

~~2014~~ 2015 STD Treatment
Guidelines
What's New?

Kees Rietmeijer

Medical Director

Denver STD Prevention Training Center



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BRIDGING

Science & Practice



Scott Pegues
Behavioral Training Coordinator

Teri Anderson
*Associate Clinical
Coordinator*

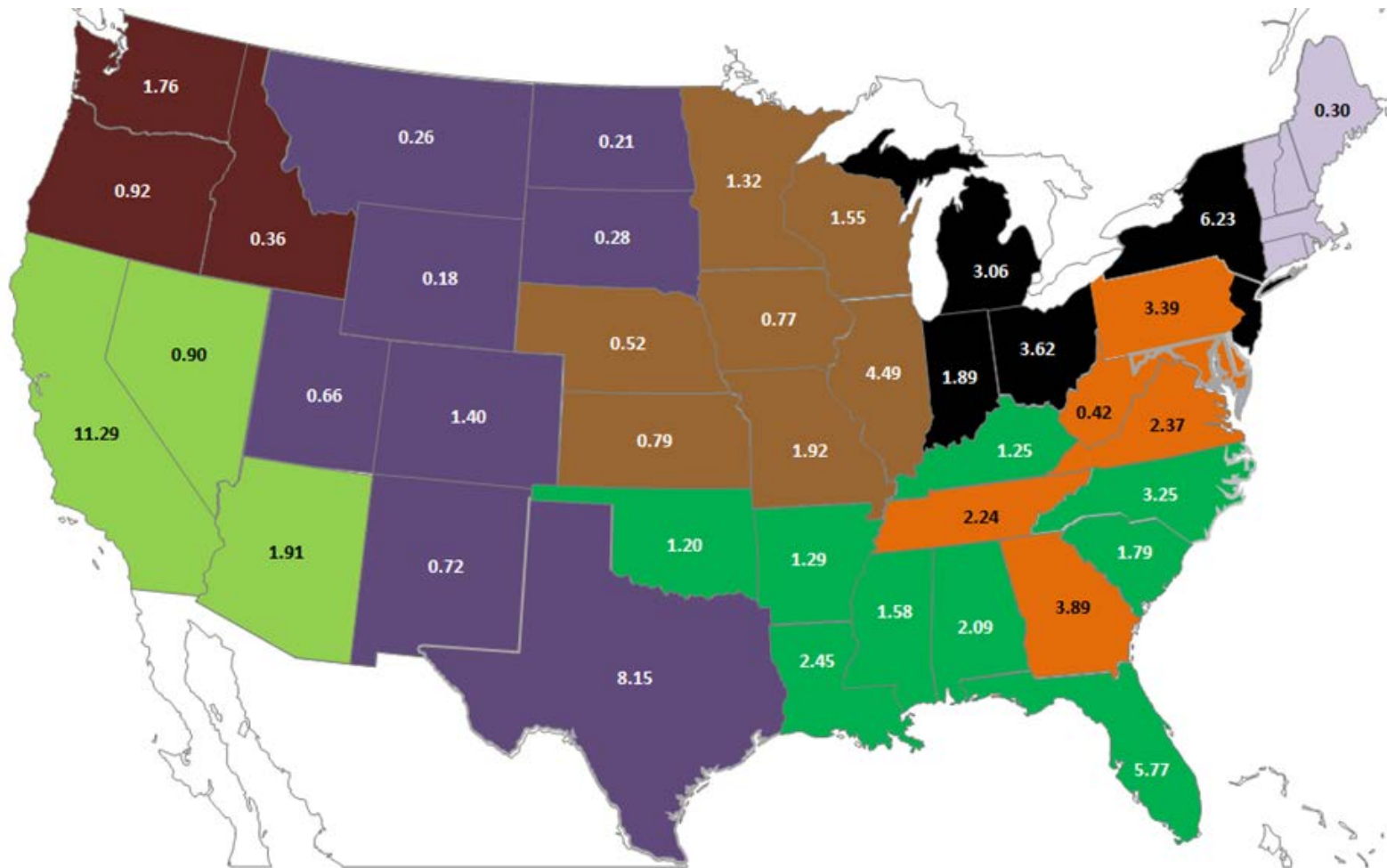


Building the capacity of health professionals through innovative training and consultation.

Source: www.denverptc.org

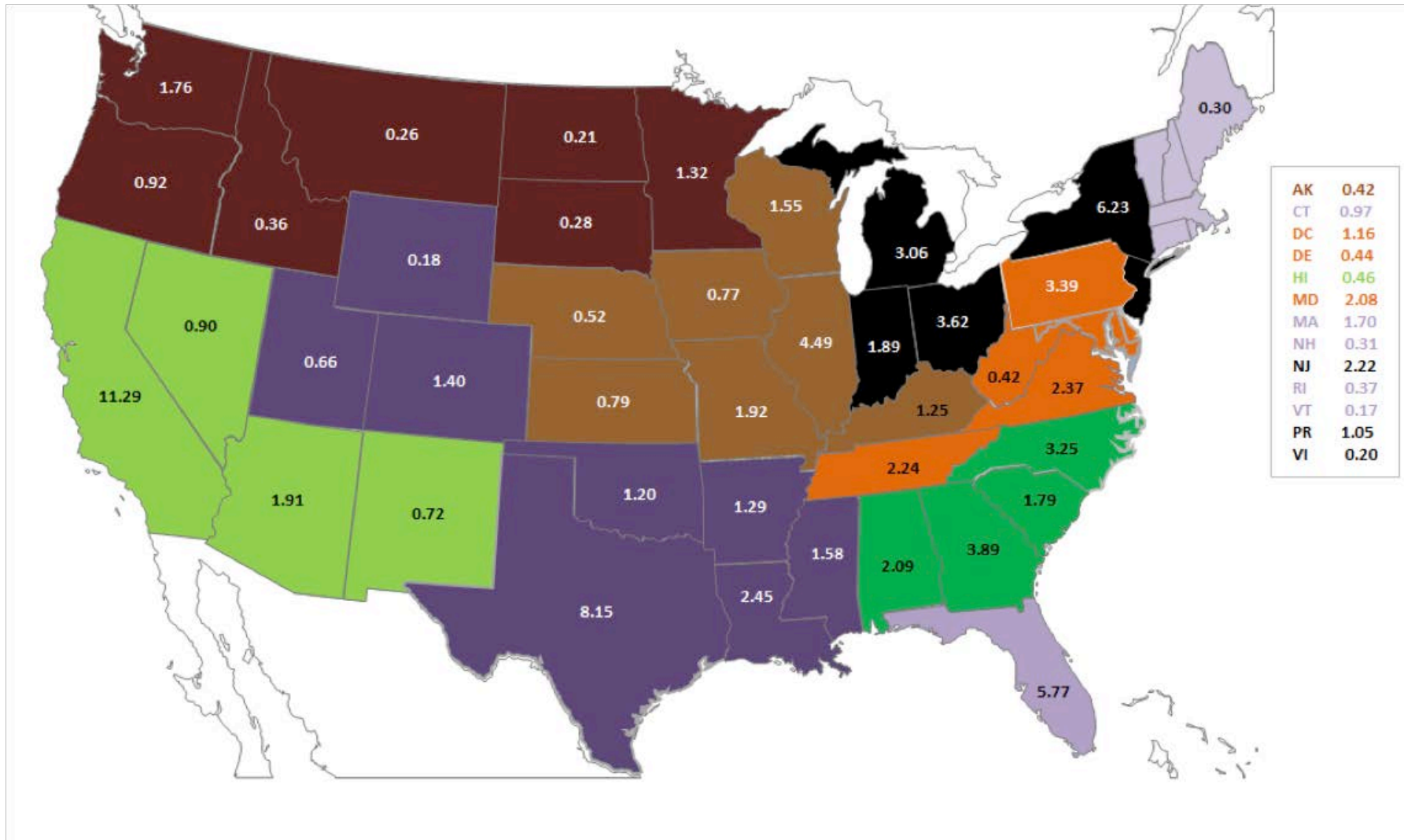


The More Things Change....



Source: NNPTC

The More They Change!



2015 CDC STD TREATMENT GUIDELINES

- ❑ **Expected release: June 5, 2015**
- ❑ **Introductory webinar: June 22, 2015**
 - www.cdc.gov/std
 - www.stdpreventiononline.org
- ❑ **Disclaimers:**

This presentation based on preliminary release

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Jeanne Mrazzazzo, MD – Seattle PTC



Treatment Guidelines Overview Webinar: June 22nd at 2:00 PM ET

May 13, 2015 NEW DATE & TIME: 2015 STD Treatment Guidelines Overview Webinar; June 22nd at 2 p.m. ET Dear Partners in Prevention: The previously announced 2015 STD Treatment Guidelines Overview Webinar has been rescheduled and will now be held on Mon

STDPO is sponsored by:



In Focus

STDPOdcast: Dr. Khalil Ghanem on Ocular Syphilis

Last week, the Centers for Disease Control and Prevention sent out a clinical advisory on an apparent increase in ocular syphilis in the United States. According to the Advisory: "Since December 2014, at least 15 cases of ocular syphilis from California and Washington have been reported to the U.S. Centers for Disease Control and Prevention. At least five other states have suspect cases under investigation. The majority of cases have been among MSM with HIV; and a

[› Learn More](#)



STDPO Partners



Want to know more about STDs? *There's an app for that.*



CDC Treatment Guidelines App
for Apple and Android

Available now, **FREE!**
(accept no competitors)

Look for “STD Tx Guide”

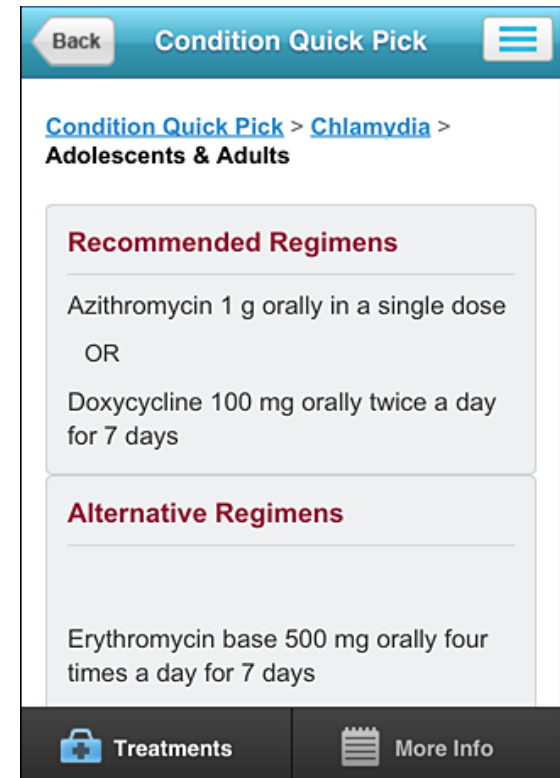
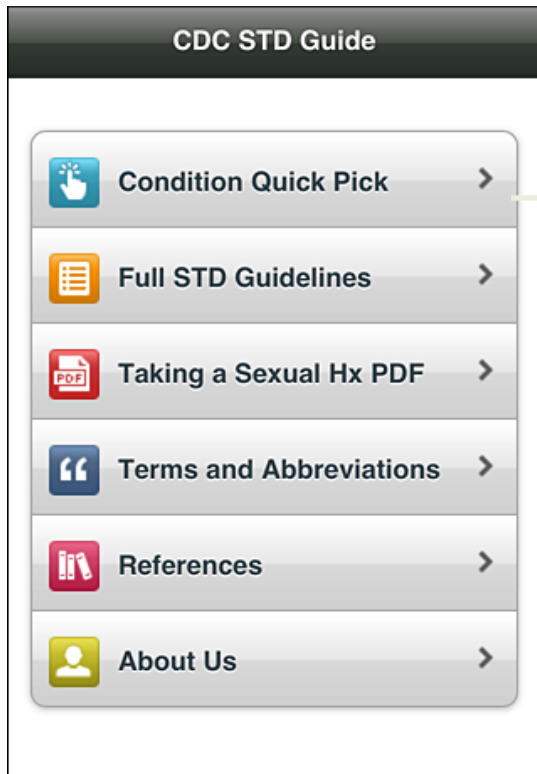
STD Treatment Mobile app



Main Menu

Condition Quick Pick

Treatment Information



STD Prevention – Key Principles

- ❑ Counseling to reduce STD acquisition
- ❑ Screening of asymptomatic persons
- ❑ Diagnosis and treatment of symptoms
- ❑ Management of sex partners
- ❑ Vaccination
 - HPV
 - Hepatitis A & B

INTRODUCTORY SECTIONS



Clinical Prevention Guidance

- Behavioral and biologic risk assessment
- High intensity behavioral counseling (USPSTF)
- Pre-exposure vaccination (HPV, HAV, HBV)
- Male latex condoms
- Male circumcision
- Microbicides
- Emergency contraception
- Pre-exposure prophylaxis for HIV**
- Retesting after treatment

Special Populations

- Pregnant women
- Adolescents
- Children
- Persons in Correctional Facilities
- MSM
- WSW
- Transgender Men and Women**

Partner Management

- Counsel on importance to client, partner(s), and community
 - Bring in your own partner (BYOP)
- Expedited partner therapy (www.cdc.gov/std/ept)
- Internet partner notification (www.inspot.org)
- Future technologies (social media)

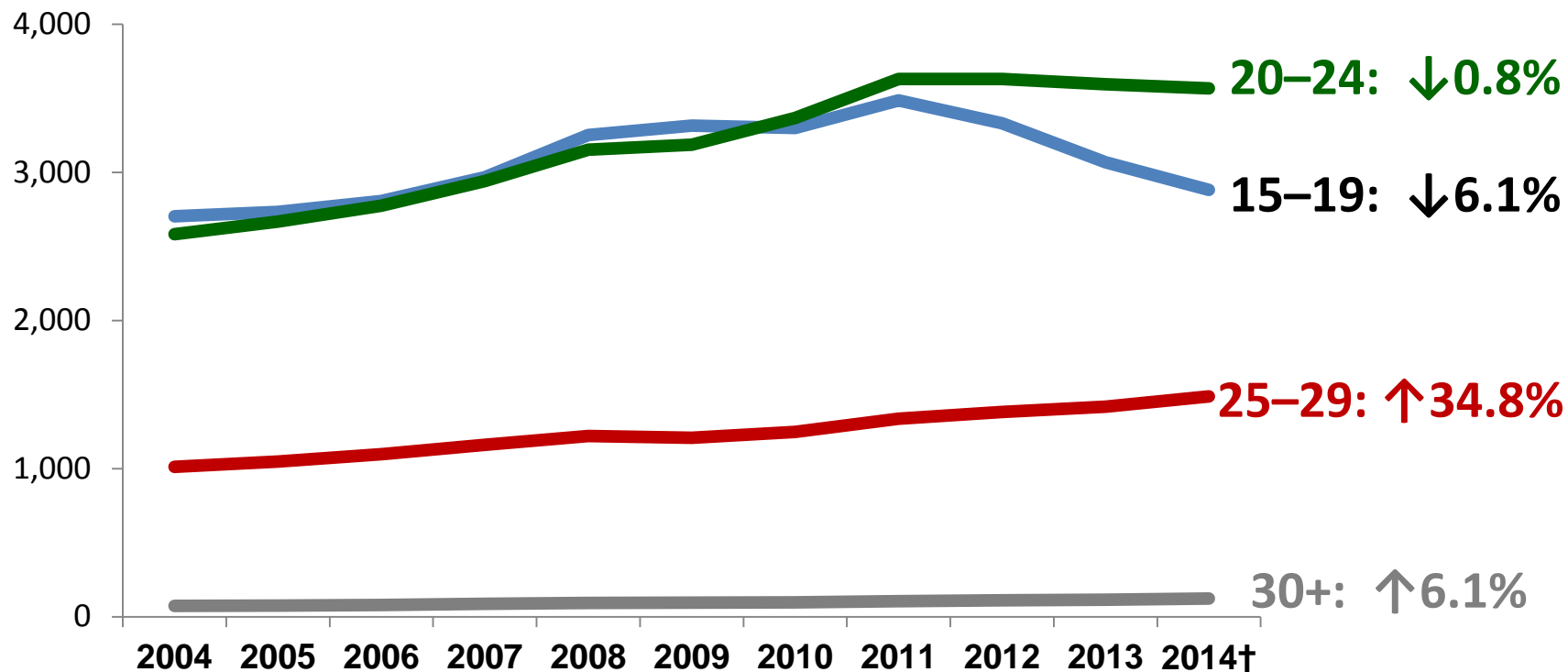
Chlamydia and Gonorrhea Screening

- ❑ Annual screening of sexually active women <25
- ❑ Screening of older women at increased risk
 - New sex partner, partner with concurrent partners or more than one partner, or partner with an STI
- ❑ Screening older women at low risk of infection not recommended
- ❑ CT screening sexually active men
 - Insufficient evidence for general screening; Consider in high prevalence (adolescent clinics, corrections, STD clinics)
- ❑ GC screening in men not recommended

Chlamydia—Rates of Reported Cases Among Women by Age Group, 2004–2014*

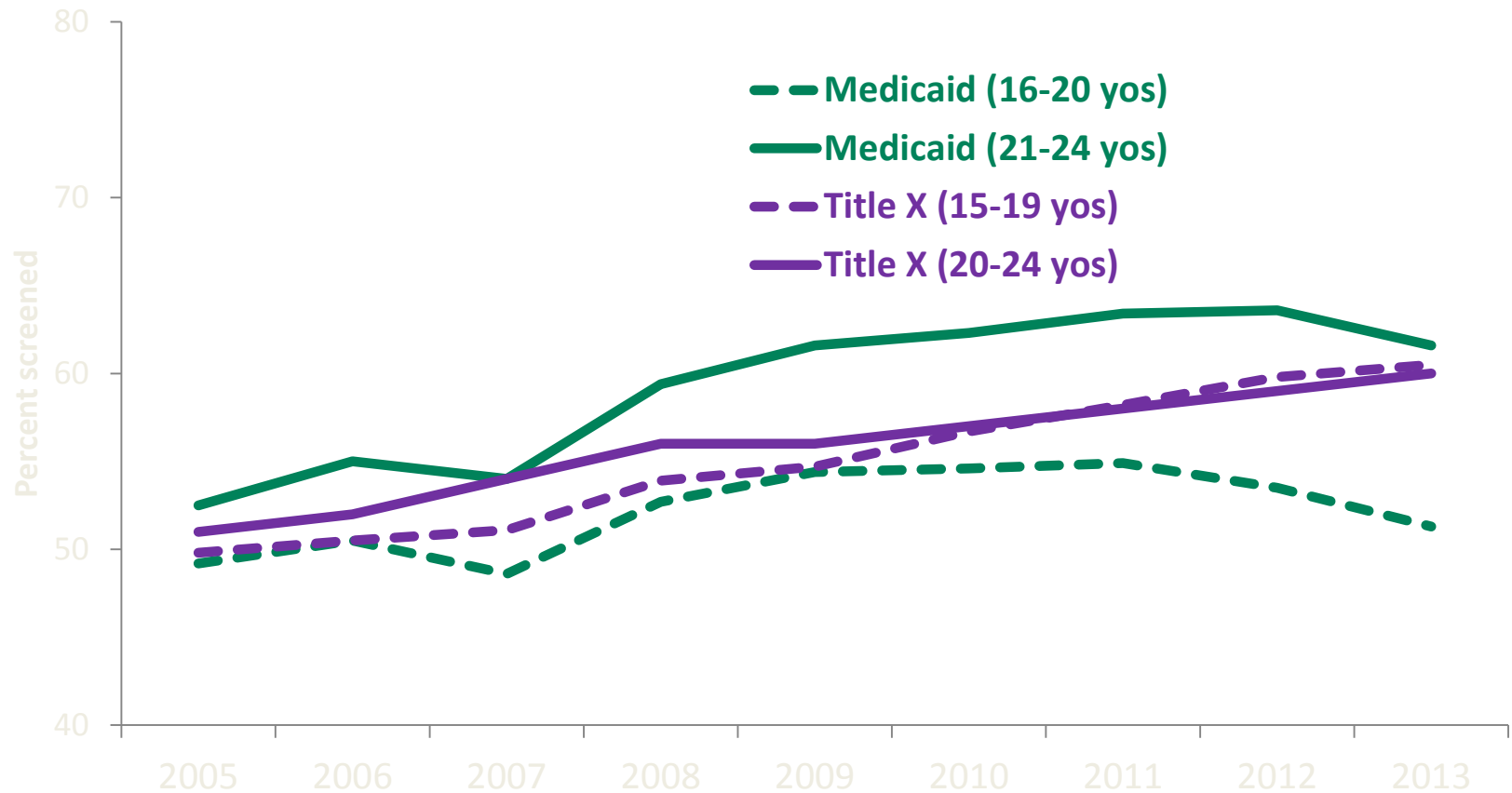
*percent change during 2013–2014

Rate per 100,000



† 2014 data are preliminary as of 5/6/2015

Chlamydia Screening Among Family Planning Clients (Title X) and Among Sexually-Active* Women enrolled in Medicaid (HEDIS), 2005–2013

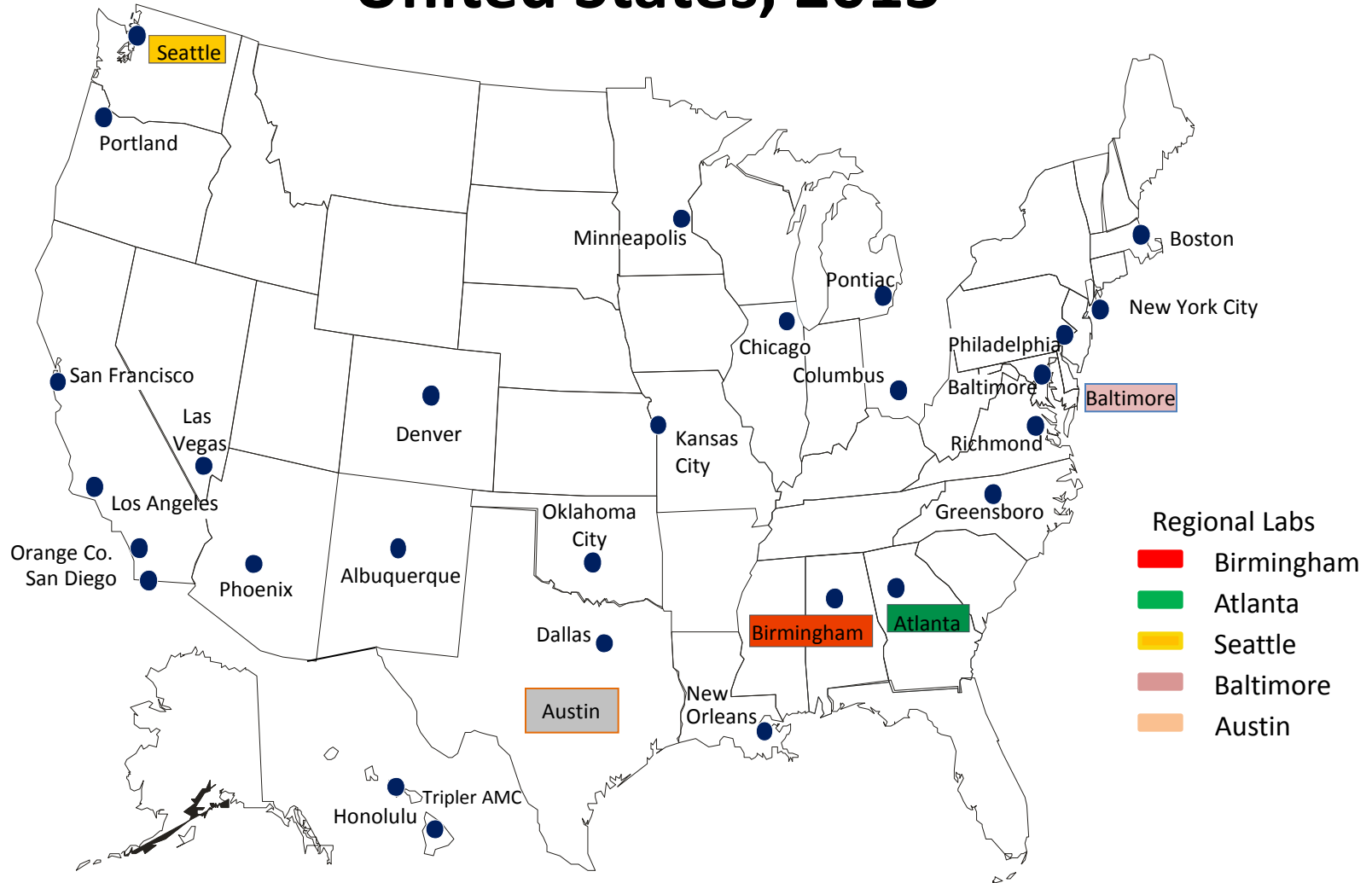


*Among women enrolled in Medicaid plans who had a visit where they were determined to be sexually active

GONORRHEA MANAGEMENT CHALLENGES: LIMITED TREATMENT OPTIONS

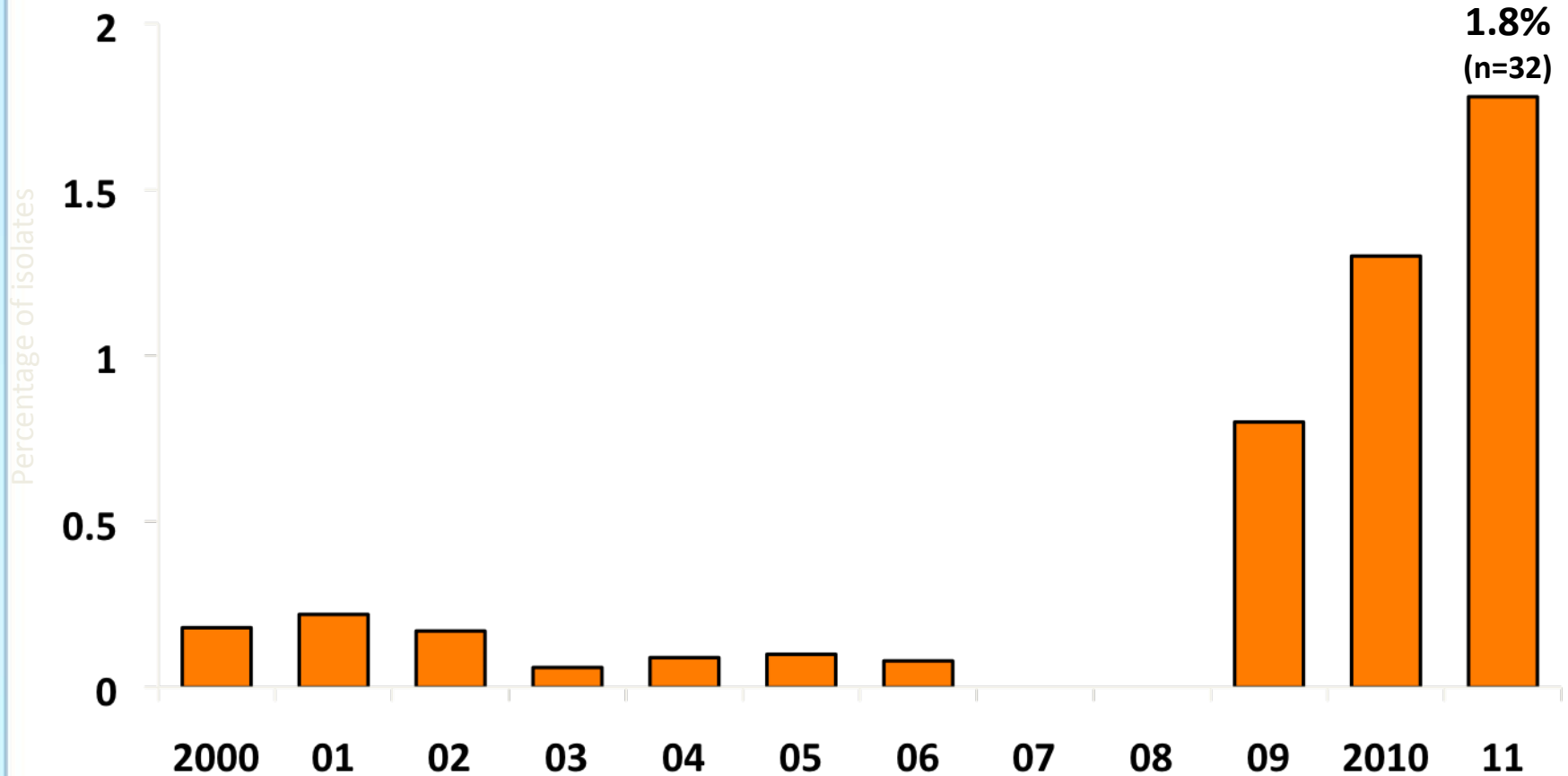


GISP Sites and Regional Laboratories United States, 2013



Proportion of isolates with Elevated MICs to Cefixime ($\geq 0.25 \mu\text{g/ml}$)

n=54,886



Antibiotic Resistance Threats in the U.S., 2013

Seven Threat Assessment Criteria:

- ❑ Clinical impact
- ❑ Economic impact
- ❑ Incidence
- ❑ 10-year projection of incidence
- ❑ Transmissibility
- ❑ Availability of effective antibiotics
- ❑ Barriers to prevention

Three Urgent Threats:

- *Clostridium difficile*
- *Carbapenem-resistant Enterobacteriaceae*
- *Drug-resistant Neisseria gonorrhoeae*

Combination GC Therapy Trial

- ❑ Two antimicrobial regimens
 1. **gentamicin (240mg IM or 5 mg/kg IM) + azithromycin 2 gm PO**
 2. **gemifloxacin 320 mg PO + azithromycin 2 gm PO**
- ❑ Rationale for regimens
 - Additive effect between gentamicin and azithromycin (*in vitro*)
 - Gemifloxacin more active against GC with known cipro resistance or mutations in the GyrA and ParC regions (*in vitro*)
 - Both drugs effective against GC and cover CT
 - One regimen is entirely oral and available in U.S.
- ❑ Randomized/open-label/non-comparative trial
- ❑ Men and women with uncomplicated urogenital gonorrhea (culture-positive) and return for test-of-cure in 10–17 days
- ❑ Outcomes:
 - Microbiological cure
 - Tolerability and microbiological cure of non-genital infections

Percentage of Participants with Microbiological Cure 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%)

	<u>Gentamicin/Azithromycin</u>		<u>Gemifloxacin/Azithromycin</u>	
	n/N	%	n/N	%
Pharynx	10/10	100%	15/15	100%
Rectum	1/1	100%	5/5	100%

Kirkcaldy RD et al. Clinical Trial Evaluating the Efficacy of Gentamicin/Azithromycin and Gemifloxacin/Azithromycin Combination Therapies as an Alternative Regimen for Gonorrhea. ISSTD , Vienna 2013

Percentage of Participants Reporting Adverse Events (AEs)

	Gentamicin/ Azithromycin n=202 (%)	Gemifloxacin/ Azithromycin n=199 (%)
Nausea	56 (27.7)	74 (37.2)
Vomiting	15 (7.4)*	10 (5.0)**
Diarrhea	39 (18.9)	46 (23.2)
Abdominal Discomfort	15 (7.5)	21 (10.5)
Any GI AE***	94 (47)	109 (54.8)

- * 10/305 (3.3%) ineligible/discontinued vomited within 1 hour
- ** 23/298 (7.7%) ineligible/discontinued vomited within 1 hour
- *** nausea, vomiting, diarrhea, abdominal pain/discomfort

Nearly all were mild-moderate
No serious adverse events occurred

Alternative Treatment Approaches Until Newer Agents or Diagnostics Available

- ❑ Increase dose or duration of cephalosporin
- ❑ Antimicrobial susceptibility profile directed therapy
 - 68% of isolates are susceptible to all antimicrobials
 - Most infections diagnosed with NAAT (no AST data)
- ❑ Antibiotic cycling
- ❑ Dual therapy
 - Ceftriaxone + azithromycin or doxycycline

Gonorrhea Treatment

Uncomplicated Genital, Rectal, or Pharyngeal Infections

PLUS*

* Regardless of CT test result

Proposed: Doxycycline may be removed from recommended to alternative

CDC 2010 STD Treatment Guidelines
www.cdc.gov/std/treatment

Gonorrhea Treatment Alternatives

Anogenital Infections

ALTERNATIVE CEPHALOSPORINS:

- ❖ Cefixime 400 mg orally once

PLUS

- ❖ Dual treatment with azithromycin 1 g (preferred) or doxycycline 100 mg BID x 7 days, regardless of CT test result

IN CASE OF SEVERE ALLERGY:

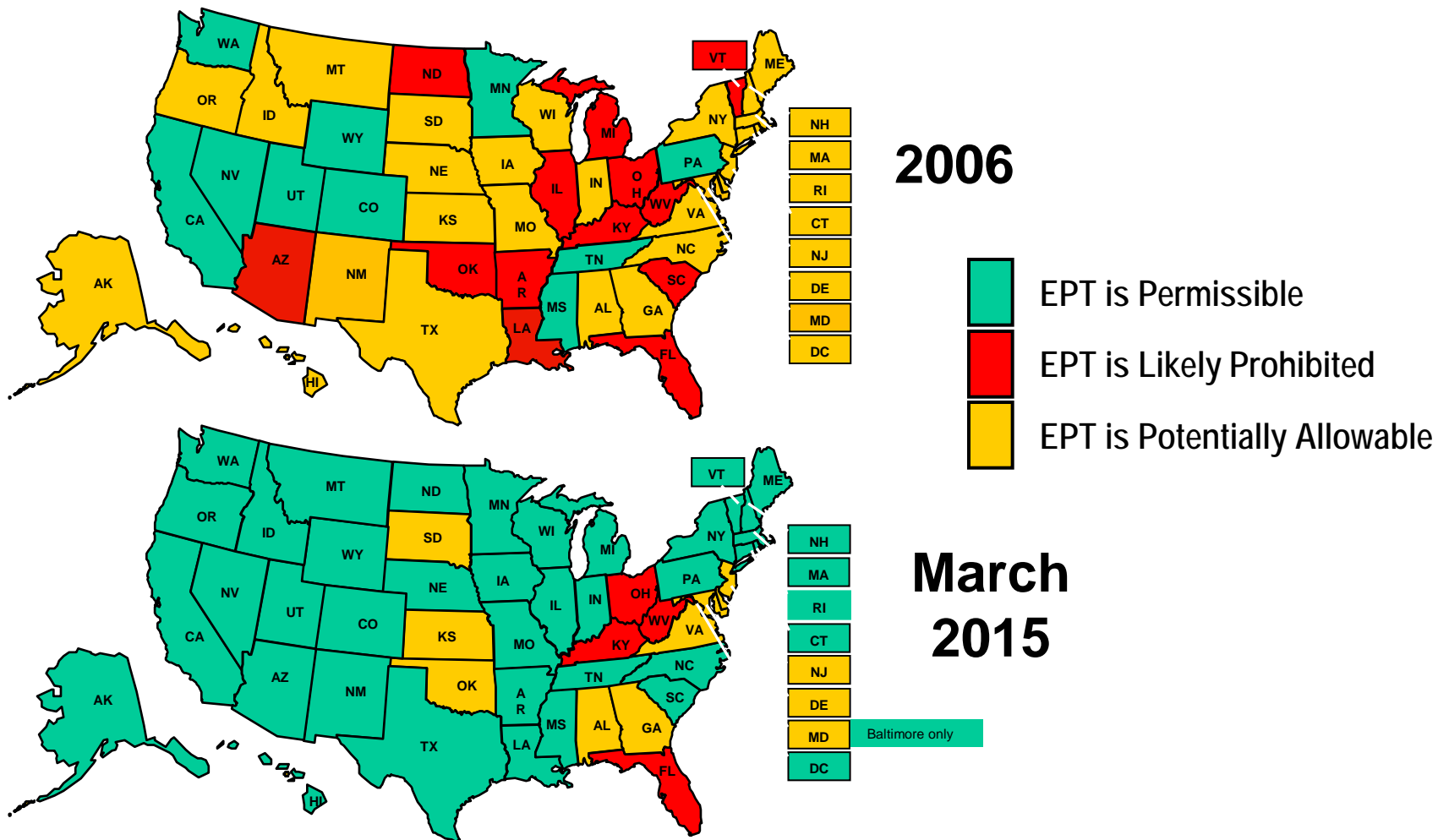
- ❖ Azithromycin 2 g orally once

(Caution: GI intolerance, emerging resistance)

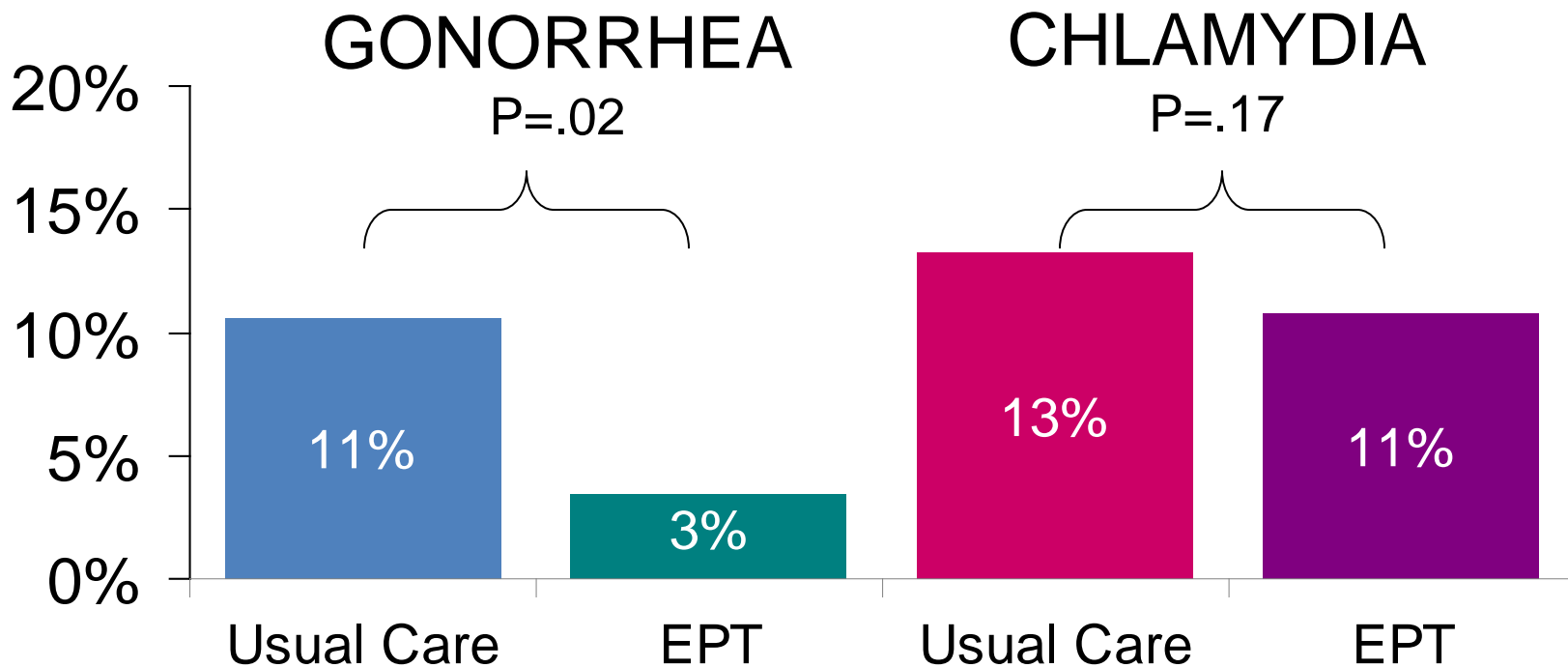
Prior TOC recommendation: Test of cure in 1 week for anyone treated w/ alternative regimens

Proposed: Limit TOC only to pharyngeal GC treated with alternative regimen, may extend interval to 14 days

Evolving Landscape of EPT, 2006 – March 2015: Legal Status Summary



The Effectiveness of Expedited Partner Treatment on Re-Infection Rates



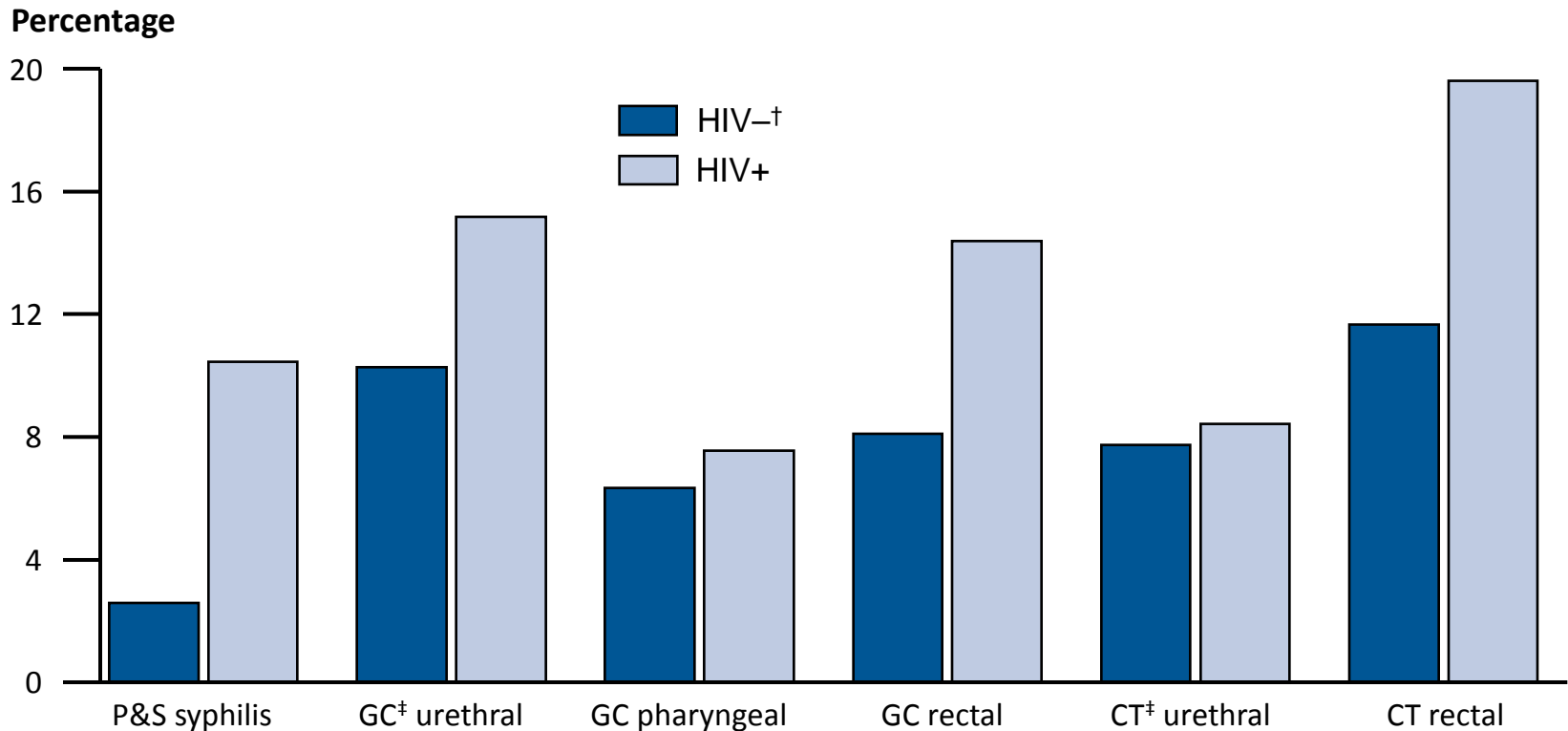
Chlamydia Treatment

- ❑ Self-collected vaginal swabs for NAATs
- ❑ Effectiveness of azithromycin may be less than doxycycline
 - Data from one NGU trial and several rectal infection studies
 - Meta-analysis of 23 RCTs by Hocking et al showed pooled cure rates: doxy 97.5%, azithro 94.4%
- ❑ Doxycycline delayed-release 200mg tablet daily for 7 days
 - Equally efficacious to generic doxycycline 100mg BID x 7 days
 - Less GI side effects but costly
- ❑ Amoxicillin moved to alternative regimen in pregnancy
 - Chlamydia persistence in vitro with PCN treatment
 - Earlier amoxicillin Rx studies in CT in pregnancy had limitations
 - RCT by Kacmar et al showed higher TOC with azithro (95%) vs. amox (80%)

Extragenital Testing for Chlamydia and Gonorrhea

Source:

STD Surveillance Network (SSuN)—Proportion of MSM* Attending STD Clinics with Primary and Secondary Syphilis, Gonorrhea or Chlamydia by HIV Status, 2010



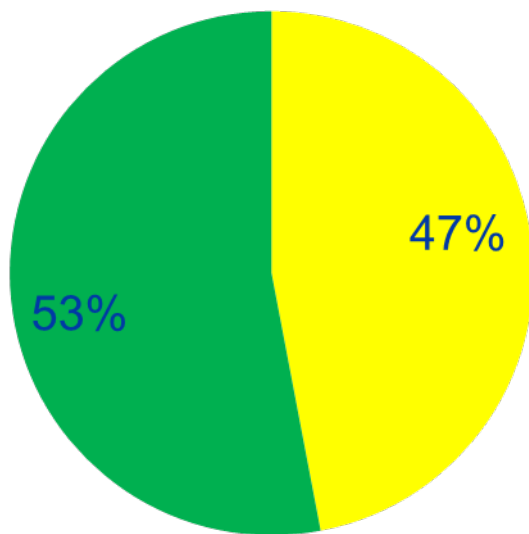
* MSM = men who have sex with men.

† HIV negative status includes persons of unknown status for this analysis.

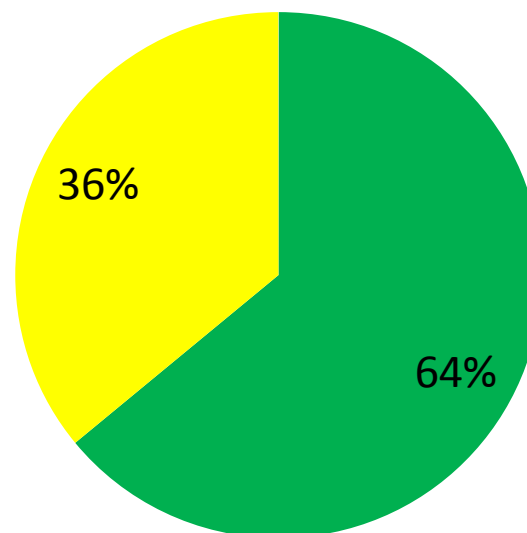
‡ GC urethral and CT urethral include results from both urethral and urine specimens.

Chlamydia and Gonorrhea Infections: Proportion not identified if screening MSM only at urine/urethral sites

Chlamydia



Gonorrhea



■ Identified ■ Not identified

NAAT Testing, Extragenital Sites

- Validation procedures can be done by labs to allow use of a non-FDA-cleared test or application
- Multiple commercial labs currently provide gonorrhea/chlamydia NAAT for rectal/pharyngeal specimens

Self-Collection of Rectal Swabs for STD Screening

- Among ~900 MSM asked to self-collect samples for performance of BD ProbeTec (SDA) assays and APTIMA COMBO-2 (AC2)
 - Prevalence of CT = 7.3%
 - Prevalence of GC = 9.4%
- Sensitivities comparable to clinician-collected swabs
 - CT: 41% vs. 44% by SDA; 71% vs. 82% by AC2
 - GC: 77% vs. 68% by SDA; 84% vs. 78% by AC2
- Both assays far superior to culture for both organisms
- Acceptable to most MSM studied (82%)

Moncada *Sex Transm Infect* 2009; Wayal *Sex Transm Infect* 2009;

NAAT Laboratory Ordering and Billing Codes

	Company-Specific Ordering Codes for Combined GC/CT Nucleic Acid Amplified Tests (NAATs)		Company-Specific Ordering Codes for CT test only
	LabCorp*	Quest*	LabCorp
Rectal	188672	16506	188706
Pharyngeal	188698	70051	188714

NAATs are offered at (or from) any location in the country with these two codes.

For information on specimen collection and transportation, clinicians should contact the local reference laboratory representative.

CPT Billing Codes	
CT detection by NAAT	87491
GC detection by NAAT	87591

CLIA verified labs* for non-genital NAATs: www.nnptc.org/PHLabs.html



Syphilis:

- ❑ Serologic response after treatment
 - 17-21% with early syphilis will not achieve a four-fold decline in nontreponemal titer at 6 months
- ❑ Role of reverse screening algorithm
- ❑ Neurosyphilis definition
 - Neurologic or ocular signs/Sx +
 - Reactive RPR +
 - CSF test abnormalities

Algorithm for reverse sequence syphilis screening

If incubating or primary syphilis is suspected, treat with benzathine penicillin G 2.4 million units IM x 1 and/or repeat in 1-2 weeks

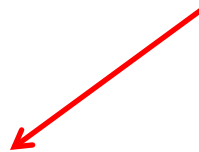
Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to CDC's STD Treatment Guidelines if not previously treated

If at risk for syphilis, repeat RPR in 2 to 4 weeks

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

High EIA/CIA Index Values May Predict TP-PA Positivity (n=255)

N=79 individuals with CIA index value
>12.0; 100% were TP-PA positive



Syphilis Treatment

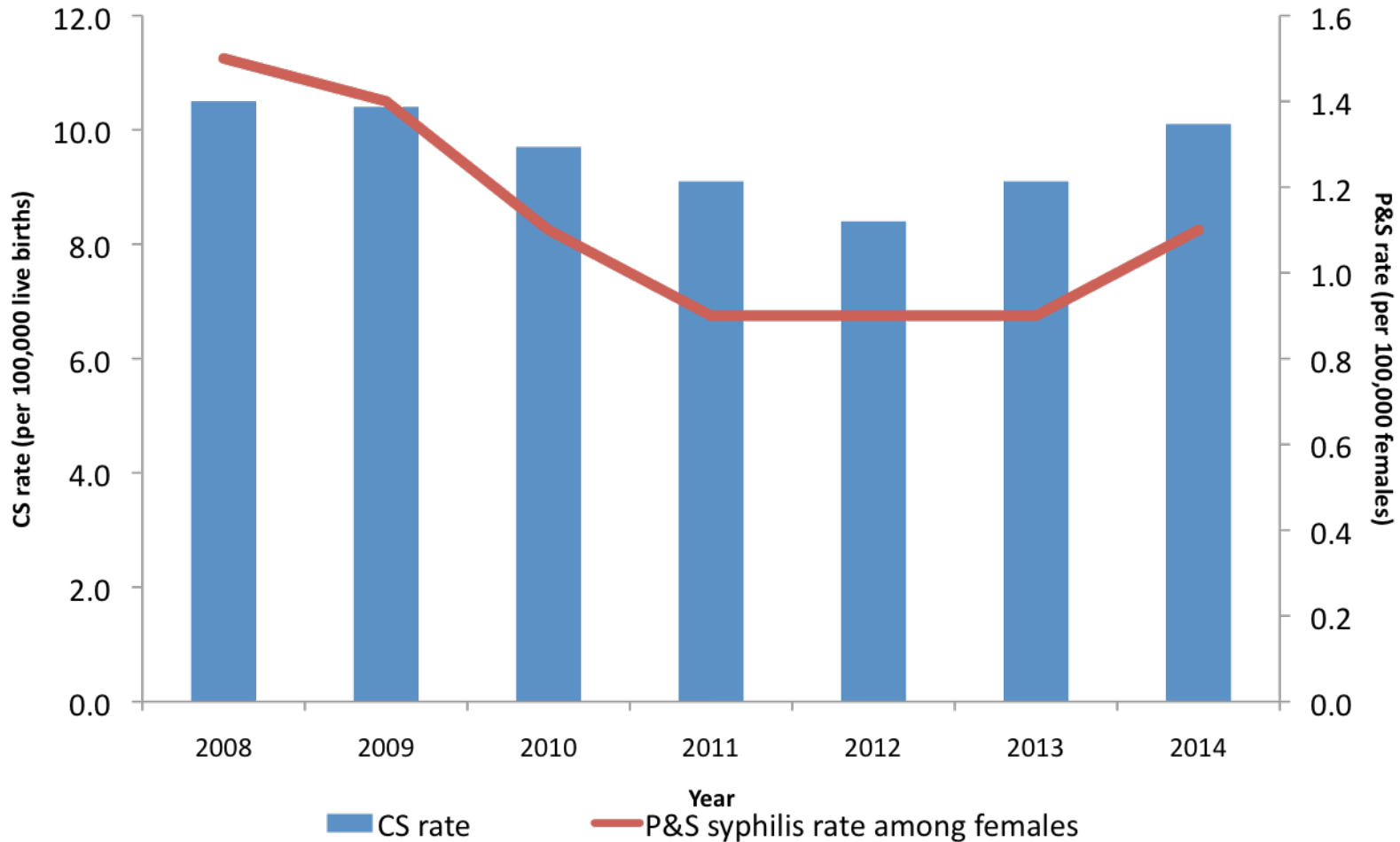
Primary, Secondary, Early Latent

- ❑ Penicillin treatment of choice +/- HIV
 - Benz PCN 2.4 mu IM x 1
 - No benefit of additional therapy

- ❑ PCN alternatives
 - Doxycycline, ceftriaxone
 - Azithromycin 2 gm (A2058G mutation/tx failure)
 - MSM>MSW
 - Do not use azithromycin in MSM or pregnancy

- ❑ PCN is the only option in pregnancy

Congenital Syphilis (CS) Rate* and Rate of Primary and Secondary (P&S) Syphilis Among Females †—United States, 2008–2014 §



*Cases of CS per 100,000 live births. Natality data available at <http://wonder.cdc.gov/nativity-current.html>

† Cases of P&S syphilis among females per 100,000 population. U.S. Census population estimates available at <http://wonder.cdc.gov/bridged-race-v2013.html>.

§ CS rates and P&S Syphilis rates for 2014 were calculated using preliminary 2014 cases counts as of March 12, 2015 & 2013 denominators.

***T. VAGINALIS* INFECTION**



Diagnostic Tests for Trichomoniasis

- Wet mount microscopy only 50-65% sensitivity
- Culture (sensitivity 75-96%; specificity ~100%)
- FDA-cleared NAATs:
 - APTIMA (sensitivity and specificity >95%)
 - vaginal/cervical swabs; urine
 - Can be used for men if CLIA validated
 - BD Probe Tec TV
 - Vaginal/cervical swabs; urine

Diagnostic Tests for Trichomoniasis

- FDA-cleared antigen detection test
 - OSOM (sensitivity 82-95%; specificity 97-100%)
 - Dip stick rapid test; could be used for self-testing in women;
 - not FDA cleared for men
 - AFFIRM VP III (sensitivity 63%; specificity 99.9%)
 - Also tests for Gardnerella and Candida
 - Not FDA cleared for men

***T. vaginalis* Infection Management**

- ❑ Lack data that screening and treatment reduces adverse events or disparities
 - Consider in high-prevalence settings (e.g., correctional facilities, STD clinics), or individuals at high risk for infection
- ❑ Retest women 3 months after TV treatment
 - NAATS may be done 2 weeks after treatment

***T. vaginalis* Infection Management**

- ❑ Tx Metronidazole 2 g or Tinidazole 2 gm
- ❑ Nitroimidazole resistance 4-10% (Kirkaldy 2012, Schwebke 2006)
 - Call CDC for management of nitroimidazole-resistant TV
- ❑ Treat Sex Partners

T vaginalis and HIV infection in Women

❑ TV is an independent risk factor for HIV acquisition

TV increases probability of acquiring HIV	OR 2.6 (CI:1.4–4.7)	Hughes, 2012
TV-infected women more likely to test positive for HIV	HR 2.1 (CI:1.1–4.0)	Mavedzenge, 2010
TV infection associated with incident HIV in women	OR 2.7 (CI:1.3–6.0)	Van der Pol, 2008

❑ Maternal TV is a risk factor for vertical transmission

Maternal TV increases HIV vertical transmission risk	RR 1.7 (CI:1.0–2.9)	Gumbo, 2010
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❑ Treating TV reduces genital HIV shedding

Women treated for TV less likely to shed HIV vaginally	RR 0.3 (CI:0.1–0.9)	Kissinger, 2009
Genital viral load decreases 0.5 (\log_{10}) after TV treatment	P<0.01	Anderson, 2012

T vaginalis and HIV infection

- ❑ Women with HIV infection should receive TV screening at entry to care and annually if sexually active
 - Associated with PID (Moodley 2002)
 - Treatment reduces genital HIV shedding (Kissinger 2009, Anderson 2012)
 - Question if HIV-infected, pregnant women should be screened at mid-gestation for TV
- ❑ Longer treatment course better in women with HIV
 - Metronidazole 500mg BID x7d (vs. 2g)-less TV at TOC/3 mo (*Kissinger, 2010*)
 - Potential factors- BV infection, changes in vaginal ecology, ARVs
- ❑ Retest women 3 mo after treatment
- ❑ No data to recommend screening or extended treatment in men with HIV

HPV INFECTION

HPV Infection Management

- ❑ HPV Vaccine recommendations updated per ACIP
 - Routine quadrivalent (HPV4) vaccination of males at age 11-12, catch up to 21 years and through age 26 years for MSM and HIV-infected
- ❑ 9-valent HPV Vaccine (HPV9) updated per ACIP discussion
 - Age groups:
 - Currently HPV4 recommended age groups vs only in the current HPV9 licensed age groups (i.e., through age 15 for males)
 - Revaccination:
 - No recommendation for routine revaccination with HPV9 vs recommend against revaccination
 - 2-dose schedule: (deferred to June meeting)

HPV Vaccine Communications during the Healthcare Encounter

- ❑ HPV vaccine is often presented as 'optional' whereas other adolescent vaccines are recommended
- ❑ Parents expressed mixed or negative opinions about the vaccine: 'new vaccine'; concerns over safety/efficacy
- ❑ When parents expressed reluctance, providers were hesitant to engage in discussion
- ❑ Some providers shared parent's views that teen was not at risk for HPV and could delay vaccination until older

Tips for Talking to Parents about HPV Vaccine

Risk to Healthcare Workers Treating Genital Warts

- ❑ HPV DNA can be found in smoke plumes after laser or electrosurgical therapy on EGW, CIN, common warts
- ❑ 2 case reports of laryngeal papillomas reported in HCW exposed to smoke plumes during treatment of GW
- ❑ Appropriate infection control to prevent possible transmission for anogenital warts and anogenital intraepithelial neoplasias (e.g. CIN) with CO2 laser or electrosurgical procedures
 - local exhaust ventilation- smoke evacuator

HPV Infection Management

- ❑ Podophyllin resin 10-25% moved to “alternative therapy” for genital warts
 - Case reports of adverse systemic toxicity with misuse
- ❑ Case reports of inflammatory responses to imiquimod
 - Worsened inflammatory or autoimmune skin disease
 - psoriasis, vitiligo, and lichenoid dermatoses
- ❑ Additional formulation of imiquimod
 - 3.75 % cream applied daily

Treatment for Genital Warts

- 2015 Recommendation
 - Patient applied
 - Podofilox 0.5% solution or gel
 - OR
 - Imiquimod 3.75% or 5% cream
 - OR
 - Sinecatechins 15% ointment

Treatment for Genital Warts

Source:

GENITAL HERPES



Genital Herpes

- ❑ Increasing proportion of anogenital infections HSV-1 (young females, MSM)
- ❑ IgM testing not useful
- ❑ Type specific serologic tests
 - ❑ HerpeSelect HSV-2 ELISA may be false + at low index values (1.2-3.5)- confirmed with Biokit or WB
 - ❑ HerpeSelect HSV-1 ELISA insensitive for HSV-1 (80%)
 - ❑ Head to head comparison of type specific assays vs WB
- ❑ No change in recommended therapy
 - ❑ Famiclovir is out of alphabetical

NEW SECTIONS

Proposed New Section: Emerging Issues

- Role of *Mycoplasma genitalium*
 - Good evidence for role in urethritis (20%)
 - May play role in cervicitis and PID
 - No commercially-available test for *M. genitalium* (in house NAATs)
 - Treatment implications
 - Azithromycin > doxycycline because of resistance to doxycycline
 - Conflicting data on single dose vs extended dosing
 - Emerging resistance to azithromycin
 - Moxifloxacin 400 mg po for 7-14 days has been studied as an alternative (cure rates 85-100%)

The Role of *Mycoplasma genitalium* in urethritis and cervicitis

M. genitalium

- Causes 15-20% of NGU cases and 30% of persistent/recurrent urethritis
- Pathogenic role in women is less clear:
 - Can be detected in 10%-30% of women with cervicitis
 - Appears to be more common in women with than women without cervicitis
 - May play a role in PID and infertility
 - Very little data on ectopic pregnancy

M. Genitalium - diagnostics

- Difficult to culture (can take up to 6 months)
- Some laboratories have developed in-house PCRs for research purposes
- No commercial NAATs yet available

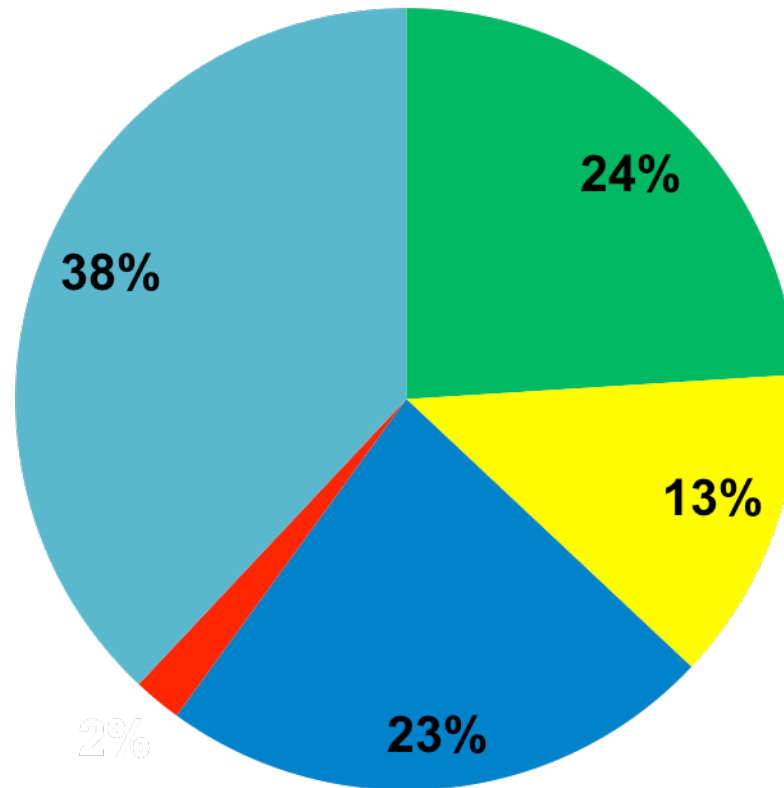
M. genitalium - Treatment

- 7-day doxycycline treatment is largely ineffective
- Azithromycin is more effective but resistance appears to be rapidly emerging (>50% in some settings)
- Moxifloxacin (400 mg x 7, 10 or 14 days) has been successfully used and may be indicated in patients who fail standard treatment for NGU or PID

Cause of Nongonococcal Urethritis

Seattle, 2007 - 2011

■ CT ■ MG ■ UU-2 ■ TV ■ None



Treatment Results

- *C. trachomatis*
- *M. genitalium*
- *U. urealyticum*

- Clinical Cure

	Azithromycin	Doxycycline
	%	%
	86	90
	40	30
	75	70
	80	76

Proposed New Section: Emerging Issues

- ❑ Sexually acquired HCV
 - Unprotected receptive anal intercourse
 - Rough or poorly lubricated unprotected anal penetration(fisting)
 - Ulcerative STIs (syphilis, LGV)
- ❑ HCV Screening in MSM
 - At initial evaluation and at least annually
 - More frequently depending on risk factors and local HCV prevalence
- ❑ Acute HCV may be HCV Ab negative (CD4 <200)
 - HCV RNA with new LFT elevation

Updated Recommendations for Diagnostic Evaluation of Urethritis

Diagnostic Criteria for Urethritis

- Mucopurulent or purulent discharge on examination
- Grams stain of urethral secretions demonstrating ≥ 2 WBCs per oil immersion field
- Positive leucocyte esterase test on first-voided urine
- Microscopic examination of first-voided urine sediment demonstrating ≥ 10 WBCs/OIF

Gram Stain Diagnosis of NGU

N = 11,422 Gram Stains

Retesting to Detect Repeat Infection

Source:

Retesting Recommendations

- Any patient who tests positive for chlamydia or gonorrhea should be rescreened 3 months after treatment
- Women who test positive for trichomonas should rescreened at 3 months
- Any patient diagnosed with syphilis should undergo follow-up serologic syphilis testing per current recommendations

Don't forget the triple dip

← Syphilis serology

← Pharyngeal GC

← Urine GC/CT

← Rectal GC/CT

Thanks

- Denver PTC Team
 - Teri Anderson
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 - John Fitch