



HPTN

HIV Prevention
Trials Network

Sexually Transmitted Infections in the Era of Effective Biomedical Prevention for HIV: Yes, We Are



HPTN Regional Meeting

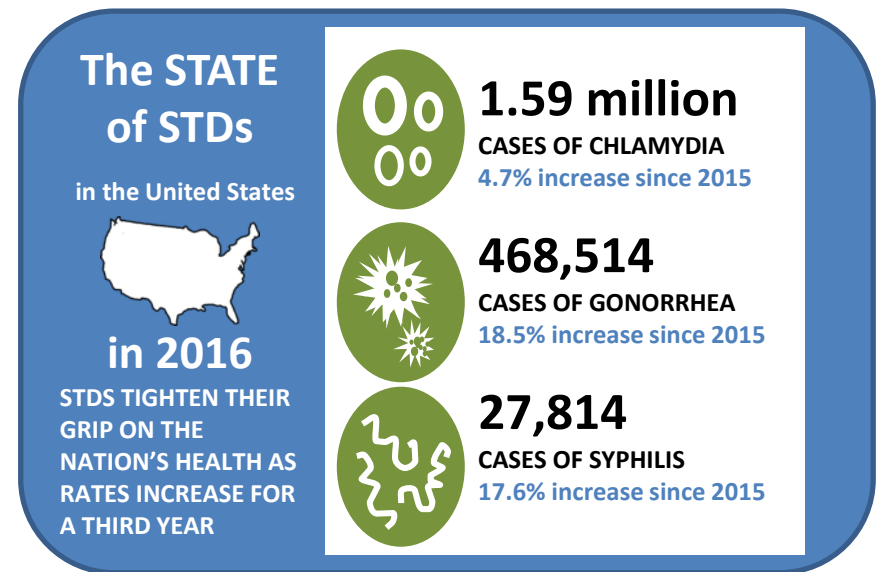
Lima, Peru, March 2018

Jeanne Marrazzo, MD, MPH

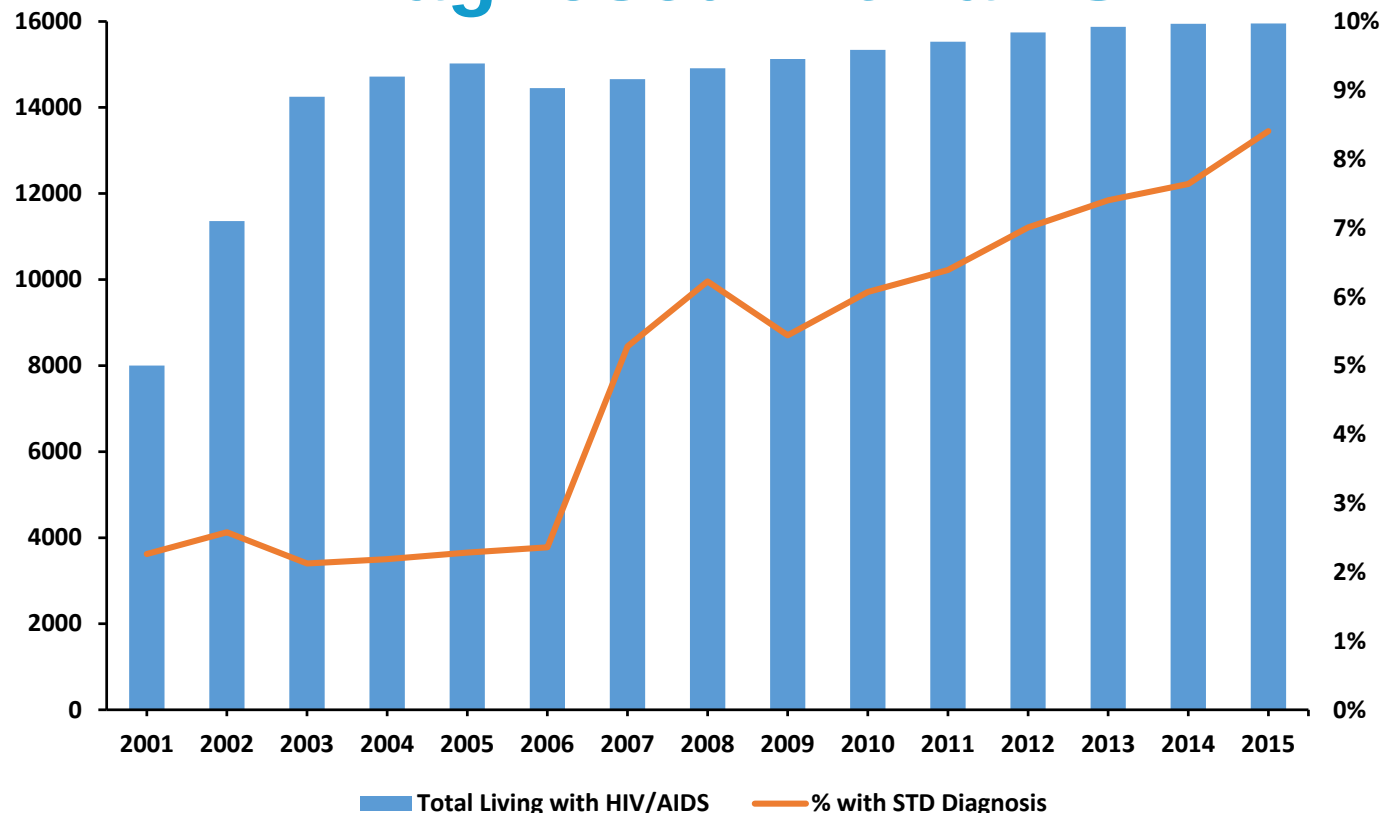
University of Alabama at Birmingham School of Medicine

What's New?

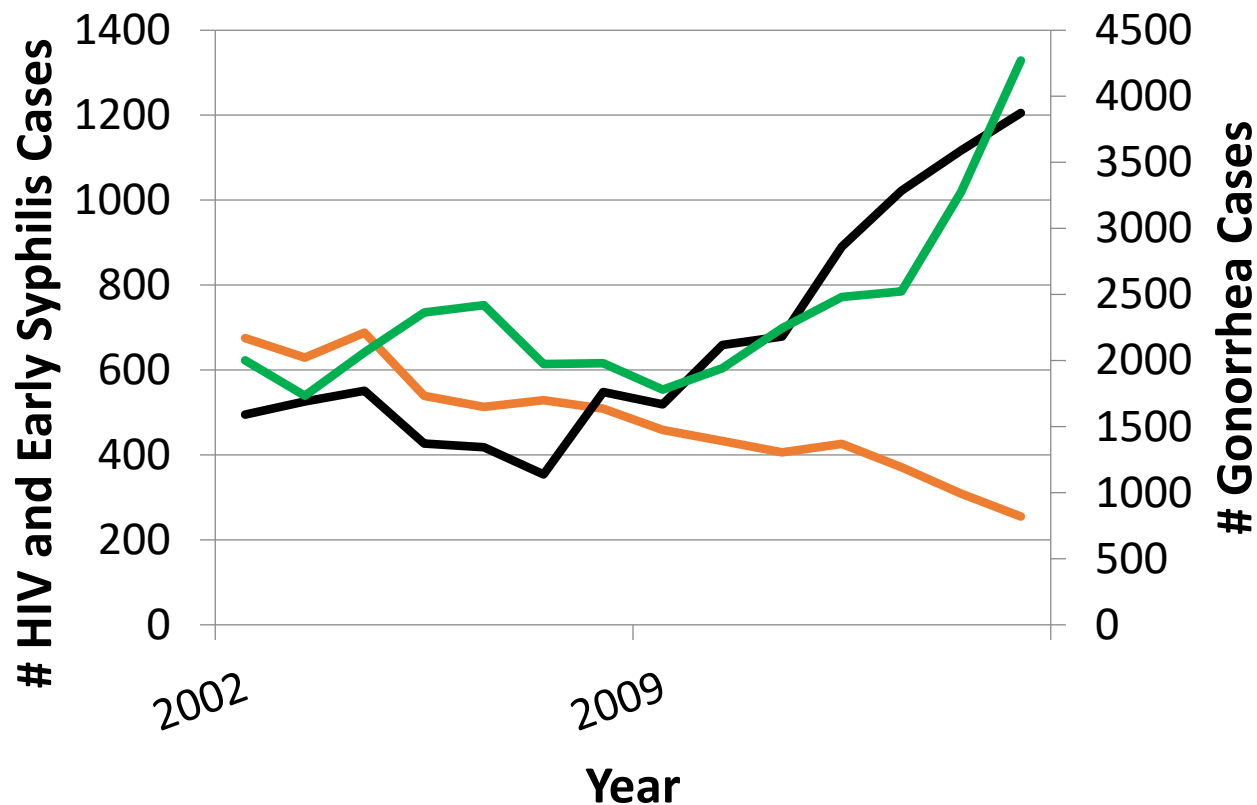
- Epidemiology in the era of PrEP/TasP
- Gonorrhea: continued antimicrobial resistance; hope for vaccine?
- Syphilis: the ongoing saga; OI guidelines
- Chlamydia: reappearance of LGV proctitis?
- STI immunizations in HIV care



More People Living with HIV are Being Diagnosed with an STD

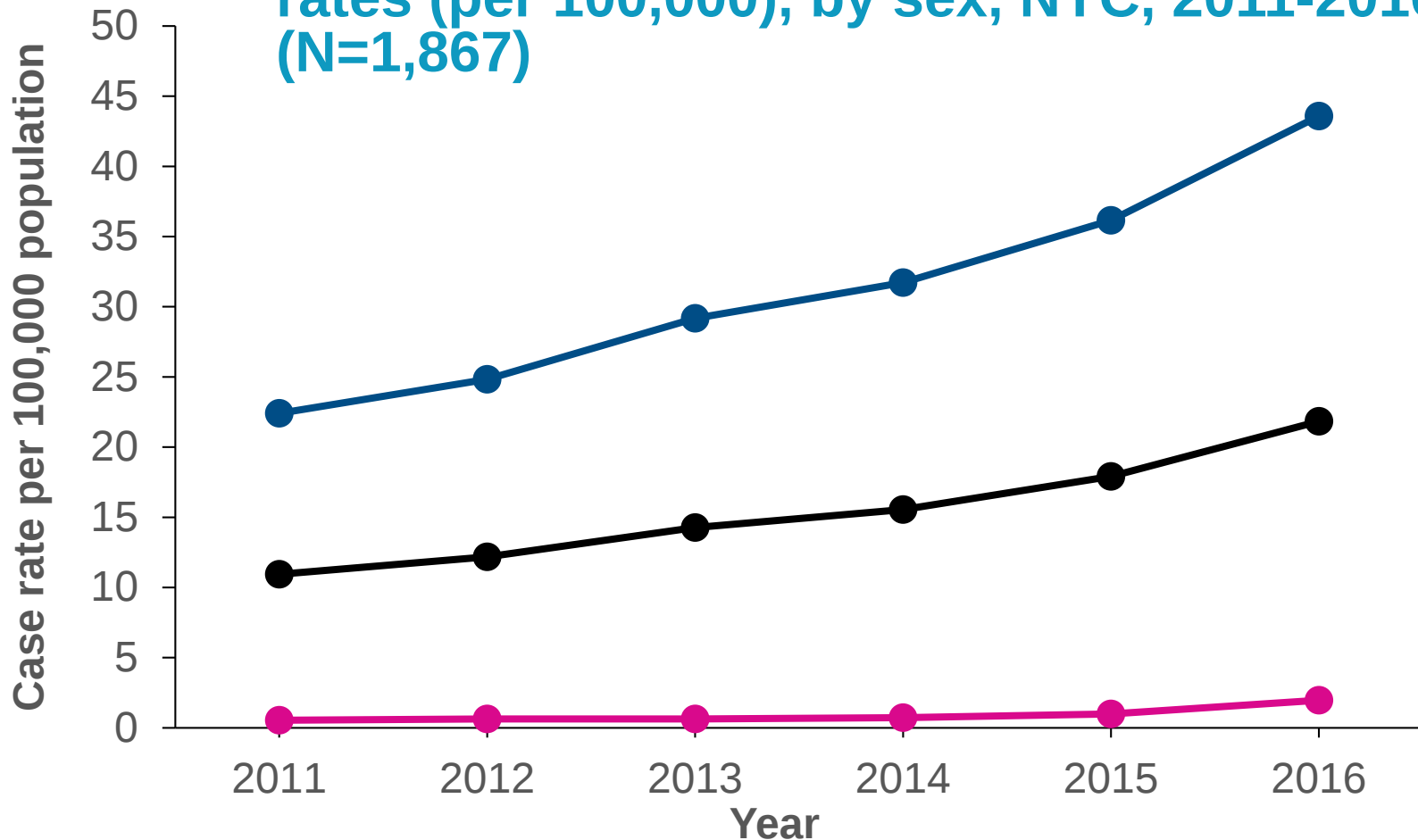


San Francisco: STD Increasing while HIV Diagnoses Decline

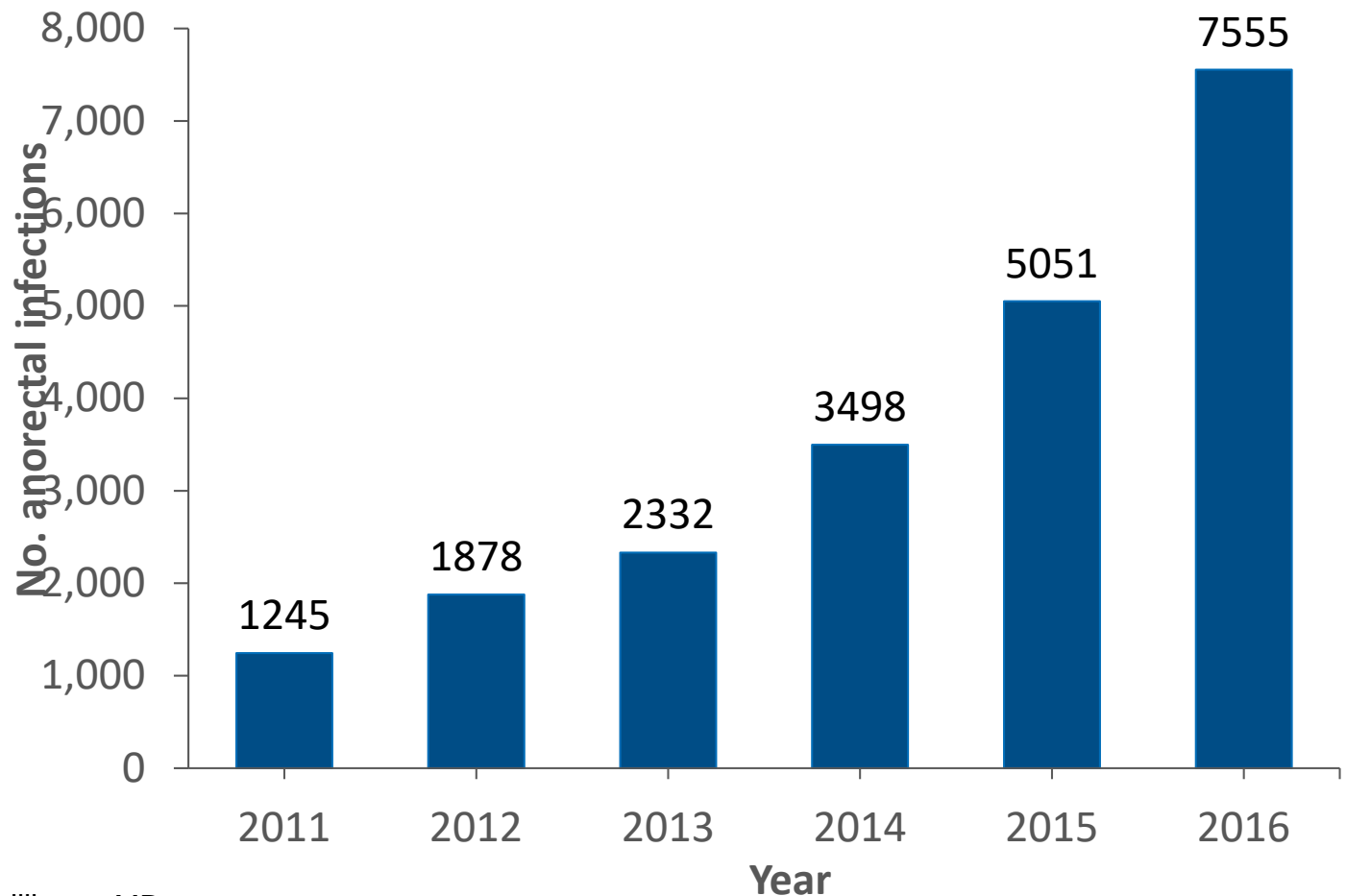


Courtesy of Susan Phillip and the SFDPH Population Health Division, Applied Research Community Health Epidemiology and Surveillance Branch

Reported primary and secondary syphilis case rates (per 100,000), by sex, NYC, 2011-2016 (N=1,867)



Male anorectal chlamydia and gonorrhea cases reported to the DOHMH, NYC, 2011-2016*

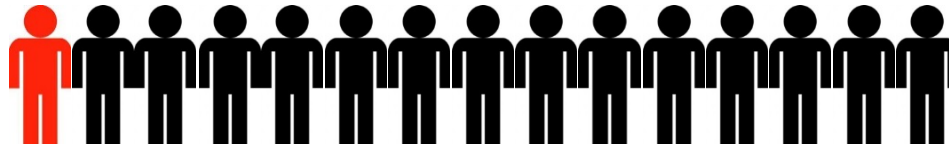


*Preliminary

Slide courtesy of Julia Schillinger, MD

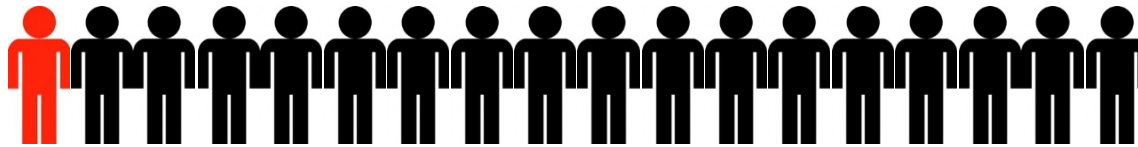
A Vicious Cycle: STDs *predict* future HIV Risk

Rectal GC
or CT



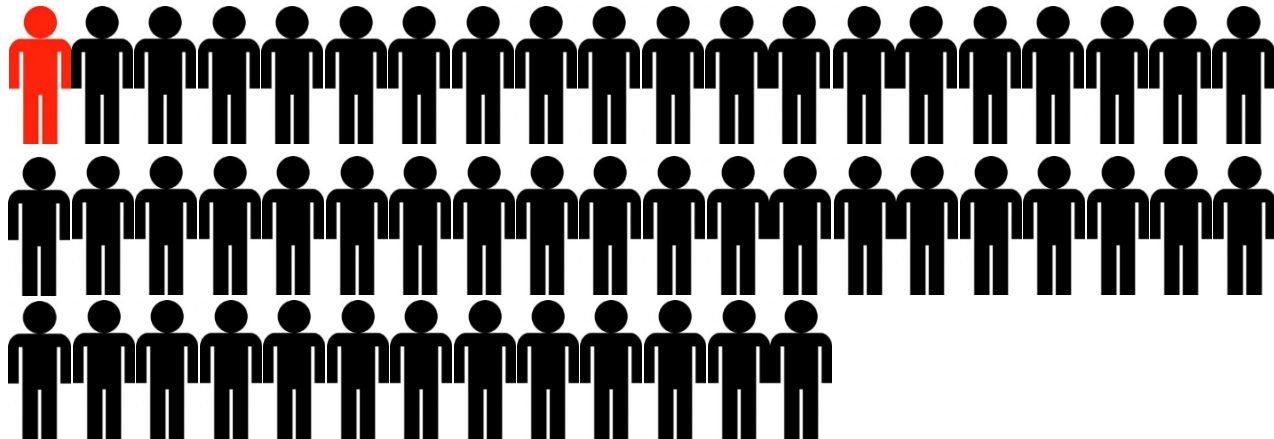
1 in 15 MSM were diagnosed with HIV within 1 year.*

Primary or
Secondary
Syphilis



1 in 18 MSM were diagnosed with HIV within 1 year.**

No rectal STD
or syphilis
infection



1 in 53 MSM were diagnosed with HIV within 1 year.*

*STD Clinic Patients, New York City. Pathela, CID 2013:57;

**Matched STD/HIV Surveillance Data, New York City. Pathela, CID 2015:61

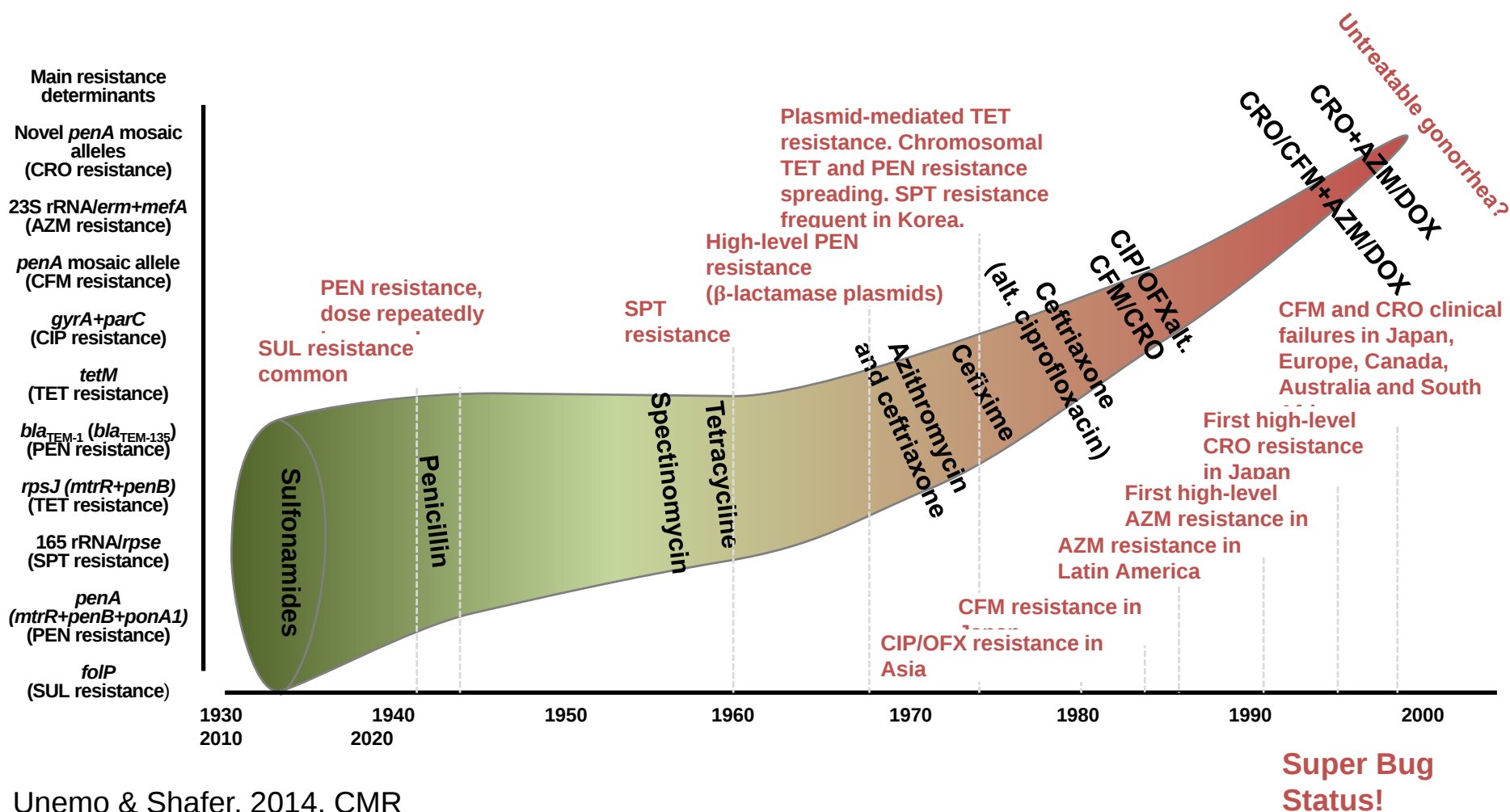




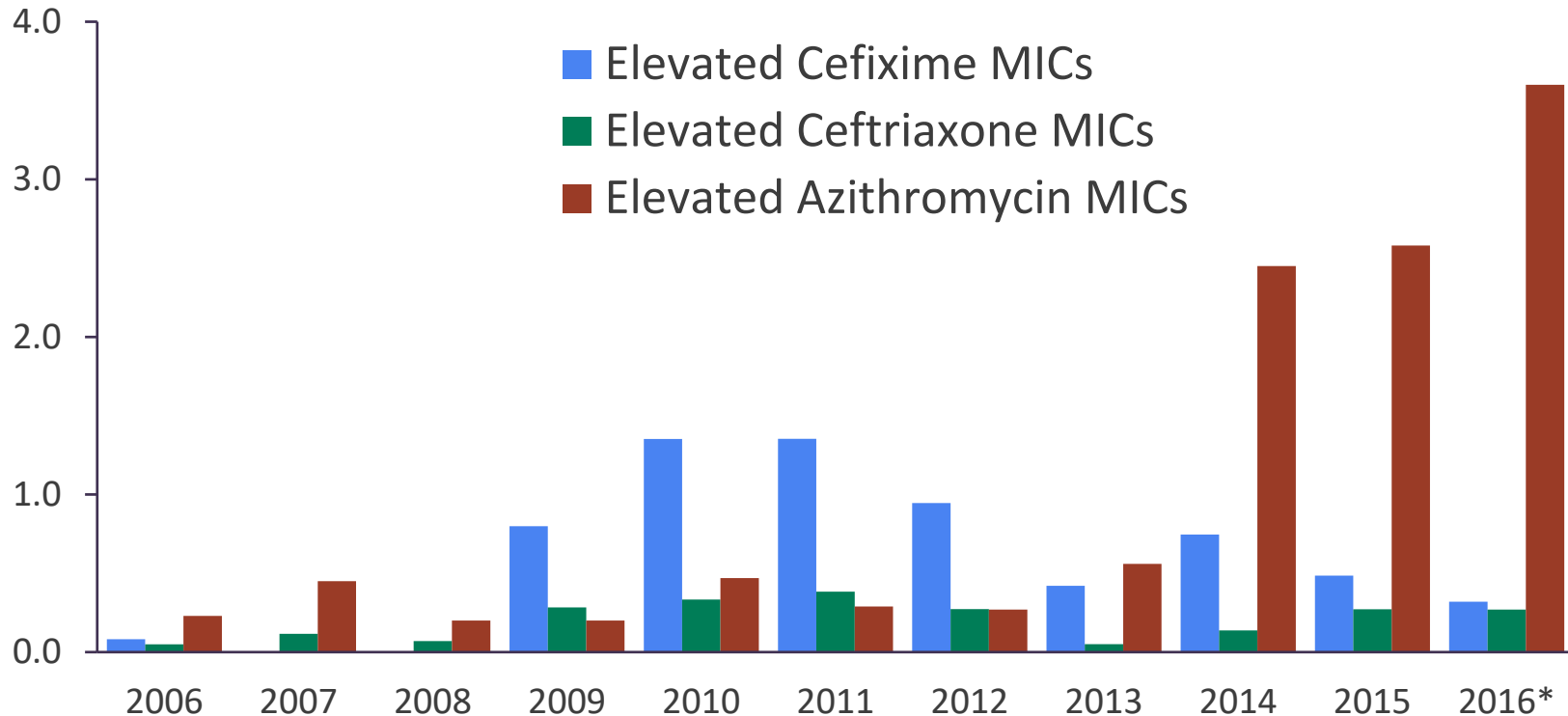
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Gonorrhea Therapy: The Shrinking Pipeline



Percentage of Isolates with Elevated Cefixime MICs, Elevated Ceftriaxone MICs, and Elevated Azithromycin MICs, GISP, 2006–2016



*Cefixime not tested in 2007 & 2008

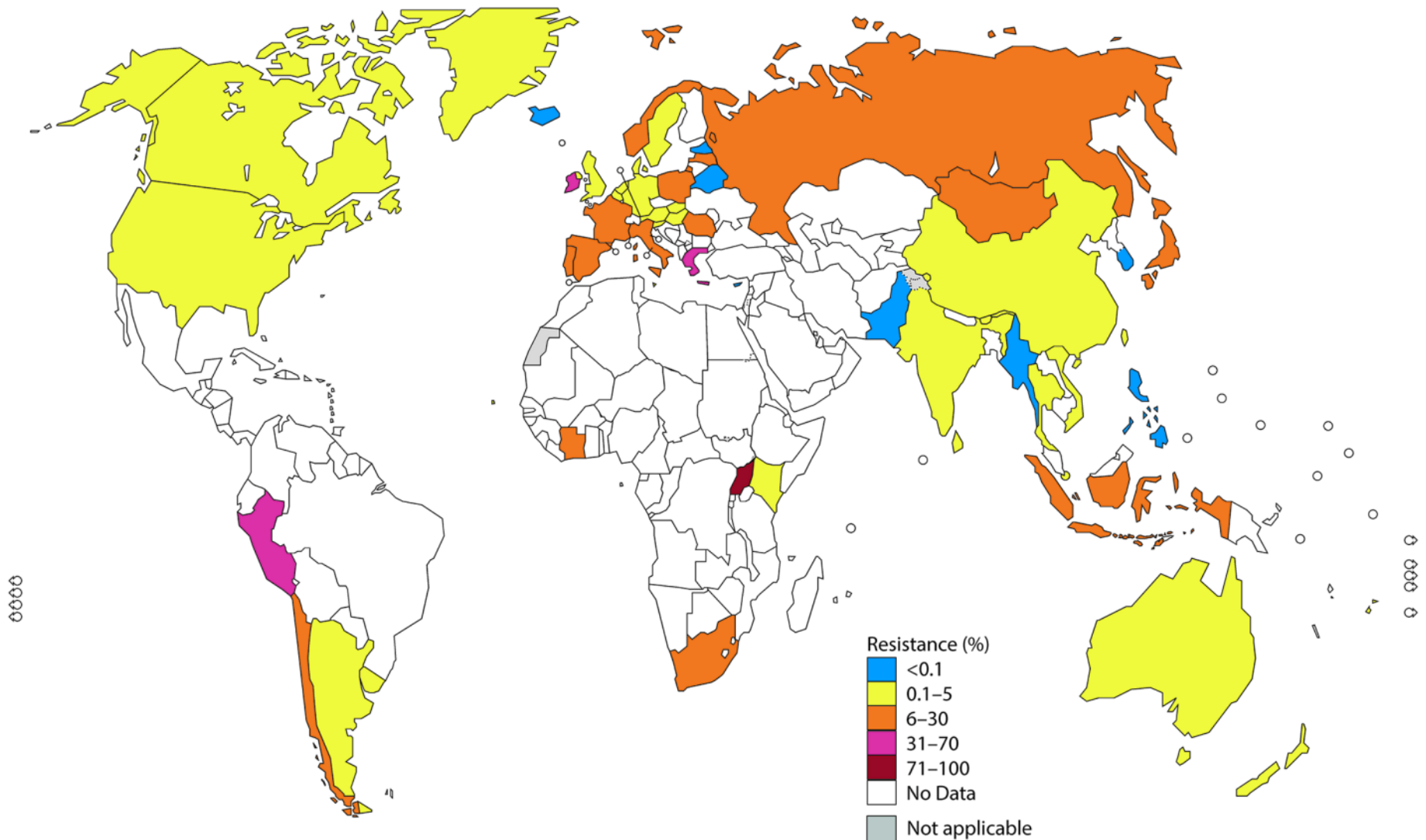


Fig 2. The percentage (%) of isolates with resistance to azithromycin according to the most recent World Health Organization (WHO) Gonococcal Antimicrobial Surveillance Programme (GASP) data (2014 for most countries, but for a few countries, only 2011–2013 data were available). Note: The areas in grey are disputed territories (e.g., Western Sahara, Jammu, and Kashmir), and no antimicrobial resistance (AMR) data are available from these regions.

2015 CDC STD Treatment Guidelines: Uncomplicated Gonorrhea Infection

- Ceftriaxone 250 mg injection x 1
- PLUS:
 - Azithromycin 1 g orally x 1

Doxycycline removed as
second agent

2015 Gonorrhea Treatment Guidelines: If Cephalosporin Allergy

Gentamicin
240 mg IM x 1

OR

Gemifloxacin
320 mg PO x 1

+

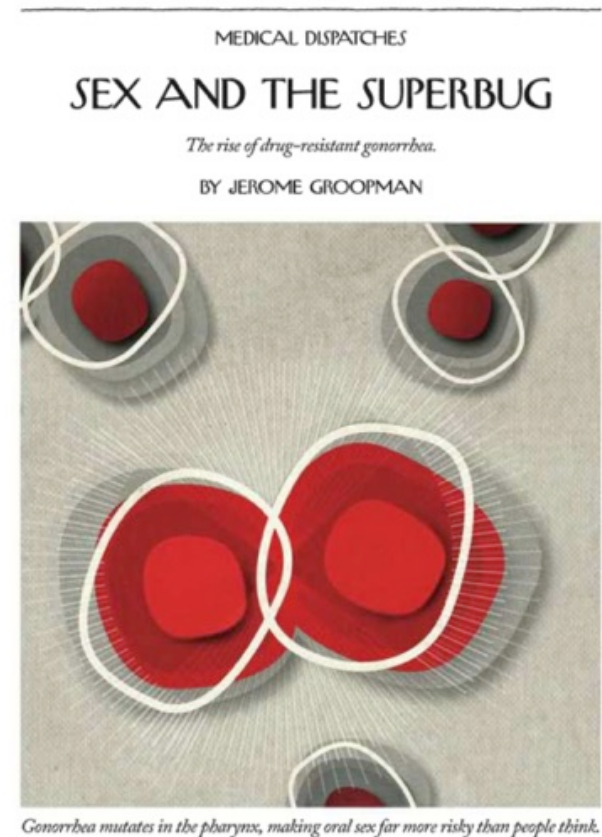
Azithromycin
2 g PO x 1

NOTES:

- Urogenital infections only
- Gemifloxacin remains in shortage

Managing Treatment Failure

- **Most treatment failure likely due to reinfection**
- If suspect treatment failure, obtain culture & susceptibility, ensure partner treatment
 - If reinfection likely (after ceftriaxone/azithro): ceftriaxone 250 mg + azithromycin 1 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)



THE NEW YORKER



"What's the next best medicine?"

What's Next for Treatment?

- Zoliflodacin (AZ D0914)
 - Spiropyrimidinetrione
 - Topoisomerase inhibitor
 - Activity at rectum; limited at pharynx
 - Apparent activity vs. *C. trachomatis*, *M. genitalium*
 - Phase II trial completed (Taylor SA et al; IDSA 2016)
- Gepotidacin (BTZ116576)
 - Triazaacenaphthylone antibiotic (topoisomerase inhibitor)
 - High efficacy potential – 3 separate ribosomal targets
 - Extra-genital activity unknown
 - Unknown activity vs. *C. trachomatis*, *M. genitalium*
 - Phase II trial completed – results pending



- Many “new” clinical manifestations
 - Ocular disease
- Indications for lumbar puncture
- Serologic non-response
- Treatment

Ocular Syphilis — Eight Jurisdictions, United States, 2014-2015

Sara E. Oliver, MD^{1,2}; Mark Aubin³; Leak Atwell, MPH⁴; James Matthias, MPH^{4,5}; Anna Cope, PhD^{5,6}; Victoria Mobley, MD⁶; Alexandra Goode, MSc⁷; Sydney Minnerly, MA⁸; Juliet Stoltey, MD⁹; Heidi M. Bauer MD⁹; Robin R. Hennessy, MPH^{5,10}; Dawne DiOrio, MPA^{5,11}; Robyn Neblett Fanfair, MD¹²; Thomas A. Peterman, MD⁵; Lauri Markowitz, MD²

MMWR 11/4/16

- 388 cases
- Most among MSM with HIV
 - A few among HIV-negative persons, including heterosexual men and women
- Several resulted in significant sequelae including blindness
- All should be reported within 24 h of diagnosis to Public Health

Suspected ocular syphilis and total syphilis cases — eight jurisdictions, United States, 2014-2015

Jurisdiction	Suspected ocular syphilis		Total surveillance syphilis cases		% surveillance syphilis cases with suspected ocular syphilis	
	2014	2015	2014	2015	2014	2015
California*	48	60	6,238	7,824	0.77	0.77
Florida	10	32	6,030	7,154	0.17	0.45
Indiana [†]	—	8	—	714	—	1.10
Maryland	10	17	1,524	1,779	0.66	0.96
New York City	14	12	5,798	6,116	0.24	0.20
North Carolina	21	42	1,799	2,435	1.20	1.70
Texas	27	16	7,337	8,400	0.37	0.19
Washington	27	44	857	1,125	3.20	3.90
Total	157	231	29,583	35,547	0.53	0.65

*California does not include syphilis reports from San Francisco or Los Angeles.

[†]Indiana reviewed data from 2015 only.

TABLE 2. Demographic characteristics of patients with suspected ocular syphilis — eight jurisdictions, United States, 2014-2015

Characteristic	No.	(%)
Total	388	(100.0)
Male	362	(93.3)
Known M561 (among 362 males)	249	(68.8)
Race		
White	217	(55.9)
Black	81	(20.9)
Hispanic	48	(12.4)
Asian	13	(3.4)
Native Hawaiian/Pacific Islander	1	(0.3)
Other/Unknown	28	(7.2)
HIV-positive	198	(51.0)

HIV, human immunodeficiency virus; MSM, men who have sex with men.

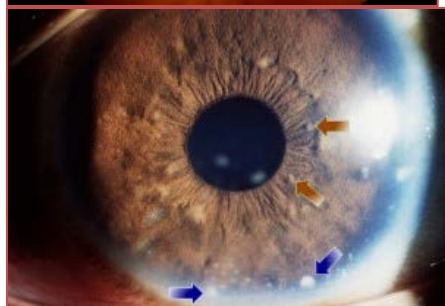


TABLE 3. Clinical characteristics, laboratory results and diagnoses for syphilis and suspected ocular syphilis — eight jurisdictions, United States, 2014-2015

Characteristic	No.	(%)
Total	388	(100.0)
Stage of syphilis		
Primary	8	(2.1)
Secondary	101	(26.0)
Early latent	79	(20.4)
Late or latent of unknown duration	193	(49.7)
Unknown	7	(1.8)
Additional symptoms of neurosyphilis	87	(22.4)
Reported ocular symptoms (among 326 with symptoms)		
Blurry vision	210	(64.4)
Vision loss	107	(32.8)
Eye pain, or red eye	46	(14.1)
Eye exam	158	(40.7)
Diagnosis (among 158 with documented eye exam)*		
Uveitis	72	(45.6)
Retinitis	20	(12.7)
Optic neuritis	18	(11.4)
Retinal detachment	6	(3.8)
CSF analysis performed	188	(48.5)
CSF VDRL (among 174 with a documented result)		
Reactive	122	(70.1)
Nonreactive	52	(29.9)
Treatment		
Aqueous penicillin G IV	230	(59.3)
Other treatment	146	(37.6)
No/Unknown treatment	12	(3.1)

CSF, cerebrospinal fluid; IV, intravenous; VDRL, Venereal Disease Research Laboratory test. *Can be included in multiple categories.

LP in Syphilis / HIV

In Favor

- CNS involvement in early syphilis is common (40%) & predicted clinical neurosyphilis in the pre-antibiotic era
- BZN PCN does not penetrate CNS
- Syphilis contained by cell-mediated immunity, and may be more severe in HIV
 - NS associated with CD4 <350, serum RPR >1:32 (Marra 2004; Libois 2007)

Against

- Frequency of serious neurosyphilis low in both untreated syphilis & early syphilis treated with BZN PCN
- PCN in CNS may not be needed to suppress early CNS invasion
- Cost & inconvenience of LP

Recommendation: careful evaluation for signs & symptoms, treatment failure

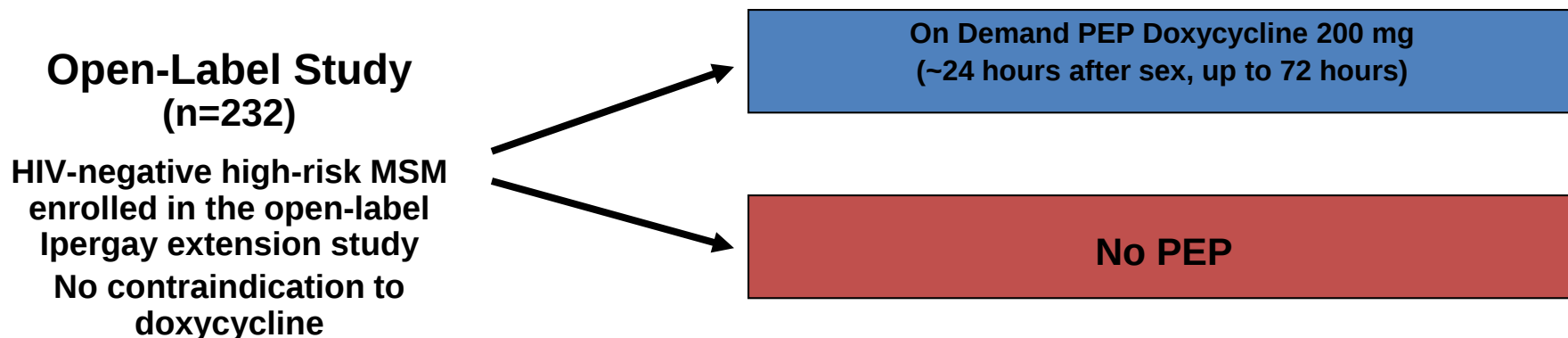
Summary

- Impressive resurgent epidemic of syphilis, especially in MSM
 - Includes neurologic syndromes, including auditory, facial nerve palsy, visual abnormalities
- Among infected MSM, at least half are co-infected with HIV
- Infection is occurring nationwide, across race / ethnicities
- Congenital syphilis events are still occurring
- Early syphilis PREDICTS HIV acquisition in those not already infected with HIV
- Serologic non-response state is probably common; careful follow-up and consideration of neurosyphilis are key

So what do we do
while we wait for a
vaccine?

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

*Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Bercot, Cécile Bébear, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Charbonneau, Alexandre Aslan, Julie Chas, Laurence Niedbalski, Bruno Spire, Luis Sagaon-Teyssier, Diane Carette, Soizic Le Mestre, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group**



Visits: baseline and every 2 months
Serologic assays for HIV and syphilis
PCR assays for chlamydia and gonorrhea
Urine, anal, and throat samples collected

Baseline characteristics:

Median age: 38-39 years

White: 95%

History of PEP use in Ipergay: 19%.

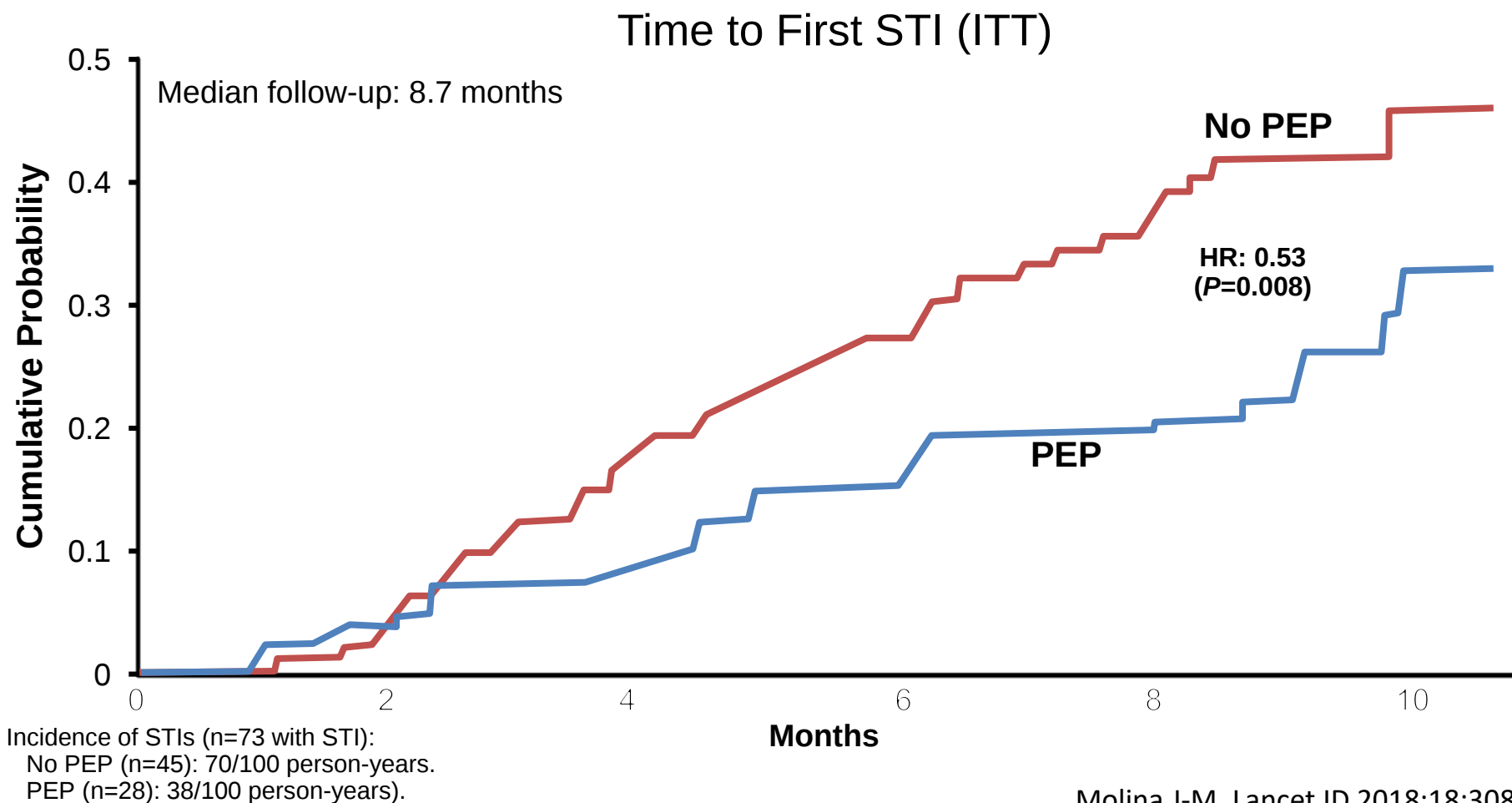
Use of psychoactive drugs (ecstasy, crack, cocaine, crystal, speed, GHB/GBL): 42%

Circumcised: 21%

Prior gonorrhea, chlamydia, syphilis infection: 16%

Number of sexual acts in prior 4 weeks: 10

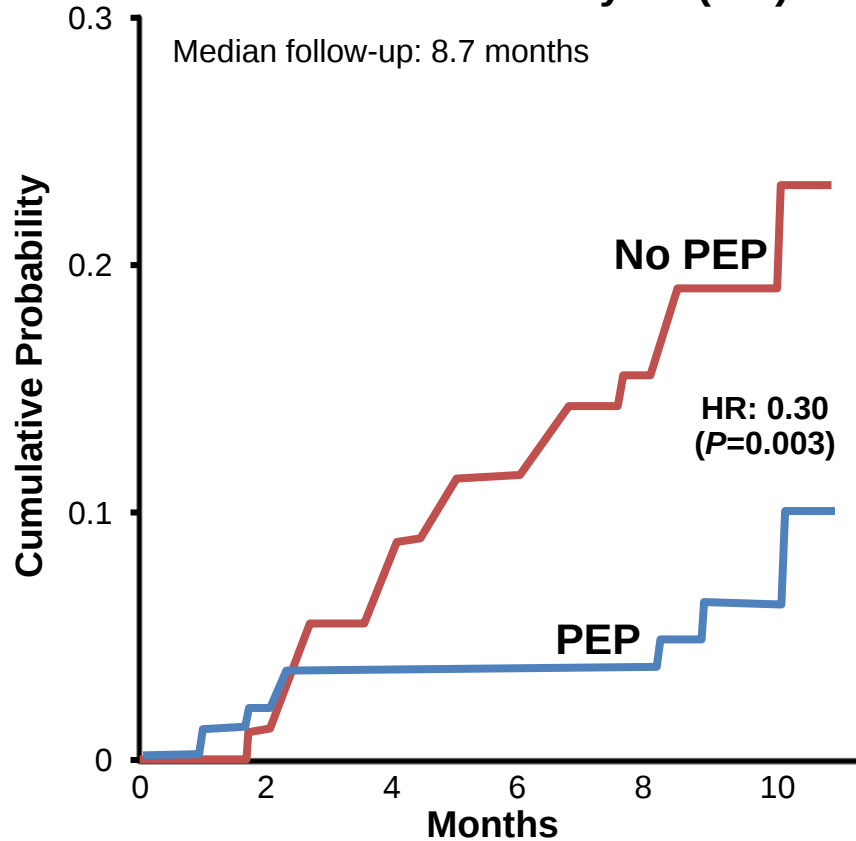
Time to First STI With On-Demand PEP With Doxycycline for MSM



Time to First Chlamydia and Syphilis With On-Demand PEP With Doxycycline for MSM

Time to First Chlamydia (ITT)

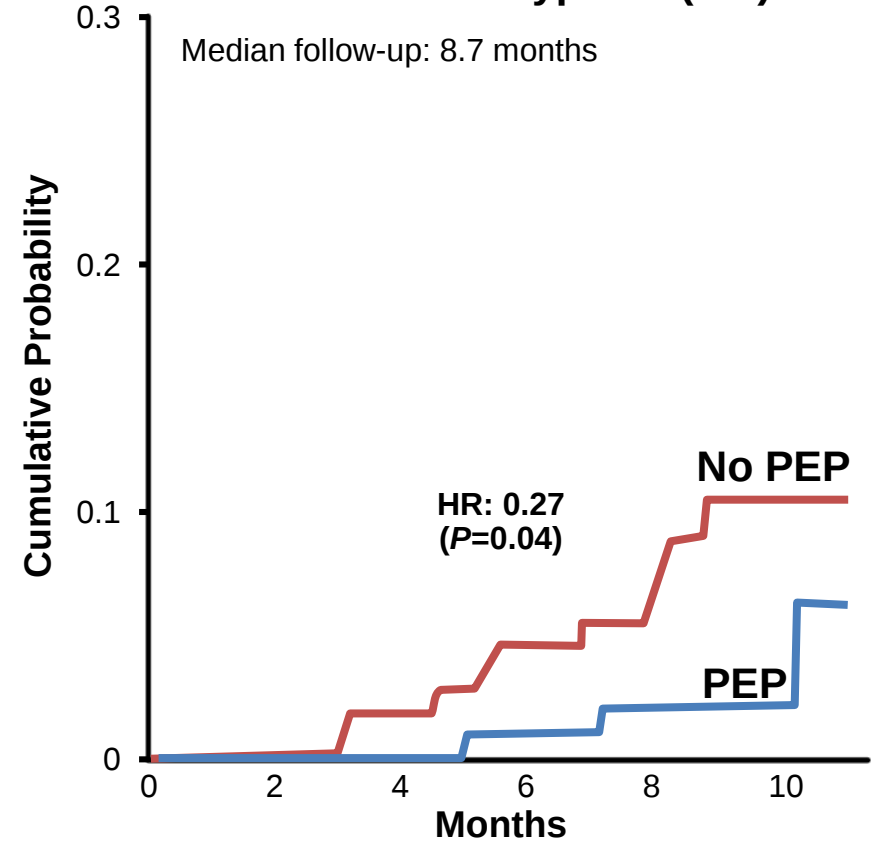
Median follow-up: 8.7 months



Incidence of chlamydia (n=28):
No PEP (n=21): 29/100 person-years.
PEP (n=7): 9/100 person-years).

Time to First Syphilis (ITT)

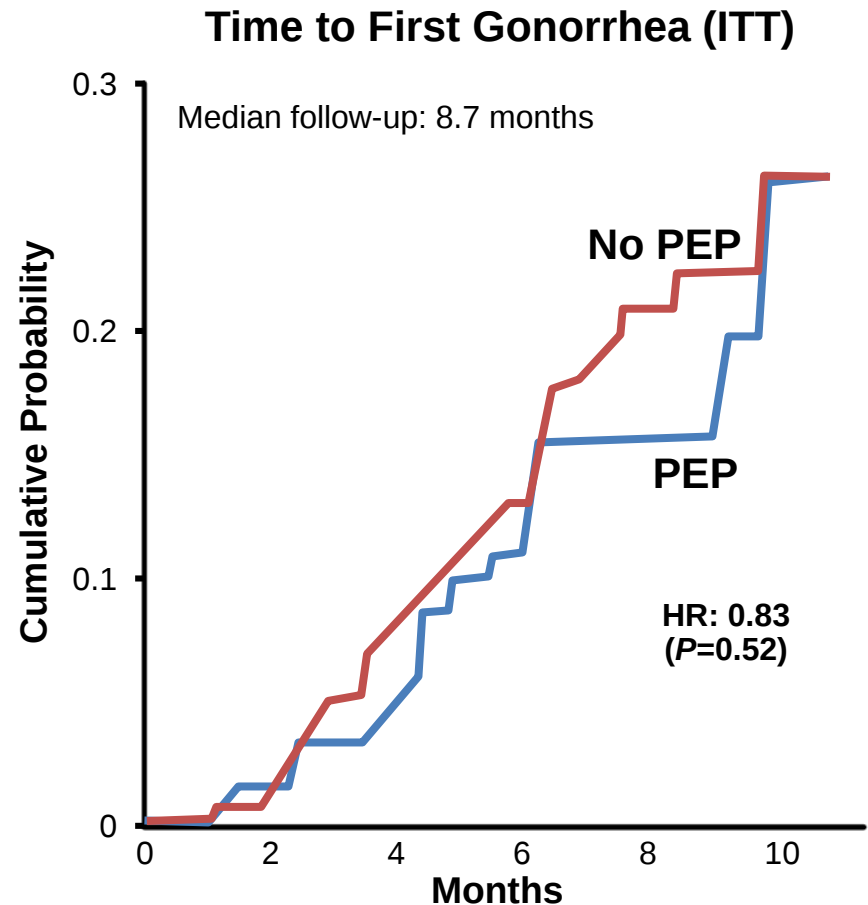
Median follow-up: 8.7 months



Incidence of syphilis (n=13):
No PEP (n=10): 13/100 person-years.
PEP (n=3): 4/100 person-years).

Time to First Gonorrhea With On-Demand PEP With Doxycycline for MSM

- No effect on gonorrhea incidence
- Number sites of gonorrhea infection (PEP versus no PEP)
 - Anus: 11 versus 19
 - Throat: 15 versus 12
 - Urine: 1 versus 7



Incidence of gonorrhea (n=47):
 No PEP (n=25): 35/100 person-years.
 PEP (n=22): 29/100 person-years).

Conclusions

- PEP reduced overall incidence of bacterial STI by 47% in MSM on PrEP (8.7 months of follow-up)
- No effect on gonorrhea, but strong reduction in chlamydia and syphilis
- Analysis of antibiotic resistance is pending
- Long-term benefit of PEP is not yet known
- More research needed
- UK BASH specifically recommended AGAINST adopting this approach clinically!

Cluster of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men — Michigan, August 2015–April 2016

Alex de Voux, PhD^{1, 2}; James B. Kent, MS³;
Kathryn Macomber, MPH³; Karen Krzanowski, MA, MPH⁴;
Dawn Jackson⁴; Tayneata Starr⁴; Sandra Johnson⁴;
Deborah Richmond, MSN⁵; Lawrence R. Crane, MD⁵;
Jonathan Cohn, MD⁵; Christopher Finch⁵; Jevon McFadden, MD⁶;
Allan Pillay, PhD²; Cheng Chen, PhD²; Laurie Anderson²;
Ellen N. Kersh, PhD²

BOX. Case definition of lymphogranuloma venereum (LGV) included
in Michigan Health Alert Network sent out on October 22, 2015

Suspected case

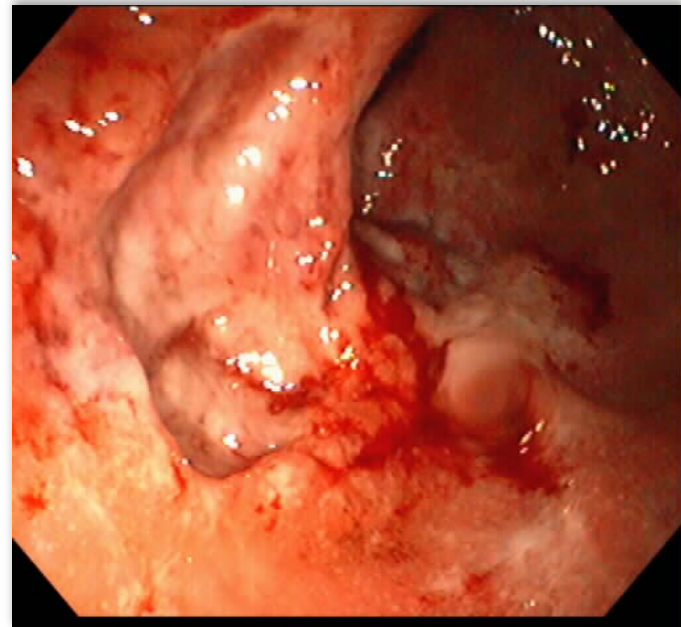
- A clinically compatible illness in a person with one or more signs or symptoms compatible with LGV (proctocolitis, inguinal/femoral lymphadenopathy, or genital or rectal ulcers), and
- A sexual partner of a person meeting the probable or confirmed case definition.

Probable case, either or both of the following:

- A patient meeting the suspected case definition, in whom other causes of LGV-like symptoms (e.g., syphilis, gonorrhea, and herpes simplex virus) have been ruled out, and a positive *Chlamydia trachomatis* from culture or nucleic acid amplification test (NAAT) from a body site associated with symptoms.
- Sexual partner of a person meeting the probable or confirmed case definition and a positive *C. trachomatis* from culture or NAAT.

Confirmed case

- A probable case with laboratory confirmation for *C. trachomatis* genotypes L1, L2, or L3 by genetic analysis (LGV-specific polymerase chain reaction or sequencing).



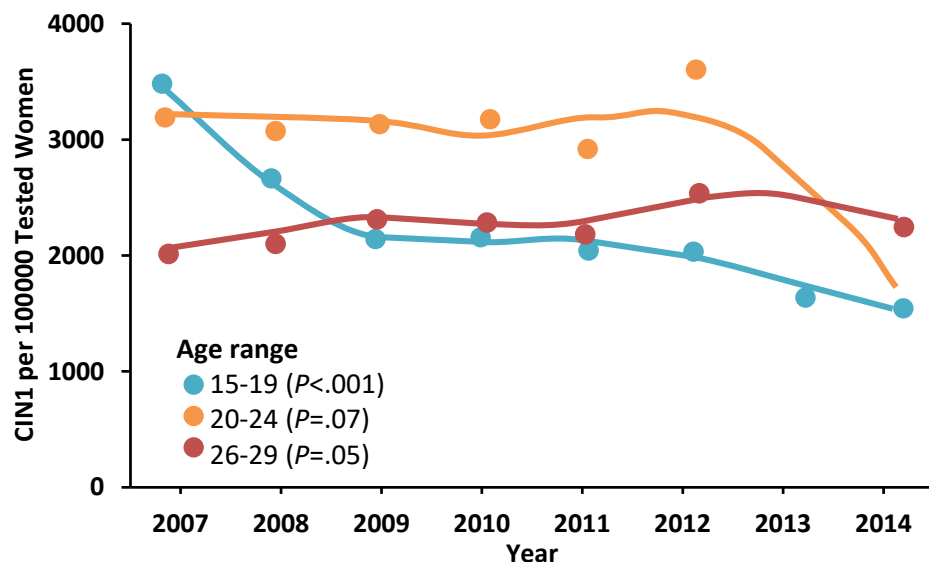
- 38 cases reported to CDC
- All HIV+ MSM
- Median CD4 483
- Suspect in severe or persistent proctitis, especially with lymphadenopathy
- Treat with doxycycline 100 mg bid x 3 weeks
- Report to local health department

“STI” Immunizations in HIV

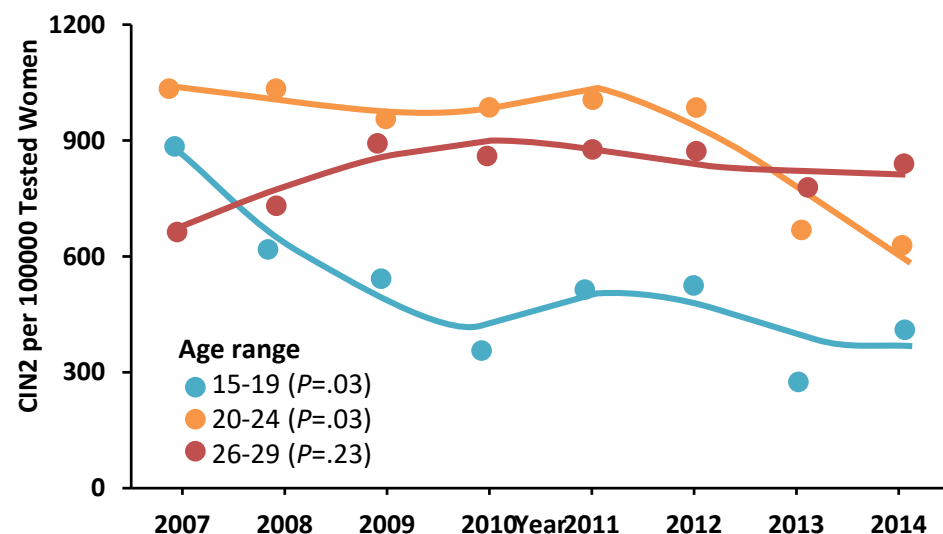
- Hepatitis A/B
- Either 9vHPV or 4vHPV vaccination through age 26 years if not vaccinated previously
- Meningococcal vaccine
 - MenACWY-D (Menactra) or MenACWY-CRM (Menveo)

Population-Based Incidence Rates of Cervical Intraepithelial Neoplasia in the Human Papillomavirus Vaccine Era

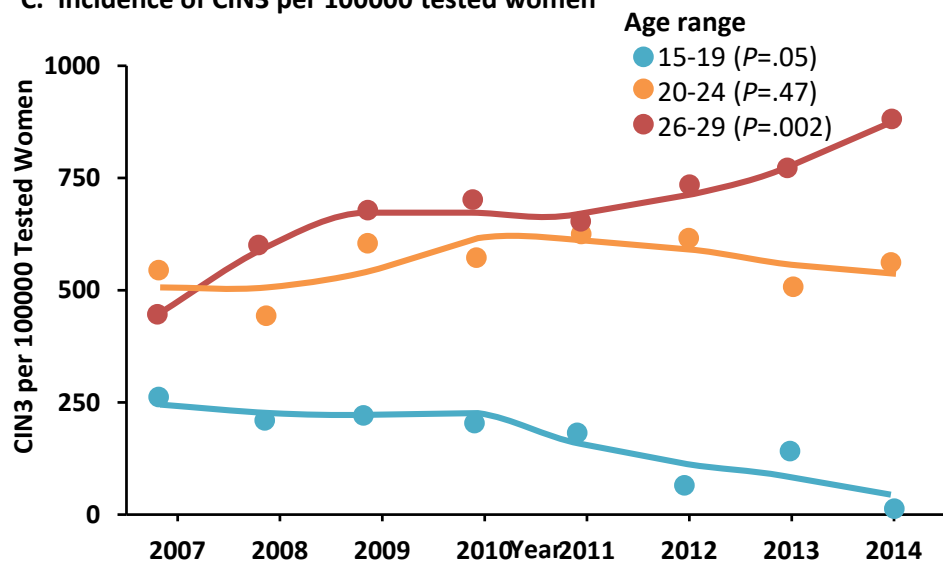
A. Incidence of CIN1 per 100000 tested women



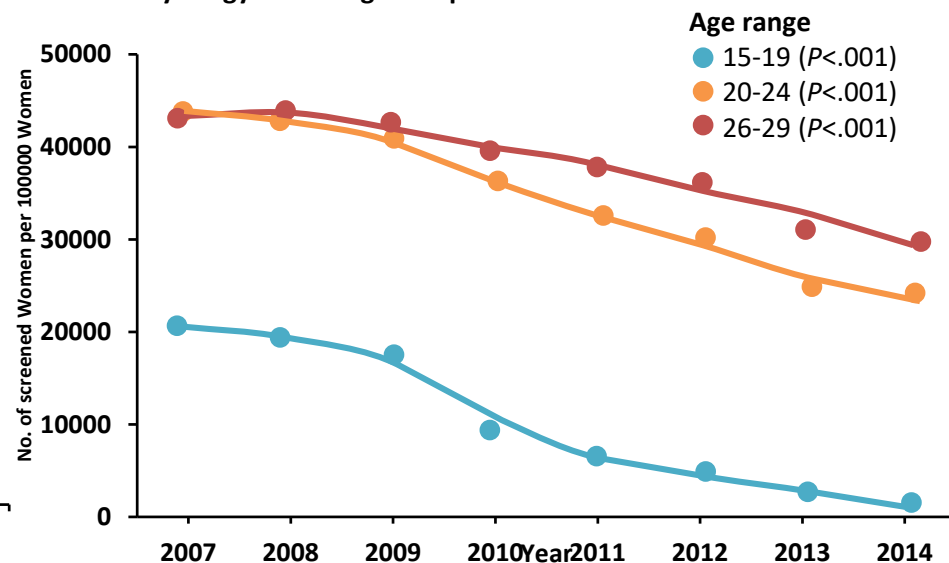
B. Incidence of CIN2 per 100000 tested women



C. Incidence of CIN3 per 100000 tested women



D. Cervical cytology screening rates per 100000 women



Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand: a retrospective case-control study

Helen Petousis-Harris, Janine Paynter, Jane Morgan, Peter Saxton, Barbara McArdle, Felicity Goodyear-Smith, Steven Black

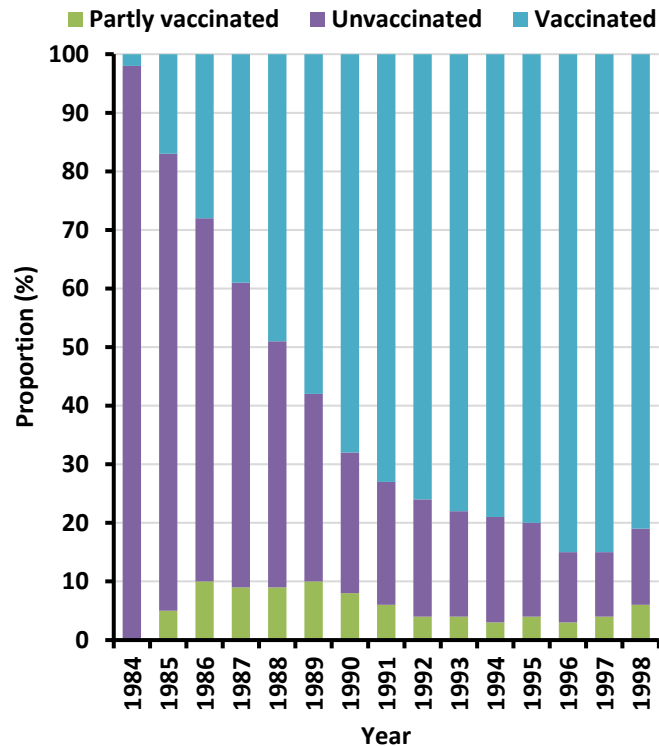


Figure 2: vaccination status of participants by year of birth

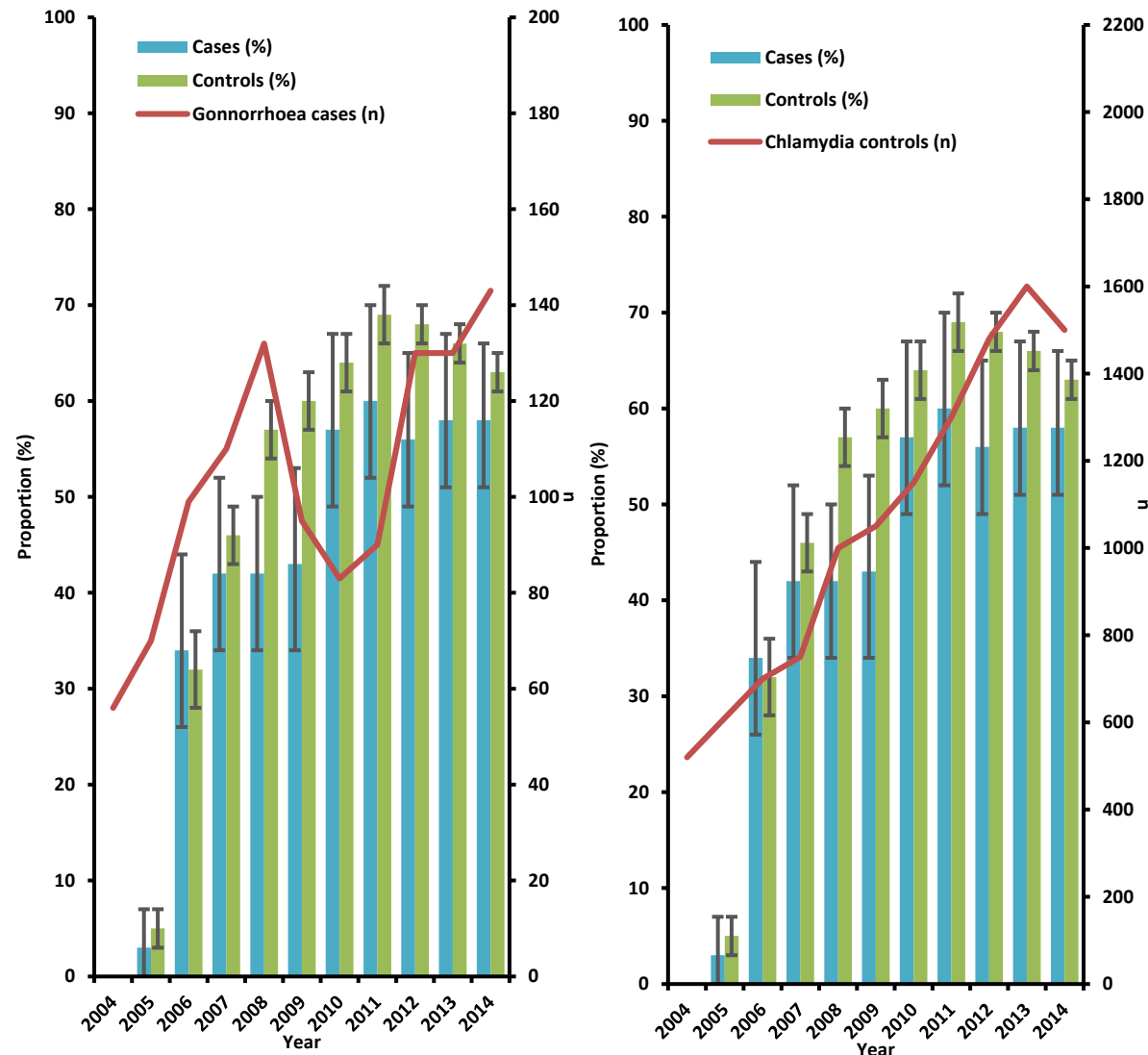


Figure 3: Year-by-year difference in the proportion of cases and controls vaccinated and number of gonorrhoea (A) and chlamydia (B) diagnoses (A) and (B) are identical except for the gonorrhoea and chlamydia counts (note the difference in right axis scales). The difference in height between each pair of columns is the unadjusted estimate of the effect of the vaccine for each year. Error bars show 95% CIs. The number of cases of gonorrhoea and chlamydia gives an indication of the sample size (and by proxy the power) in the estimate for each year. The strongest measured effect occurred in the years immediately after the vaccination program, then fell over time, suggest a possible waning of the vaccine effect.

STD Screening for MSM

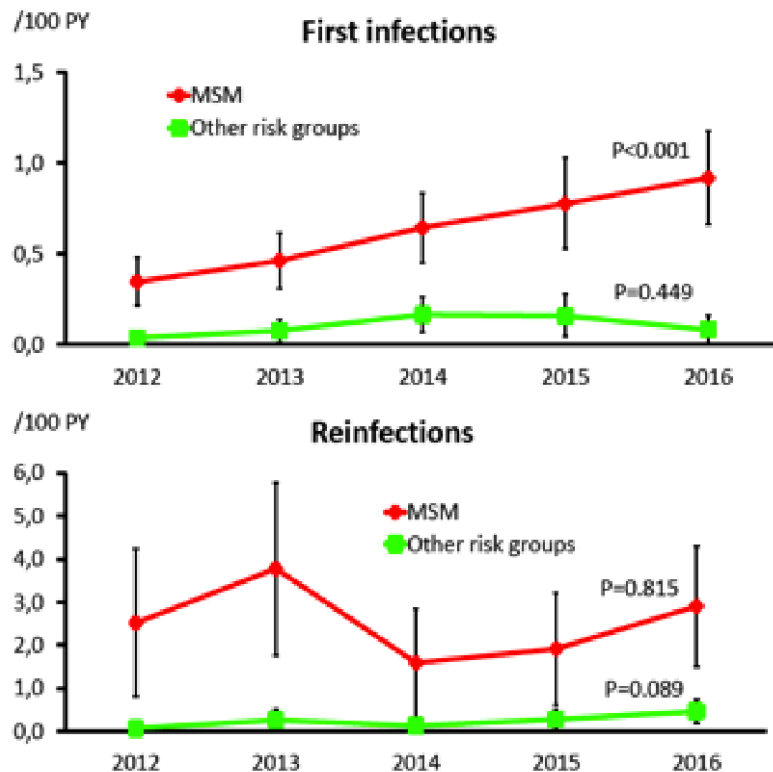
- HIV
 - Syphilis
 - Urethral GC and CT
 - Rectal GC and CT (if RAI)
 - Pharyngeal GC (if oral sex)
- 
- HSV-2 serology (consider)
 - Hepatitis B (HBsAg, freq not specified)
 - **Hepatitis C (HIV+MSM, at least annually)**

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

HCV Incidence in MSM

HCV incidence (1st infection / reinfection)



- Dat'AIDS cohort includes 25% of HIV+ people in care in France
- 38,217 HIV+ people with known HCV status, 5559 of whom (15%) already had HCV infection.
- Among people with detectable HCV RNA, 43% began DAA therapy by 2016, and 82% achieved cure either spontaneously or through DAA therapy.
- HCV incidence (new infection or reinfection) rose significantly in MSM from <0.5 per 100 p--y in 2012 to >1.0 per 100 p-y in 2016 ($P = 0.001$).
- In contrast, in a Swiss cohort, wide DAA use halved HCV incidence in HIV+ MSM (Braun DL, CROI 2018; abstract 81LB)

Serologic Screening for Genital Herpes Infection

US Preventive Services Task Force

Recommendation Statement

IMPORTANCE Genital herpes is a prevalent sexually transmitted infection in the United States, occurring in almost 1 in 6 persons aged 14 to 49 years. Infection is caused by 2 subtypes of the herpes simplex virus (HSV), HSV-1 and HSV-2. Antiviral medications may provide symptomatic relief from outbreaks but do not cure HSV infection. Neonatal herpes infection, while uncommon, can result in substantial morbidity and mortality.

OBJECTIVE To update the 2005 US Preventive Services Task Force (USPSTF) recommendation on screening for genital herpes.

EVIDENCE REVIEW The USPSTF reviewed the evidence on the accuracy, benefits, and harms of serologic screening for HSV-2 infection in asymptomatic persons, including those who are pregnant, as well as the effectiveness and harms of preventive medications and behavioral counseling interventions to reduce future symptomatic episodes and transmission to others.

FINDINGS Based on the natural history of HSV infection, its epidemiology, and the available evidence on the accuracy of serologic screening tests, the USPSTF concluded that the harms outweigh the benefits of serologic screening for genital HSV infection in asymptomatic adolescents and adults, including those who are pregnant.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends against routine serologic screening for genital HSV infection in asymptomatic adolescents and adults, including those who are pregnant. (D recommendation)

JAMA. 2016;316(23):2525-2530. doi:10.1001/jama.2016.16776

<https://jamanetwork.com/journals/jama/fullarticle/2593575>

University of Washington STI Self-Testing Program

Seattle STD Prevention Training Center

<http://www.uwptc.org>

TEST YOURSELF
The Visual Guide for a Self-collected Rectal Swab



1. Wash your hands with soap and water.
2. Remove the transport tube and collection swab from packaging.
3. Label the transport tube with your Patient label.
4. Label the transport tube with the Rectal label.
5. Open the package containing the collection swab.
6. Firmly hold the collection swab above the desired site closer to the rectum.
7. Get into a comfortable position that allows you access to your anus. Putting your foot on the step stick may help.
8. Gently insert the swab 1 inch into the rectum and twist the swab in a circle at least 5 times.
9. Remove the cap from the transport tube.
10. Place the collection swab into the transport tube, wrapping it at least 3 times.
11. Put the cap back on the transport tube and twist it closed to prevent leaks.
12. Put the transport tube into the biohazard bag.
13. Wash your hands with soap and water.

TEST YOURSELF
The Visual Guide for a Self-collected Throat Swab



1. Wash your hands with soap and water.
2. Remove the transport tube and collection swab from packaging.
3. Label the transport tube with your Patient label.
4. Label the transport tube with the Throat label.
5. Open the package containing the collection swab.
6. Hold the collection swab far enough from the tip.
7. Say "Ah," and reach the collection swab into your mouth to gently touch your throat.
8. Gently roll the swab up on your throat side to side, up and down at least 5 times.
9. Remove the cap from the transport tube.
10. Place the collection swab into the transport tube, wrapping it at least 3 times.
11. Put the cap back on the transport tube and twist it closed to prevent leaks.
12. Put the transport tube into the biohazard bag.
13. Wash your hands with soap and water.

Table 1. Key research questions.

Overall	• Is the high incidence of STI likely to undermine the success of TasP or PrEP in the long term, in certain populations, or with new PrEP agents? • Can approaches focused on broader spectrum prevention (i.e., agents that inhibit HIV and other viruses) be effective for both HIV and STI PrEP? • What are the broad implications, including funding and trial design, for clinical research in STIs and HIV?
Biology and HIV–STI synergy	• When mucosal injury occurs, does the immune environment influence healing time? • What does hormonal contraception do to the interaction of STI and HIV and to the vaginal microbiome? • Are these processes different in the adolescent genital tract? • How does asymptomatic rectal STI and its treatment perturb the rectal mucosal environment and its receptivity to HIV infection? • For non-TDF-FTC PrEP regimens, can inflammation facilitate breakthrough replication that could overcome the effect of PrEP or promote the risk of HIV/STI transmission? • Could HIV cure strategies that involve interventions to “shock” the virus from latent reservoirs release transmissible virus in the genital tract?
Epidemiology of STIs and sexual behavior in the PrEP era	• To what degree is the increased detection of STI in persons on PrEP due to increase screening (ascertainment bias) versus a true increase in acquisition? • How will prolonged PrEP use impact sexual behavior and sexual networks? • How is PrEP utilized in the context of multiple sexual partnerships? • What is the relative contribution of enhanced detection through routine screening among PrEP users and HIV-infected MSM in care versus absolute increases in STI acquisition due to increases in unprotected sex?
Implementation science	• What innovative testing strategies improve STI diagnosis among individuals on PrEP? • What will be the economic and workforce implications of the increase in STI screening we will continue to see with expanding use of PrEP? • Can STI clinics integrate the provision of PrEP as part of their menu of services? • Can primary care settings seeing patients at risk for HIV improve the quality of STI screening and service provision? • What interventions decrease racial/ethnic disparities in PrEP uptake and STIs?
Study design	• How can we leverage HIV prevention studies using the factorial design strategy to “layer on” STI prevention interventions? • What STI prevention strategies are amenable to more efficient studies focused on operational endpoints (i.e., coverage) instead of effectiveness? • Can the stepped wedge cluster randomized trial approach be used more widely to study clinic-based and population-based STI prevention strategies?

Abbreviations: PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; TasP, treatment as prevention; TDF-FTC, tenofovir-emtricitabine

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Implications for the STI-HIV Research Agenda

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Take-Home Messages

- Screen, appropriately!
- Be aware of antibiotic-resistant GC
- Syphilis: it's not going away. Recognize neuroinvasive disease & don't treat serofast individuals infinitely
- Hepatitis C is an ongoing STI, increasing in some populations despite effective treatment
- Sexual health
 - Vaccinate for HPV, meningococcus, hepatitis A/B
 - Continue Pap screening, and watch for evolving guidelines
 - Prevention messages

Thank you!

- Ken Mayer
- Ned Hook
- Susan Philip
- Ina Park
- Julie Schillinger



Single Dose Versus 3 Doses of Intramuscular Benzathine Penicillin for Early Syphilis in HIV: A Randomized Clinical Trial

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- Open-label randomized trial enrolling 64 participants; mean CD4 388
- Serologic treatment success 12 mos.
 - 28 of 35 (80%) in single-dose regimen
 - 27 of 29 (93%) in 3-dose regimen
 - Per-protocol analysis: 93% vs. 100%; absolute difference 7% (95% C.I. -7%, 22%); $P=0.49$
 - Not modified by CD4 count, RPR titer, syphilis stage
- Not powered to demonstrate non-inferiority

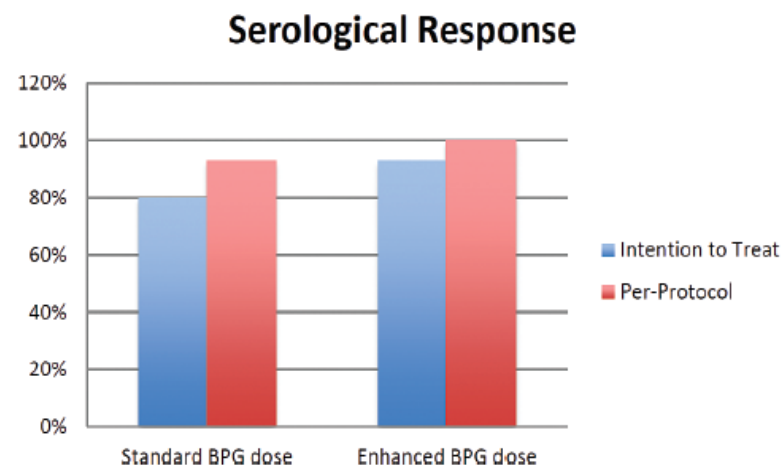


Figure 2. Intention-to-treat and per-protocol analyses of the comparison between a single dose vs 3 doses of 2.4 million units of intramuscular benzathine penicillin G (BPG) for early syphilis in human immunodeficiency virus-infected individuals. Abbreviation: BPG, benzathine penicillin G.

RESEARCH ARTICLE

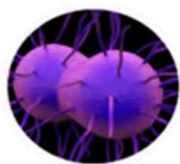
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A systematic review of syphilis serological treatment outcomes in HIV-infected and HIV-uninfected persons: rethinking the significance of serological non-responsiveness and the serofast state after therapy

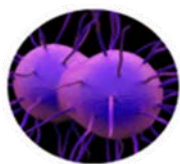
Arlene C. Seña^{1†}, Xiao-Hui Zhang^{2†}, Trudy Li³, He-Ping Zheng², Bin Yang², Li-Gang Yang², Juan C. Salazar⁴, Myron S. Cohen¹, M. Anthony Moody^{5,6}, Justin D. Radolf^{4,7} and Joseph D. Tucker¹

- Identified 1693 reports in the literature, reviewed 20
- Median proportion of patients with serological 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 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 not associated with serologic cure



ETX0914 Urogenital Microbiological Per Protocol Cure Rates

Therapy	Confirmed Infections	Cures	Micro. Cure Rate %	Micro. Cure % 95% CI
ETX0914 2g	49	48	97.96	89.15, 99.95
ETX0914 3g	47	47	100.00	92.45, 100.00
Ceftriaxone 500 mg	21	21	100.00	83.89, 100.00



ETX0914 Pharyngeal Microbiological Per Protocol Cure Rates

Therapy	Confirmed Infections	Cures	Micro. Cure Rate %	Micro. Cure % 95% CI
ETX0914 2g	6	4	66.67	22.28, 95.67
ETX0914 3g	9	7	77.78	39.99, 97.19
Ceftriaxone 500 mg	4	4	100.00	39.76, 100.00

Emerging Issues: *Mycoplasma genitalium*

- Recognized cause of urethritis
- Role in cervicitis and PID emerging
- No diagnostic test FDA cleared for use
 - NAAT available in some large medical centers and commercial laboratories
- Suspect in persistent or recurrent urethritis and consider in persistent cervicitis and PID
- Treatment implications
 - Azithromycin better than doxycycline, but...
 - Emerging resistance to azithromycin
 - Moxifloxacin for recurrence

Non-Gonococcal Urethritis (NGU) Treatment

- Azithromycin or doxycycline
- Limited data on the public health impact of *M. genitalium* to demote doxycycline
- Persistent or recurrent urethritis
 - *M. genitalium* most common cause
 - Higher azithromycin doses not effective
 - *Trichomonas vaginalis*
 - Metronidazole or tinidazole for men who have sex with women in areas of high prevalence
 - Urology referral with persistence after treatment

Persistent / Recurrent NGU Treatment

- If initially tx'd with doxy → Azithromycin
- If failed azithro → moxifloxacin 400mg qday x 7 days
- If sexually active with women & high trich prevalence add → Metronidazole or tinidazole

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