The Appliance of Science: A Review of Recent Advances in STI (STD) Research

Bill Miller

Editor-in-Chief

Sexually Transmitted Diseases

Observed Treatment Responses to Short-Course Doxycycline Therapy for Rectal Lymphogranuloma Venereum in Men Who Have Sex With Men

Rebecca Simons, MRCP, Sophie Candfield, MRCP,†*
*Patrick French, FRCP,† and John A. White, FRCP**

From the *Guy's and St Thomas' NHS Foundation Trust; and †Central and North West London NHS Foundation Trust, London, United Kingdom

rebecca.simons@doctors.org.uk.

The issue: Does rectal infection with LGV biovars always require 21 days of doxycycline?

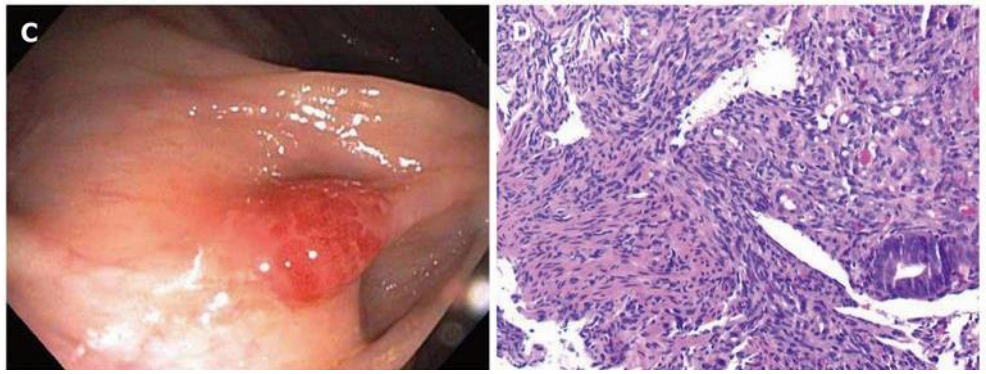
LGV biovars of *Chlamydia trachomatis* (Ct) cause severe proctitis

Increasing reports of symptomatic and asymptomatic rectal infection with LGV biovars

Over 25% of rectal infection with LGV biovars may be asymptomatic

Recommended 21 days of treatment for rectal LGV has “efficacy” of 98.5%, but no RCT

Not clear that asymptomatic infection with LGV biovars needs to be treated with same duration as symptomatic proctitis



Gallegos, et al. *World J Gastroenterol* 2012

Study setting

Two genitourinary medicine clinics in London

Study design

Retrospective case series, based on medical record review

Identified all MSM with LGV biovar DNA by PCR

Selected those with <21 days of initial treatment

Excluded MSM with no test of cure or with 21 days of treatment

After confirmation of LGV biovar, MSM invited back for TOC and offered 3 weeks of doxycycline

Study population characteristics (n=60)

Characteristic	Median/Percentage
Age (median)	38
Race	
White	82%
Black	8%
Other	10%
HIV infection	
HIV-infected	93%
HIV-uninfected	7%
Symptoms	
Asymptomatic	50%
Anorectal symptoms	45%
Genitourinary symptoms	5%
Severe proctitis (e.g. tenesmus)	12%

Duration of treatment and co-medication

Duration of doxycycline treatment	%		
7 days	83% (50/60)		
14 days	17% (10/60)		
Comedication			
None	45%		
Ceftriaxone	30%		
Benzathine penicillin	3%		
Ceftriaxone + azithromycin	13%	}	All azithromycin = 18%
Ceftriaxone + azithromycin + benzathine penicillin	3%		
Azithromycin	2%		
Other (acyclovir or tinidazole, albendazole)	4%		

Test of cure results

	Time to TOC Median (range)		Negative TOC	(n/N)
No azithromycin	28 days (7-200)		96%	47/49*
Azithromycin	37 days (12-162)		100%	11/11
Severe proctitis				
7 days doxy			100%	4/4
14 days doxy			100%	3/3

*One patient positive for non-LGV Ct strain only at 114 days;
Second patient positive for LGV Ct strain and non-LGV strain at 28 days

Considerations

No RCT for treatment duration in rectal LGV

Duration has been based primarily on invasive nature of disease

Non-LGV biovars treated with 7 days doxycycline

Selection bias: more asymptomatic disease here than expected; most symptomatic cases probably received 21 days

Should I change my practice?

For consideration:

Rectal Ct detected (regardless of strain) with mild or no symptoms → treat for 7 days; if LGV strain detected → TOC

Need a multicenter RCT

ORIGINAL STUDY

Observed Treatment Responses to Short-Course Doxycycline Therapy for Rectal Lymphogranuloma Venereum in Men Who Have Sex With Men

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EDITORIAL

Lymphogranuloma Venereum Treatment and Terminology

H. Hunter Handsfield, MD

A side issue: Asymptomatic/mild LGV?

~50% of MSM with LGV biovars have mild or no symptoms

The question: Does mild or asymptomatic infection with an LGV biovar constitute LGV?

Our informal survey

With resurgence of LGV as a rectal infection in MSM, and with frequently available typing to diagnose infection with L strains of *C. trachomatis*, the term lymphogranuloma venereum (LGV) is increasingly used to refer to any infection with such strains. But some might argue that the term should be clinically defined, i.e. LGV should refer only to the classical inguinal syndrome or severe proctitis and not asympomatic or minimally symptomatic infections, either genital or rectal, detected mostly by screening. Among other things, anecdotal and retrospective data are emerging that many such infections respond to less intensive treatment than 3 weeks of doxycycline, including a paper soon to be published in *Sexually Transmitted Diseases*.

What are your views on the issue?

Would you support or argue against limiting “LGV” to traditional clinical syndromes?

What are your primary arguments for or against limiting LGV to traditional clinical syndromes?

Study population

11 STD experts, most with primarily chlamydia expertise

9 US based

1 UK

1 Netherlands

Results

Support using LGV to reflect clinical syndrome only:	5 (45%)
Support using LGV to include asymptomatic rectal infection:	5 (45%)
Deferred:	1 (45%)

Qualitative results:

Those supporting inclusion of asymptomatic rectal infection tended to voice opinions more strongly

Key recognition

Most mild or asymptomatic rectal Ct infections are not typed.

These will routinely be treated with 7 days of doxycycline.

So, some rectal infections with LGV biovars will, through routine clinical practice, receive only 7 days of doxycycline.

A Population-Based Study to Compare Treatment Outcomes Among Women With Urogenital Chlamydial Infection in Washington State, 1992 to 2015

Christine M. Khosropour, PhD, MPH, Teal R. Bell, MPH,† James P. Hughes, PhD,‡ Lisa E. Manhart, PhD, MPH,*§ and Matthew R. Golden, MD, MPH*¶||*

From the *Department of Epidemiology, University of Washington, Seattle; †Washington State Department of Health, Olympia; Departments of ‡Biostatistics, §Global Health, and ¶Medicine, University of Washington; and ||Public Health—Seattle and King County HIV/STD Program, Seattle, WA

ckhosro@uw.edu.

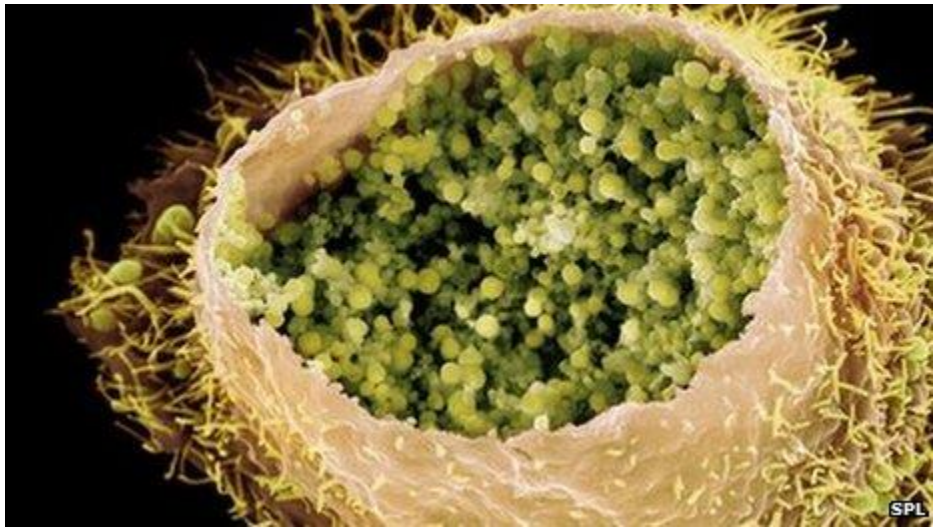
The issue: Azithromycin or doxycycline for Ct in women?

CDC recommends azithromycin (1g x1) or doxycycline (100mg bid x 7d) for treatment of urogenital Ct

For urogenital Ct, the drugs appear similarly efficacious

But, azithromycin appears less effective for rectal Ct.

http://www.bbc.co.uk/science/0/21858967



The issue: Rectal Ct and autoinfection in women

Rectal Ct is common in women, including among women without anal intercourse

Autoinfection of Ct from vagina to rectum and rectum to vagina occurs

70-89% of women with urogenital Ct have concurrent rectal Ct

If a women has concurrent vaginal and rectal Ct and azithromycin does not adequately treat the rectal Ct, then autoinfection could occur leading to persistent/recurrent urogenital Ct

Study design

Retrospective cohort study using statewide chlamydia surveillance data

Date range 1/1/1992 – 12/31/2015 (23 years)

http://www.ipl.org/div/stateknow/wa1.html

Study population

All women in State of Washington, aged 14 years or older

Positive test for urogenital Ct

Received azithromycin or doxycycline consistent with CDC guidelines

Definitions

Urogenital Ct: Positive, laboratory-confirmed Ct test from cervix, urethra, urine, or vagina

Primary outcome: first positive urogenital Ct test result after treatment of initial infection, between 14 and 180 days

- Women without a positive test in that interval include women who were not retested or who had a negative repeat test

Sensitivity analyses: 21-180 days; 28-180 days

Final analytical sample

234,733 women with urogenital Ct treated with azithromycin or doxycycline

168,301 treated with azithromycin

66,432 treated with doxycycline

Women's characteristics

	Azithromycin		Doxycycline
Age, years			
14-17	17%		19%
18-24	57%		58%
25-29	15%		13%
30-34	6%		5%
≥35	5%		5%
Race/ethnicity			
White	46%		56%
Black	10%		10%
Hispanic/Latina	16%		12%
Other/unknown	30%		27%
Concurrent gonorrhea			
Yes	3%		4%
No	97%		96%

Azithromycin versus doxycycline

	Risk over 180 days		Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Risk of persistent/recurrent Ct				
Overall	6.1%			
Azithromycin	6.7%		1.41 (1.36-1.47)	1.24 (1.19-1.30)*
Doxycycline	4.7%		--	--

*Adjusted for age, race/ethnicity, year of diagnosis, pregnancy status, gonorrhea coinfection, reason for initial CT test, and county where the case was reported

Changing the retesting window had no effect on the adjusted RR

Repeat positive: # of days since treatment

	Azithromycin	Doxycycline
Overall (14-180 days)	6.7%	4.7%
14-30 days	0.6%	0.4%
31-60 days	1.4%	0.9%
61-90 days	1.5%	0.9%
91-180 days	3.3%	2.5%
No repeat positive test	93.3%	95.3%

Considerations

Less recurrence/persistence with doxycycline compared to azithromycin

Longer follow-up window used than in many RCT (1-6 weeks)

Study likely underestimates recurrence/persistence because of passive testing

Autoinfection is plausible explanation

Timing for autoinfection unknown; longer window suggested in this study

Should I change my practice?

Undiagnosed rectal Ct is common → more testing in women?

Doxycycline has less persistence/recurrence → more doxycycline?

Should Asymptomatic Men Who Have Sex With Men Be Screened for Oropharyngeal Chlamydia? Clinical Outcomes From a Cross-Sectional Study

Jason J. Ong, PhD,†‡ Eric P.F. Chow, PhD,*† Vesna De Petra, DipApp Sc,§ Deborah Williamson, PhD,§ Irene Pelatosis, Assoc DipAppSc,§ Ben Howden, PhD,§ Lei Zhang, PhD,*†¶‖ Marcus Y. Chen, PhD,*† Catriona S. Bradshaw, PhD,*† Jane Hocking, PhD,** and Christopher K. Fairley, PhD*†*

From the *Melbourne Sexual Health Centre, Alfred Health, Carlton; †Central Clinical School, Monash University, Melbourne; ‡Department of General Practice, Faculty of Medicine, Dentistry and Health Sciences; §Microbiological Diagnostic Unit Public Health Laboratory, University of Melbourne, Parkville; ¶School of Public Health and Preventive Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia; ‖Research Center for Public Health, Tsinghua University, Beijing, China; and **School of Population and Global Health, University of Melbourne, Parkville, Victoria, Australia

JOng@mshc.org.au.

The issue: Oral Ct in MSM

Australian & British guidelines recommend screening for *Chlamydia trachomatis (Ct)* in asymptomatic MSM

U.S. guidelines do not

Prevalence is typically low: ~1%

Prevalence of concomitant anogenital infection seems variable

Study design

Cross-sectional, retrospective audit

All MSM with an oropharyngeal swab over 14 months

Study setting

Melbourne Sexual Health Centre, Melbourne, Australia

https://www.slideshare.net/ccsmonash/20150813-amrep-student-information-night-rolling-slides-51568013

Study population

4877 oropharyngeal swabs

4877 consultations

2606 distinct MSM

	median	(IQR)
Age	29	(25-37)
Number of casual partners, 3 mos	2	(1-4)
	n	(%)
Born in Australia	1360	(52)
Speaks English at home	2054	(79)
Overseas visitor	18	(0.7)
Past STI	919	(42)
Current regular partner	833	(38)
Casual partner in last 3 months	1603	(78)

Oropharyngeal Ct

	n/N	%	95% CI
Oropharyngeal Ct	72/4877	1.5%	(1.2-1.9)
Concurrent urethral	3/72	4%	
Concurrent anorectal	8/72	11%	
Concurrent urethral or anorectal	10/72	14%	
Oropharyngeal gonorrhea	2/72	3%	
Anorectal gonorrhea	5/72	7%	
Urethral gonorrhea	1/72	1%	
Any concurrent gonorrhea	6/72	8%	
Untreated if no screening	56/72	78%	(67-86)

Site-specific Ct

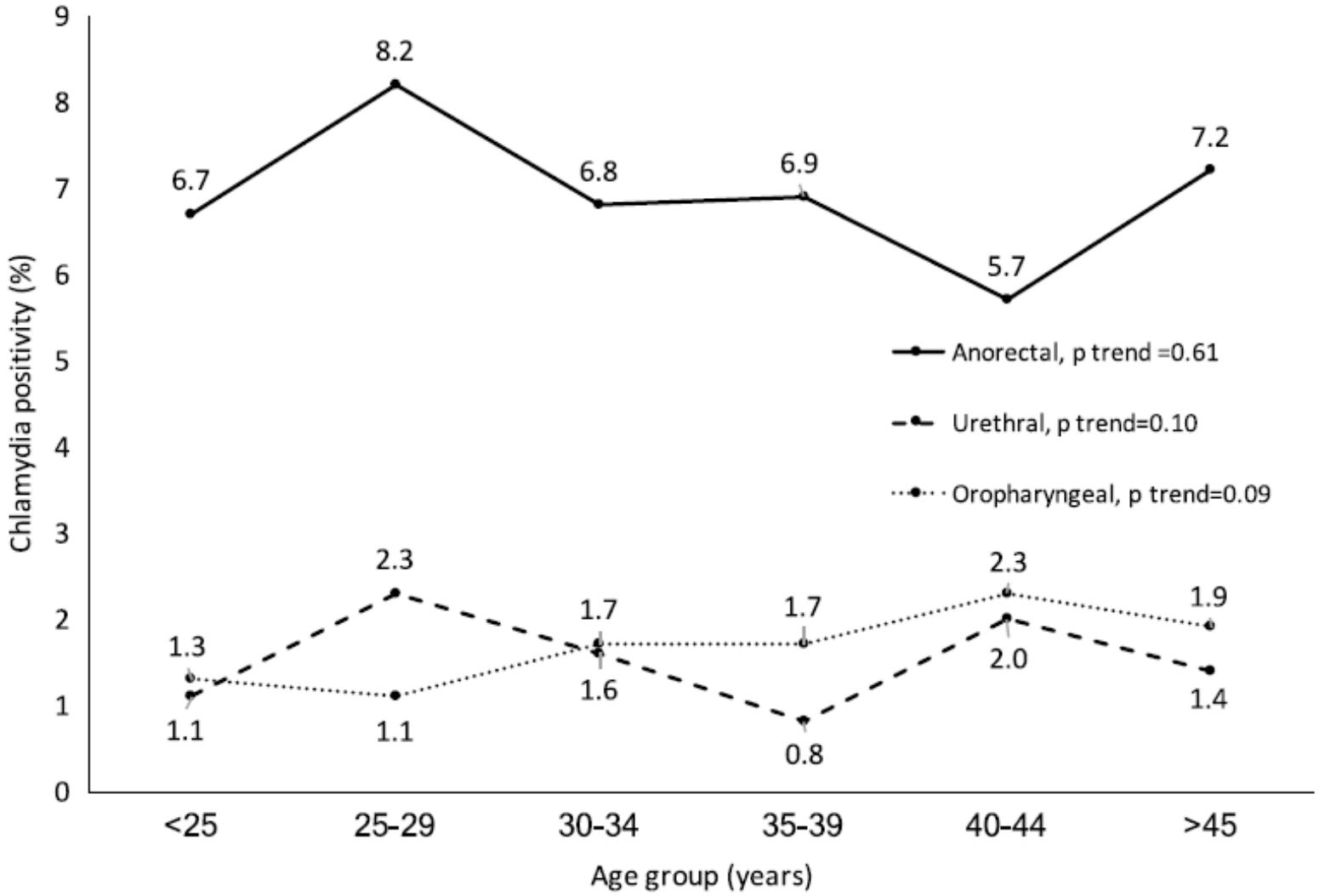


Figure 1. Site-specific chlamydia positivity stratified by age group. *P* values were calculated using the χ^2 test for trend.

Oropharyngeal Ct and GC

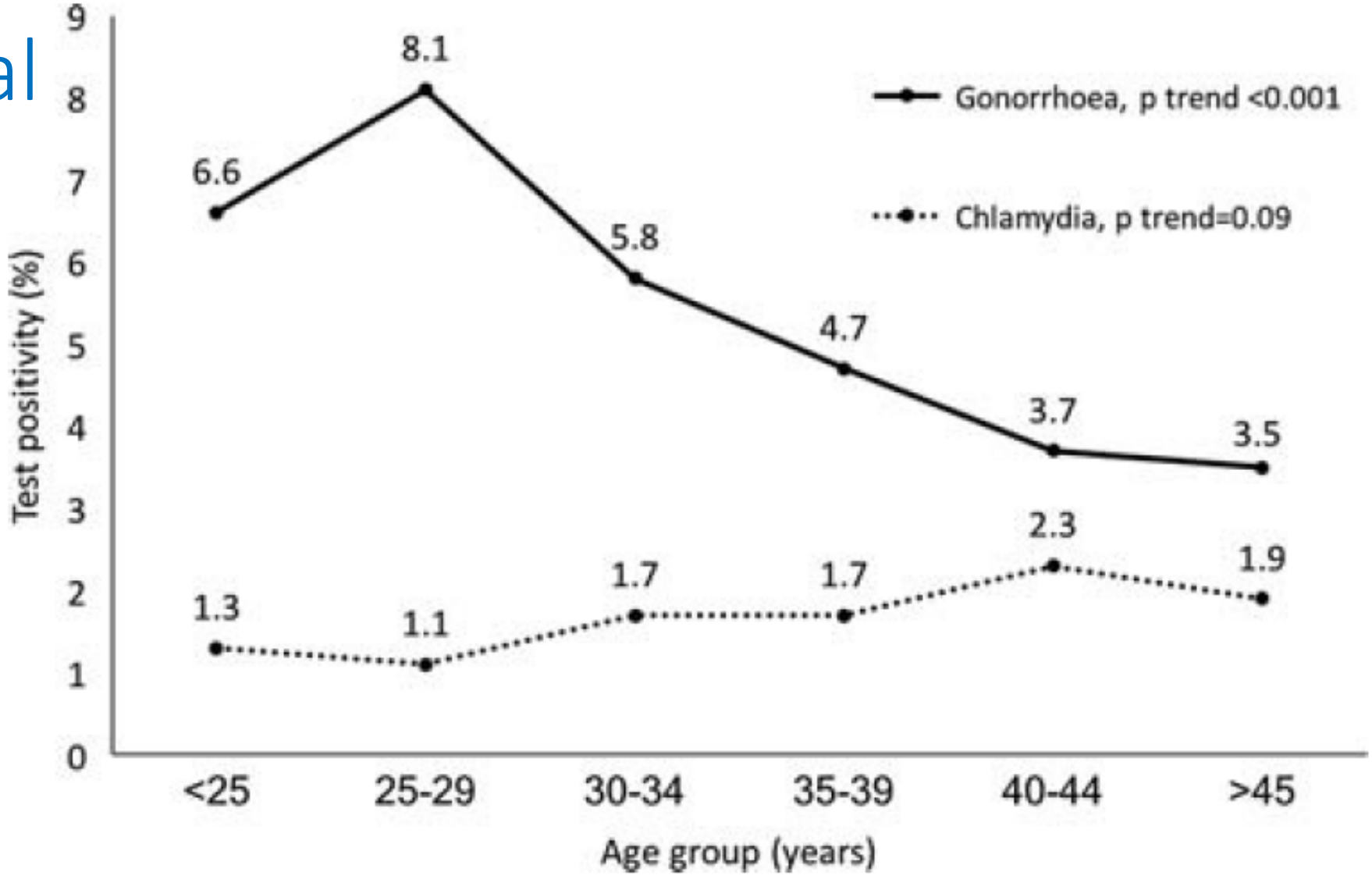


Figure 2. Oropharyngeal chlamydia and gonorrhea positivity according to age group. *P* values were calculated using the χ^2 test for trend.

Considerations

Prevalence of oropharyngeal Ct in a sexual health clinic was relatively low.

But…over three-fourths of cases were not accompanied by Ct or GC at another site—these would go untreated.

Limited information on the performance of NAAT in oropharynx. Concern is specificity.

How does oropharyngeal Ct contribute to the broader epidemiology of Ct in MSM?

Will this change U.S. guidelines?

Probably not…yet

Should I change my practice?

Ct prevalence will vary from community to community

Screening asymptomatic men likely to be beneficial in many contexts

When screening is performed, oropharyngeal screening should likely be included

THANK YOU!

Bill Miller
Editor-in-Chief
Sexually Transmitted Diseases
@STD_Journal
miller.8332@osu.edu
std@ucsf.edu