 2015.64(3).

Gonorrhea Treatment: Summary

- Dual therapy recommended
  - Enhance treatment effectiveness
  - Prevent transmission of resistant organisms
  - Azithromycin preferred over doxycycline due to high prevalence of tetracycline resistance (23.7% in 2013)
- No clinical data to support increasing dose of ceftriaxone or azithromycin as part of dual therapy
- Ceftriaxone treatment failures rare, all outside U.S.
- Azithromycin monotherapy not recommended due to ease of resistance
- Test of cure **not** needed after treatment for urogenital or rectal infection; **recommended for pharynx (alternative)**

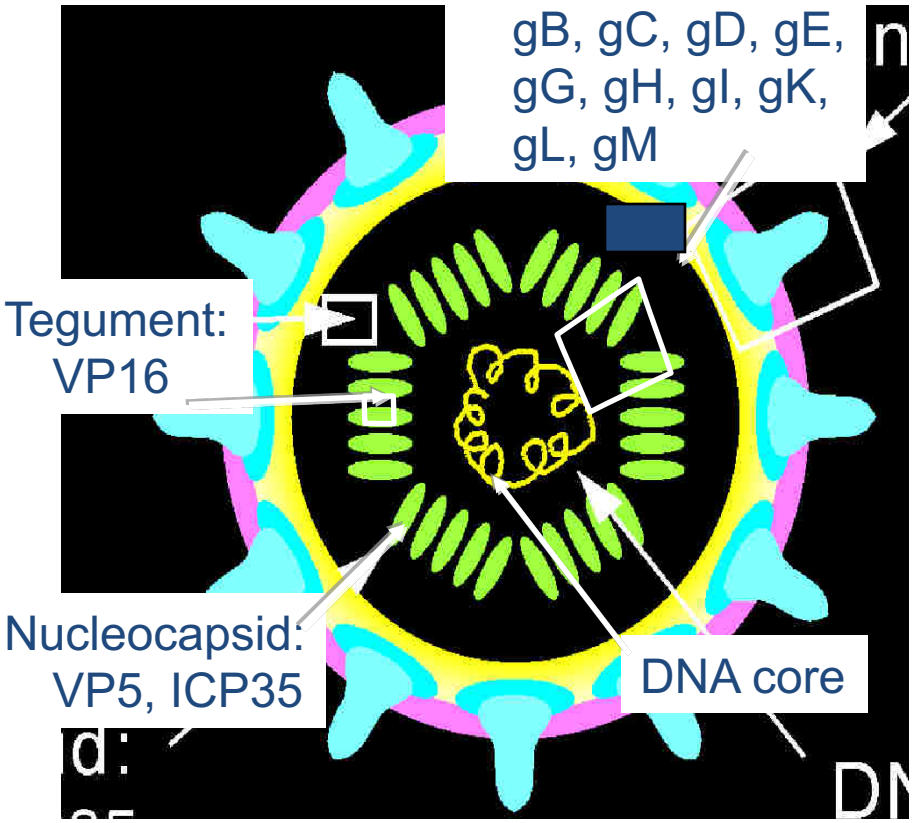
Managing Treatment Failures

- **Most treatment failure likely due to reinfection**
- If suspect treatment failure, obtain culture & susceptibility
  - If reinfection likely (after ceftriaxone/azi): Rx ceftriaxone 250 mg + azithromycin 1 g
  - If reinfection likely (after cefixime/azi): Rx ceftriaxone 250 mg + azithromycin 2 g
  - If treatment failure suspected, gemifloxacin 320 mg + azithromycin 2 g or gentamicin 240 IM + azithromycin 2g
- Report to local or state health department; call us!
- Test of cure 7-14 days after retreatment (culture/susceptibility test with NAAT)
- Ensure partner treatment

Genital Herpes

- 35 yo man initiated HIV care 6 months earlier
- Doing well on ART with suppression
  - TDF/FTC/DRV/r
  - CD4 488
- History of gonorrhea 2 years prior
- Starting a new relationship with a man who has genital herpes
- Asks what he should do

Accurate HSV Serology: Type Specific



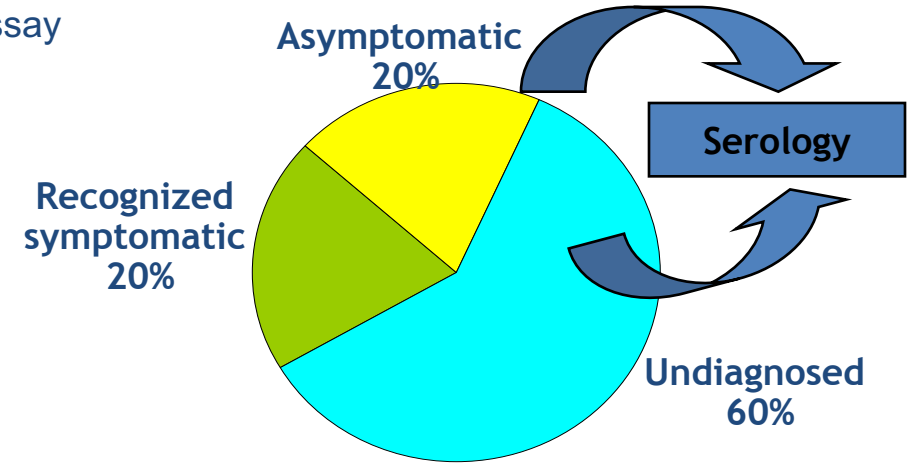
Glycoprotein gG tests

- Western blot
- gG ELISA
- gG-membrane tests
- gG immunoblot

Type-Specific gG-based Serology Commercial Kits

Test name	Company	Sensitivity (%)	Specificity (%)
HerpeSelect–2 ELISA	Focus	96–100	97–100
HerpeSelect immunoblot	Focus	97–100	98
POCkit-HSV-2	Diagnology	93–100	94–97
Cobas-HSV-2	Roche	93	98
Captia Select-HSV-2	Trinity	90–92	91–99

NOTE. ELISA, enzyme-linked immunosorbent assay
Gold Standard: Western blot



Wald & Ashley, CID 2002

HSV Serology

- False negatives can occur

- In primary infection
  - Window period: development of antibodies-can take from 2 weeks to 3 months (>90% seroconvert by 3 mo)
  - Paired sera at time of suspected primary outbreak and 12 weeks later can show seroconversion (first negative, then positive)

Genital Herpes: What's New in HIV OI Guidelines? Preventing Recurrence

- Suppressive therapy for HSV may be continued indefinitely, without regard for improved CD4 cell count, although need for continuation should be addressed on an annual basis, particularly if immune reconstitution has occurred (BIII).

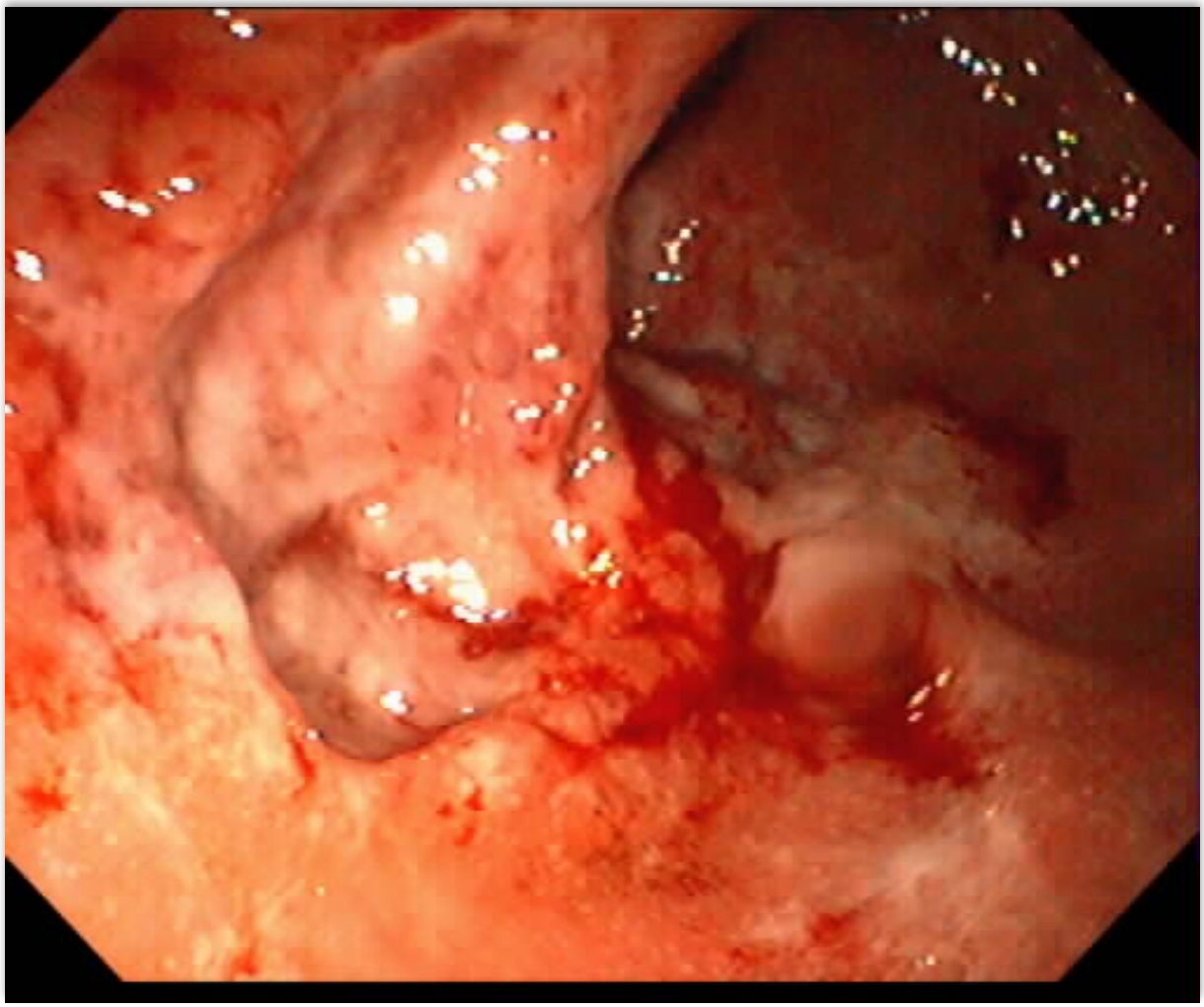
- In persons starting ART with CD4 cell counts <250 cells/mm3, there is in increased risk of HSV-2 shedding and genital ulcer disease in the first 6 months; suppressive ACV decreases the risk of GUD nearly 60% compared to placebo, and may be recommended for persons with CD4 cell counts <250 cells/mm3 starting ART (BI).

- The use of daily suppressive therapy (when compared to episodic therapy) has been associated with a lower risk of development of acyclovir-resistant HSV in hematopoietic stem cell recipients; there are no specific data for persons with HIV infection.

U.S. O.I. Guidelines, September 2015

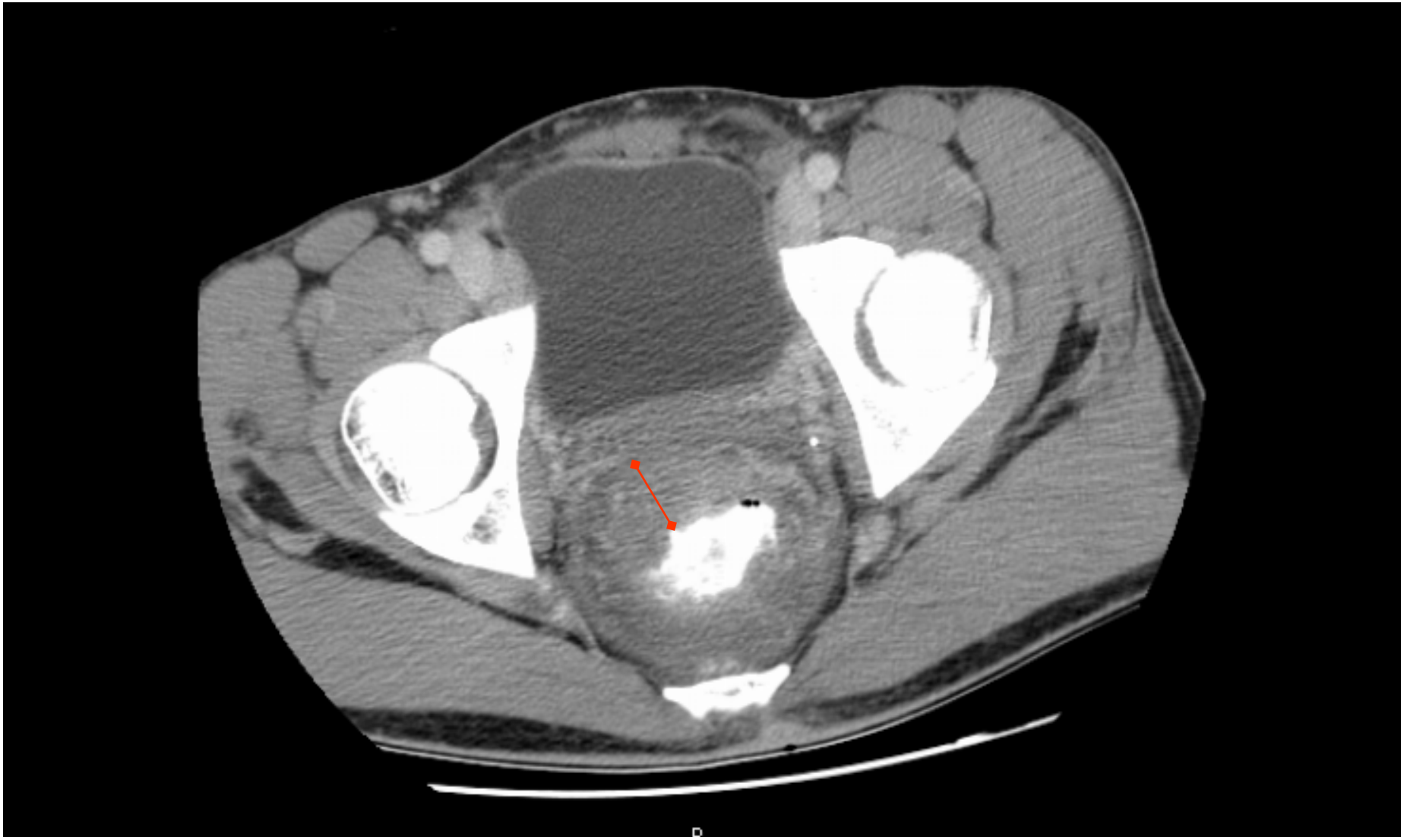
Case History

- 34 y.o. HIV+ (CD4 200) man w/ rectal discharge, bleeding, pain that first occurred 2 mos prior, off ART
- Given routine GC, chlamydia, & syphilis treatment
- Symptoms recur with severe pelvic pain radiating to back
- Monogamous with male partner; family history of Crohn's disease and colon cancer



Colonoscopy: rectal ulcers with inflammation, friable mucosa; no abscess

Contributed by Catherine McLean, CDC



CT scan: Perirectal wall thickening and surrounding inflammatory changes.
Limited local lymphadenopathy

Results

- Colon Bx: fibropurulent debris, granulation tissue; special stains-AFB, PAS, Steiner negative
- Rectal swab of ulcer: *Chlamydia trachomatis* (NAAT); negative for HSV, GC, chancroid, enteric pathogens
- Urine negative for *C. trachomatis*, GC
- Sent for genotyping to CDC

Download the CDC STD treatment guidelines app

Many thanks!

- Ina Park
- Gail Bolan
- Hillary Liss

Syphilis Treatment
Primary, Secondary, Early Latent

- **Penicillin treatment of choice**
  - Benzathine penicillin 2.4 mu IM x 1
- **No benefit of additional therapy**
  - Enhanced (IM + oral)
- **Penicillin alternatives**
  - Doxycycline, ceftriaxone
  - Azithromycin 2 gm (A2058G mutation/treatment failure)
    - Most common in MSM
    - Not recommended in MSM or pregnancy
  - Possible prophylactic effect of doxycycline? Bolan RK *STD* 2015

HIV infected ? LP or not…

- Studies document clinical and CSF abnormalities consistent with neurosyphilis in HIV + with low CD4 (≤350) or RPR ≥ 1:32
  - No change in clinical outcomes if asymptomatic
- Unless neurologic symptoms, no evidence that CSF exam is associated with improved outcomes, so not recommended
  - Assess for neurologic/opthalamic/otologic symptoms
  - LP all HIV + with syphilis and neurologic symptoms

Marra, JID* 2004; 189: 369-76; Libois, *STD* 2007; 34 (3): 141-4; Ghanem, *CID 2009; 49:162-3;