Mycoplasma genitalium (MG)

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slides courtesy of Lisa E. Manhart, PhD

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Disclosures

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Disclaimer

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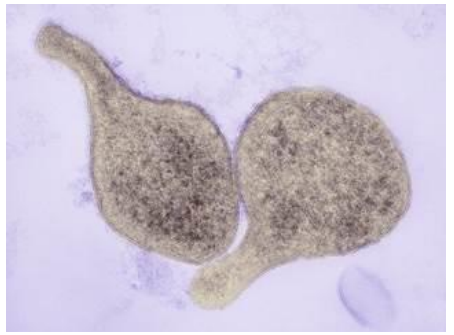
AETC AIDS Education & Training Center Program Mountain West

Mycoplasma genitalium (MG) & HIV

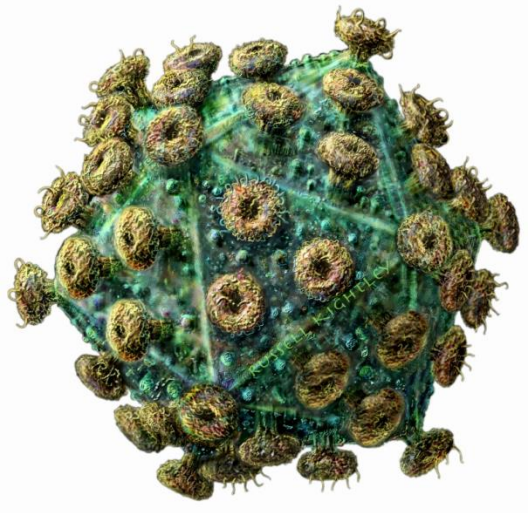
Meta-analysis (19 studies)[1]
Two-fold increased risk of HIV infection w/MG
Summary OR = 2.01; 1.4-2.8

2 studies of **HIV-incidence**
Prior MG associated with HIV-1 acquisition
AOR 2.4; 2.0-5.8 (Zimbabwe/Uganda)[2]
AHR 2.2; 1.1-4.4 (Uganda)[3]

2-fold increased risk of **HIV shedding** in HIV-positive persons (3 studies)



Thomas Deerinck, NCMIR/UCSD



[1] Napierala-Mavedzenge, 2009; [2]Mavedzenge 2012; [3]Vandepitte 2013, No studies in men who have sex with men (MSM)

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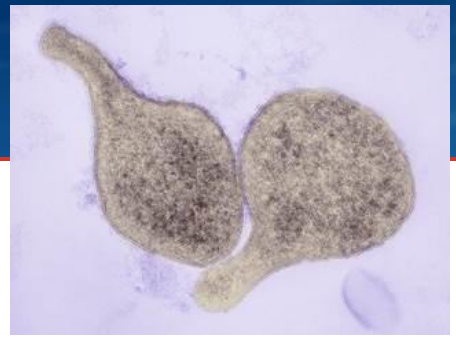
What is *Mycoplasma genitalium*?



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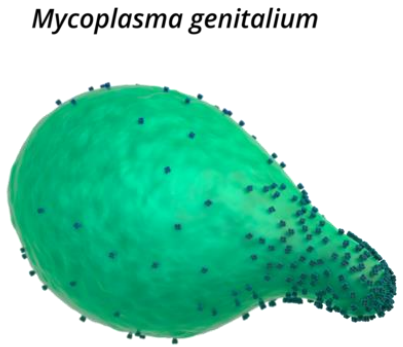
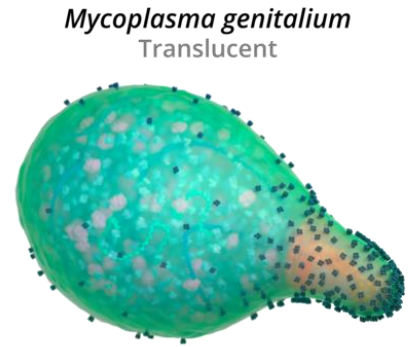
Mollicute – Tiny and lacks a cell wall

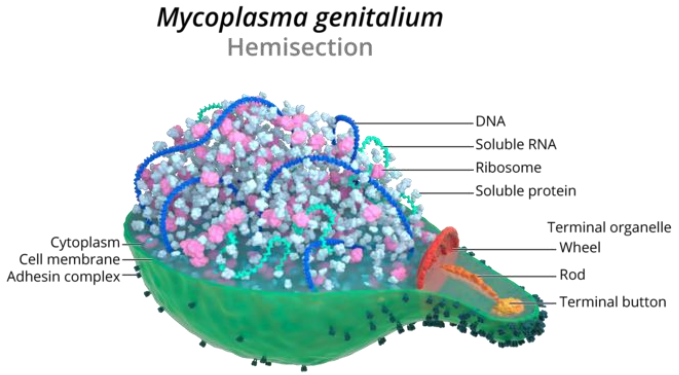
Cannot be diagnosed by microscopy
(NAATs required for detection)

One of smallest known genomes
580 kb, translating to <500 genes

Extremely fastidious and slow growing
Culture only accomplished by a few laboratories in the world
Depends on host or complex growth media for nutrients







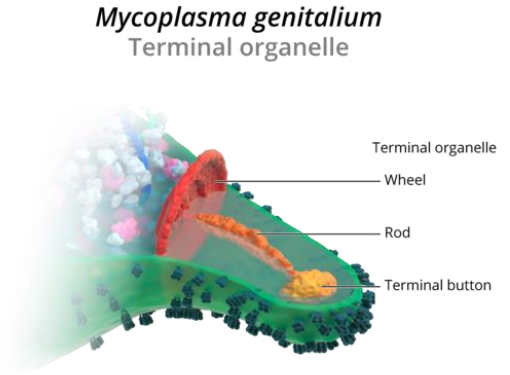


Illustration credit: Cognition Studio, Inc.; Gwendolyn E. Wood, PhD; Lisa E. Manhart, PhD, MPH; and David H. Spach, MD

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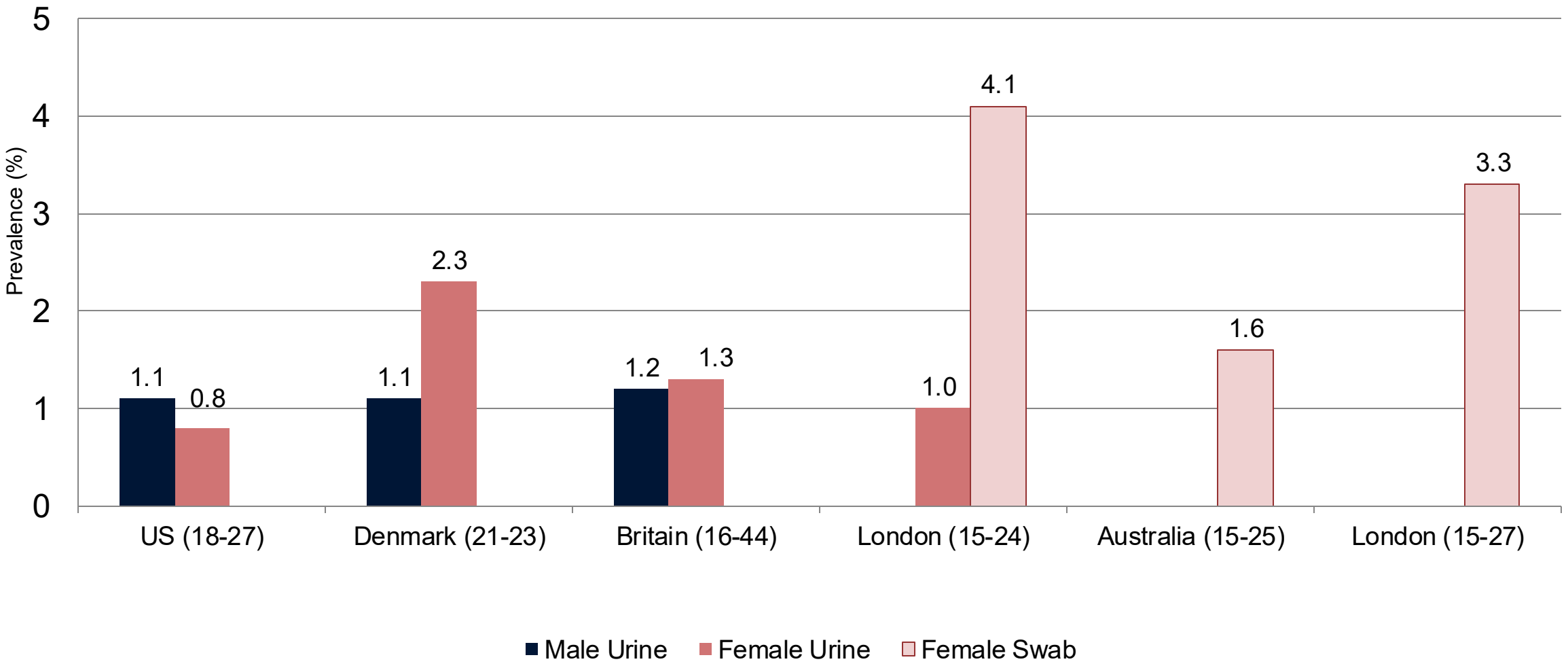
How common is it?

~ 1 - 3% low risk persons infected



Manhart 2007; Andersen 2007; Sonnenberg 2015; Svenstrup 2010; Walker 2011; Oakeshott 2010

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How common is it?

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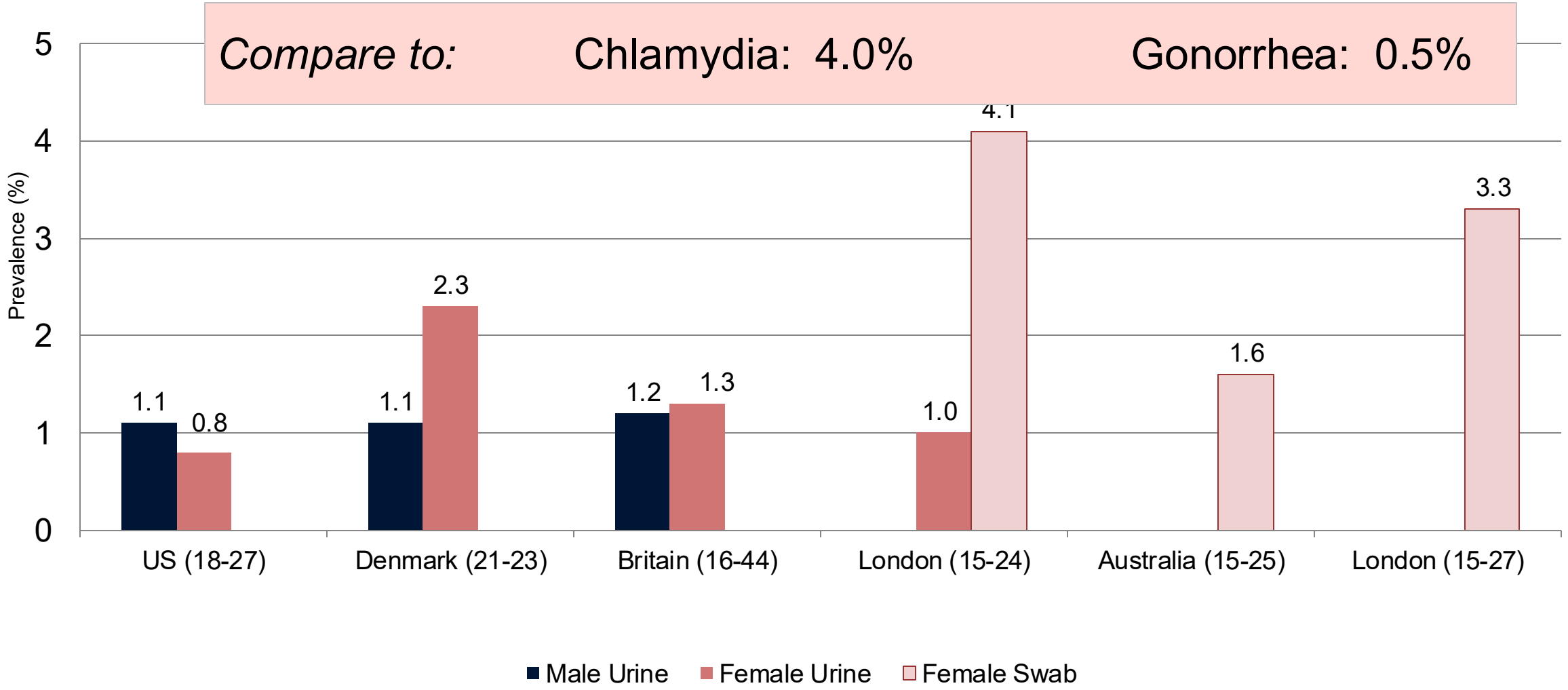

Manhart 2007; Andersen 2007; Sonnenberg 2015; Svenstrup 2010; Walker 2011; Oakeshott 2010

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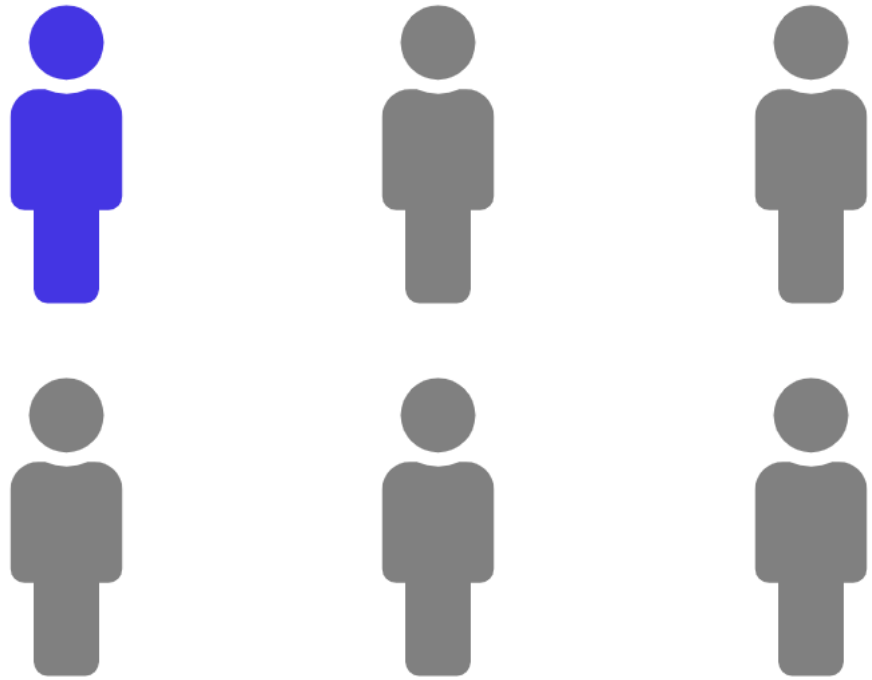
Recent MG Epidemiology - *MyGeniUS*

Surveillance testing* of 1,743 urogenital specimens obtained from persons seen in sexual health clinics in the United States showed 1 in 6 persons had a positive test for *Mycoplasma genitalium*.

*Testing was conducted in October-December 2020 in 6 cities and testing included asymptomatic patients (56%) and symptomatic patients (44%).



Manhart LE, Leipertz G, Soge OO, et al. *Mycoplasma genitalium* in the US (MyGeniUS): Surveillance Data From Sexual Health Clinics in 4 US Regions. *Clin Infect Dis*. 2023;77:1449-59.

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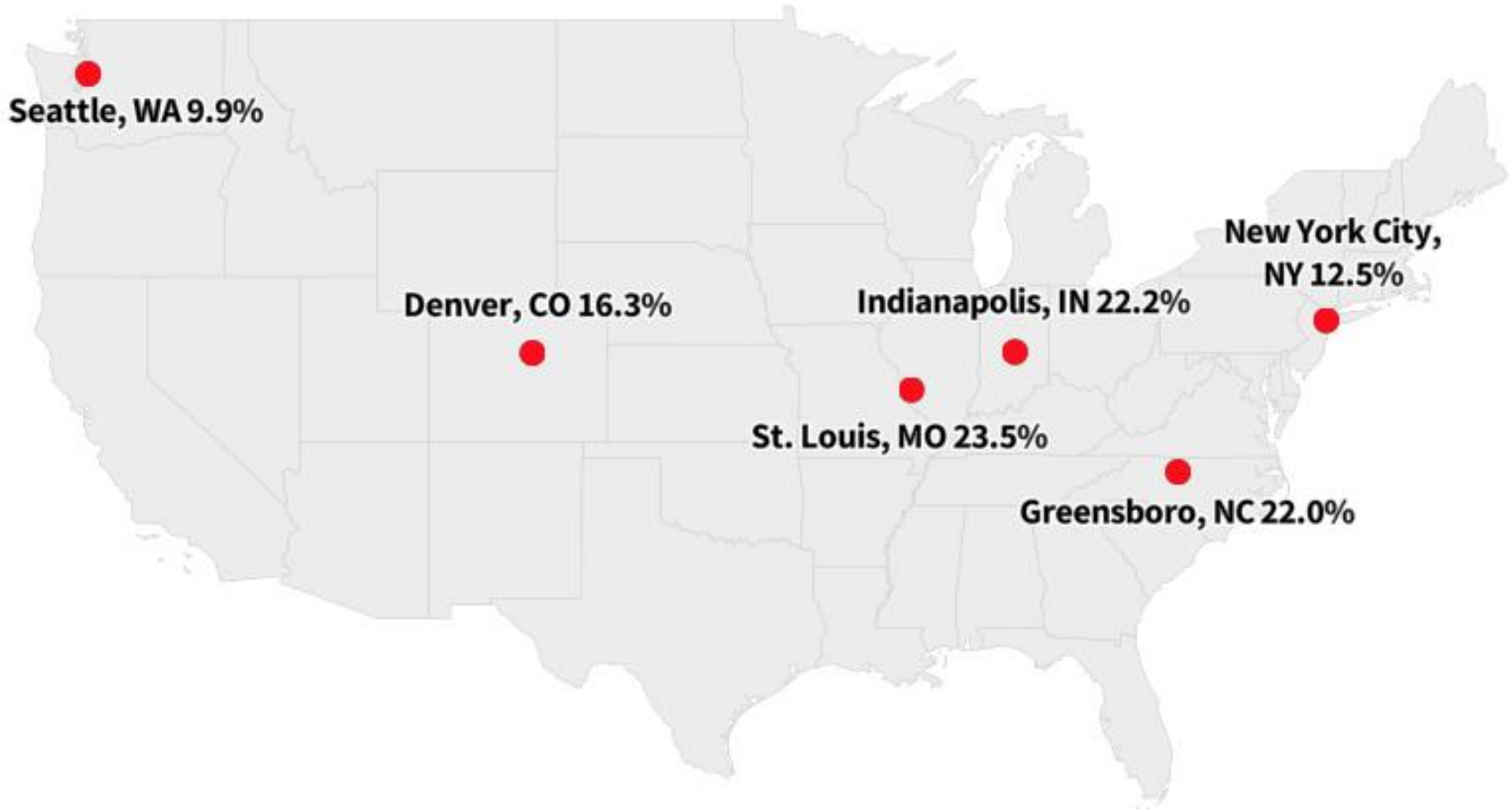
Recent MG Epidemiology - *MyGeniUS*

***Mycoplasma genitalium* prevalence varied significantly among the 6 surveillance sites.**



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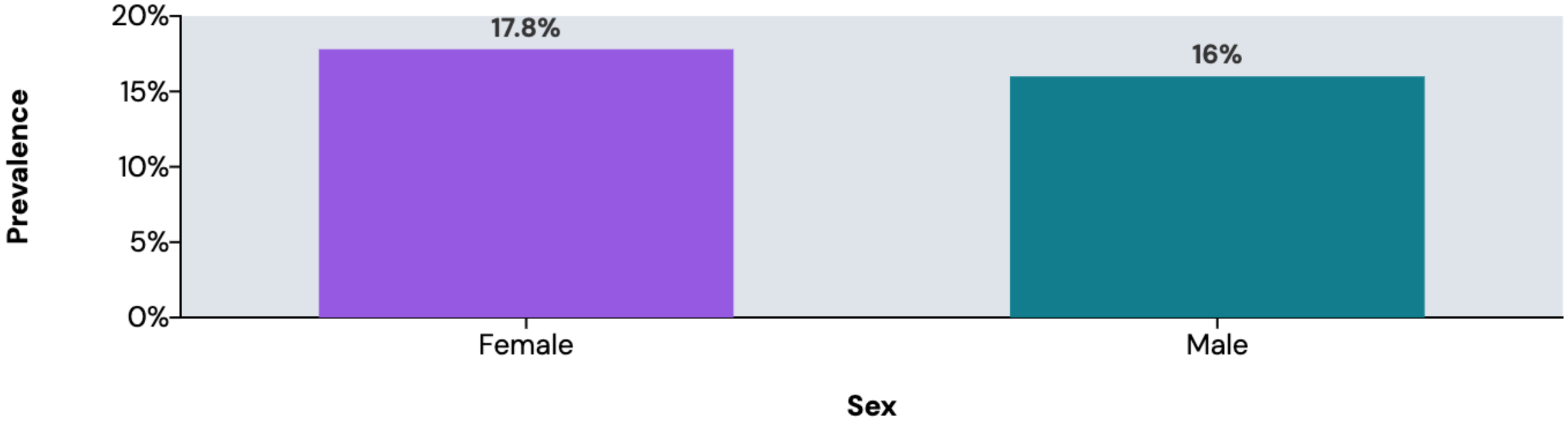
Recent MG Epidemiology - *MyGeniUS*

Mycoplasma genitalium prevalence was about the same in females and males.



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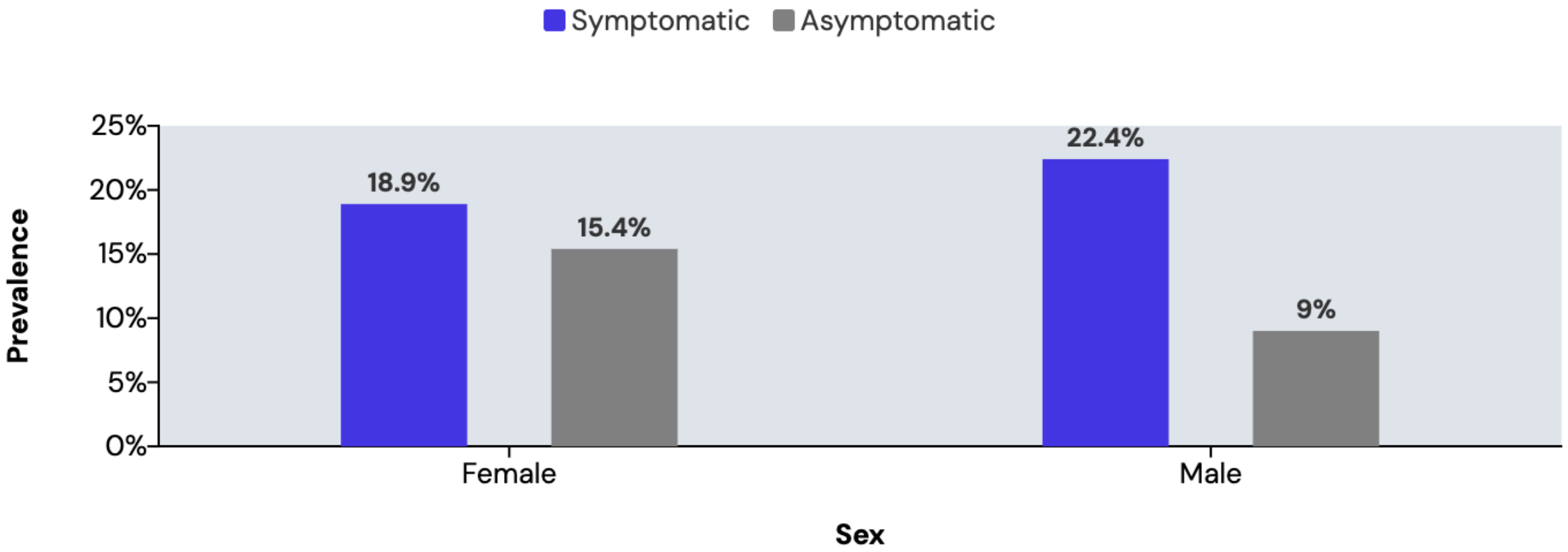
Recent MG Epidemiology - *MyGeniUS*

Mycoplasma genitalium prevalence was higher in persons who were symptomatic.



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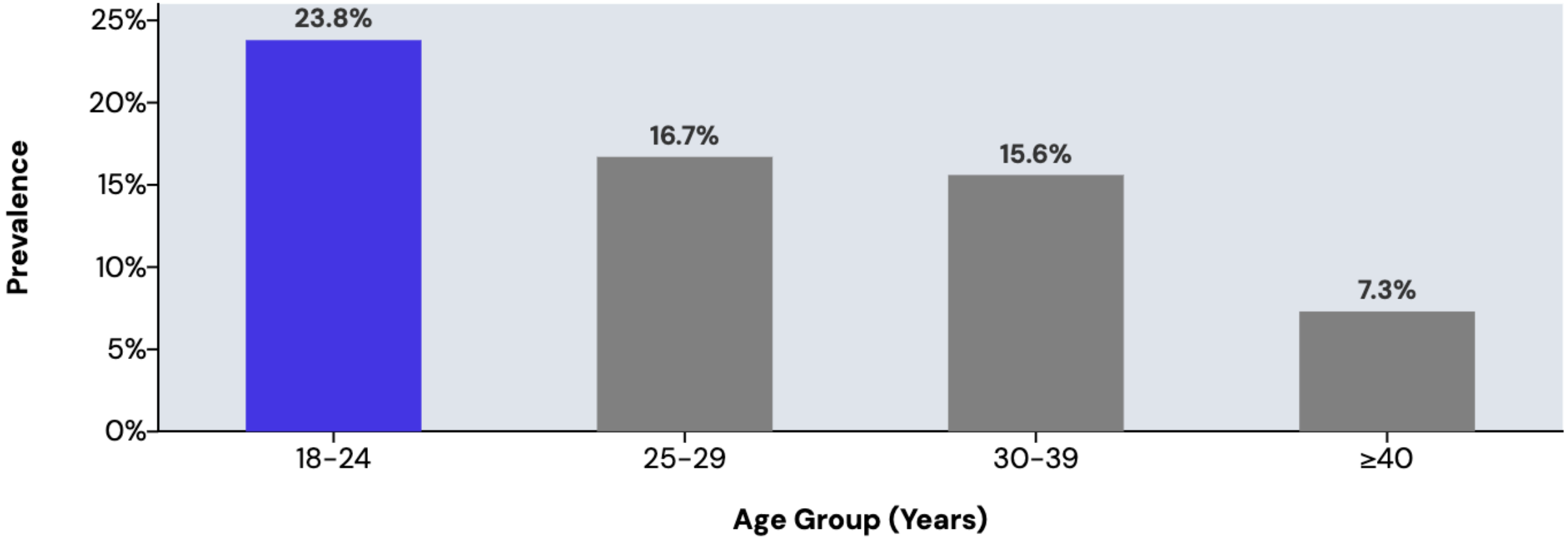
Recent MG Epidemiology - *MyGeniUS*

Among adults, *Mycoplasma genitalium* prevalence was highest in persons 18-24 years of age.



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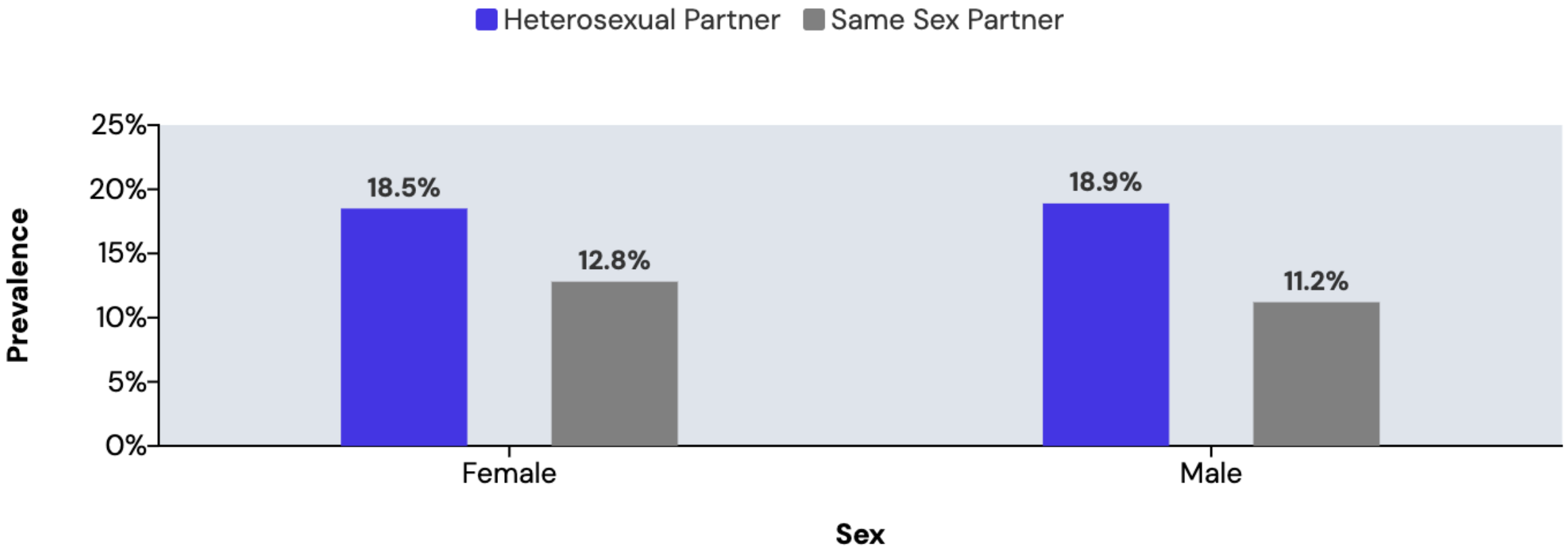
Recent MG Epidemiology - *MyGeniUS*

Mycoplasma genitalium prevalence was higher in persons with heterosexual partners than in those with same sex partners.



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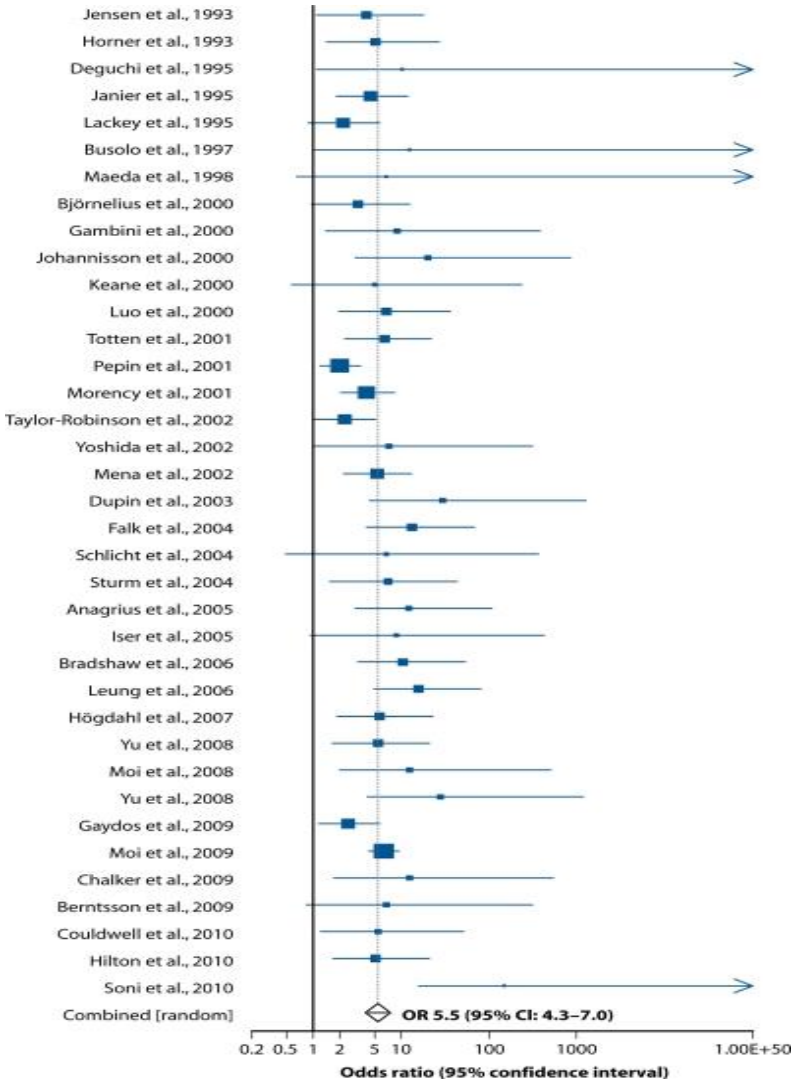
Male urethritis & *M. genitalium*



Acute urethritis[1]

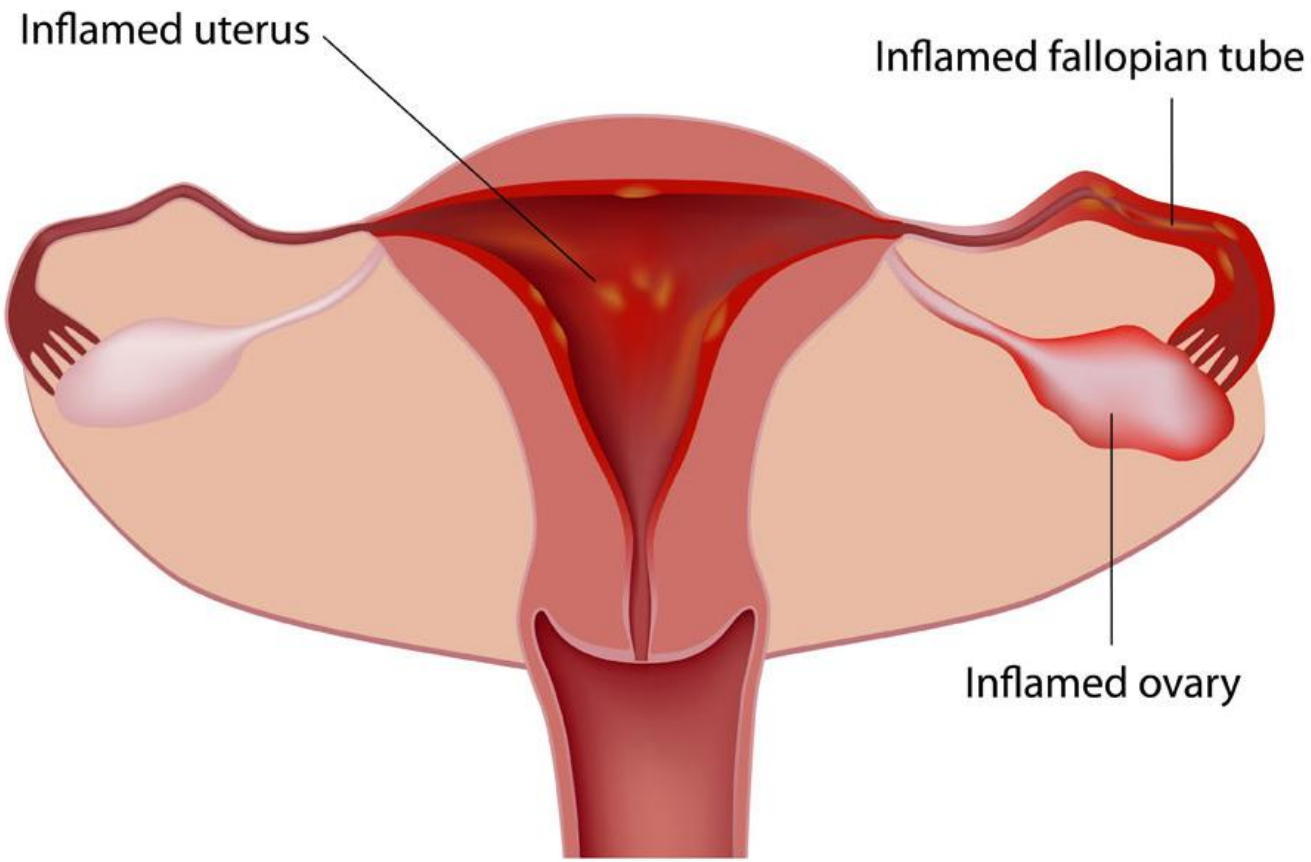
- 15% MG+ in urethritis
- 22% MG+ in urethritis not due to CT or NG
- Summary **OR = 5.5 (4.3-7.0)**

Persistent urethritis[2]

- **13 – 41%** of men with persistent/recurrent urethritis MG+

[1] Taylor-Robinson & Jensen, *Clin Microbiol* Rev, 2011; [2] Sena et al, *JID* 2012

General Agreement about Association with PID



4 – 22% of women with PID have *M. genitalium*

Meta-analysis[1]

- **11** studies
- Pooled Odds Ratio = **1.9 (1.31 - 3.49)**

Stronger relationship in studies adjusting for CT

OR = **2.0 (0.95 – 4.01)**

[1] Lis et al, *Clin Infect Dis* 2015 - updated by Dr. Manhart ~2021

Recent Meta-analysis confirms PID is higher in those with MG

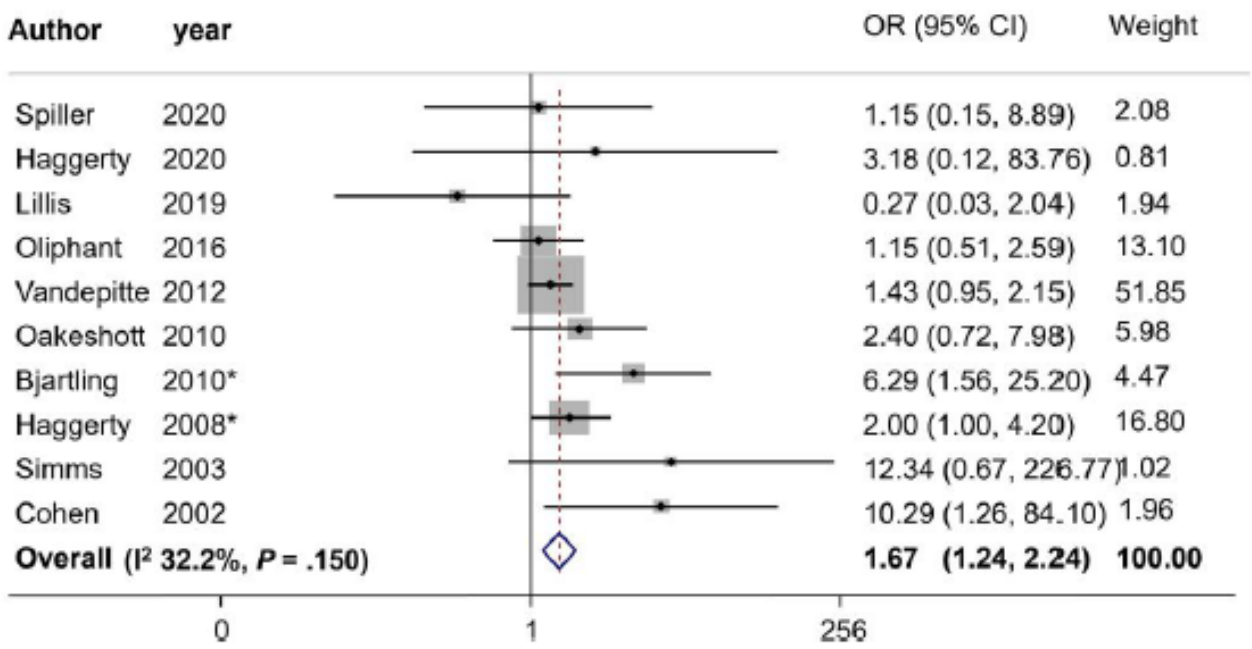


Figure 2. Forest plot of the association between *Mycoplasma genitalium* and PID cases. *Published odds ratio. Dotted line represents pooled OR. Weights are from Random effects model. Abbreviations: CI, confidence interval; OR, odds ratio; PID, pelvic inflammatory disease.

1/10 women with PID have MG

MG is associated with a 67% increase in odds of PID

OR 1.67 is slightly lower and CI narrower than the 2015 Meta-analysis (OR 2.14)

Htaik K, Vodstrcil LA, Plummer EL, Sfameni AM, Machalek DA, Manhart LE, Bradshaw CS. Systematic review and meta-analysis of the association between *Mycoplasma genitalium* and Pelvic inflammatory disease (PID). *Clin Infect Dis*. 2024 Jun 7:ciae295.

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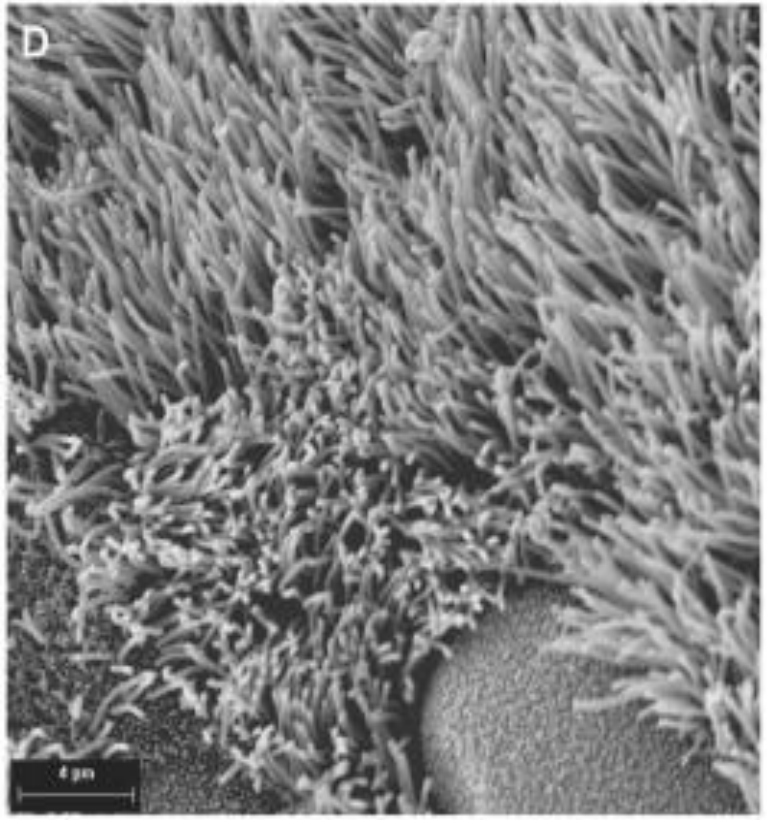
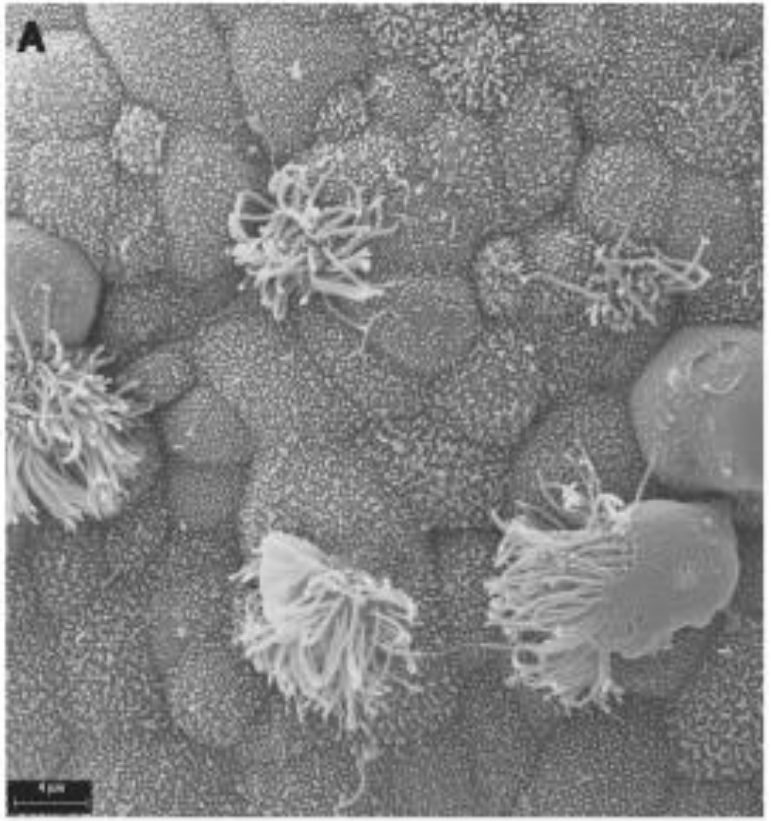
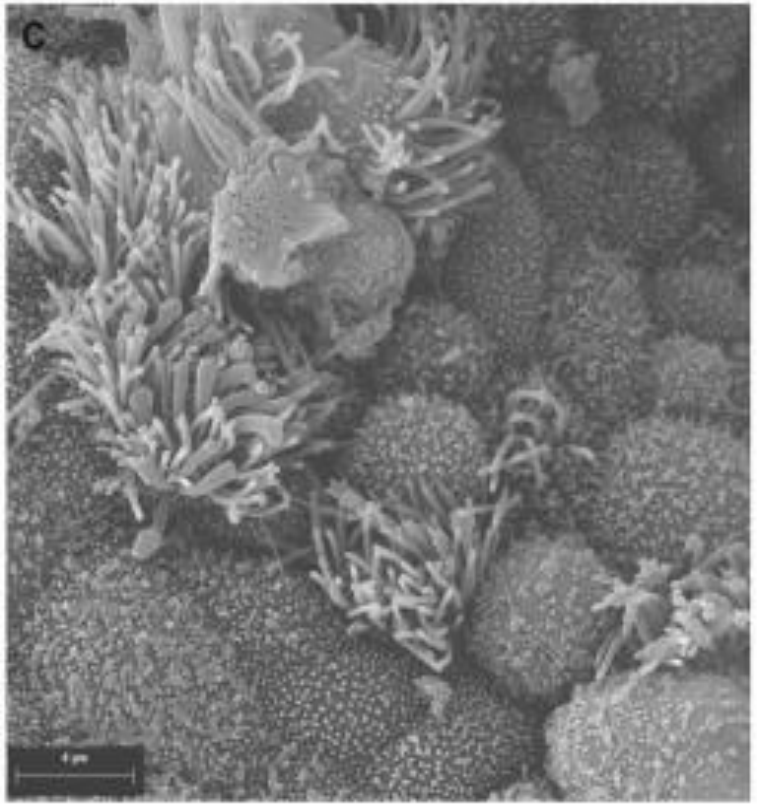
M. genitalium & Fallopian Tube Tissue

Normal (control) tissue	Infection with ***C. trachomatis***	Infection with ***M. genitalium***







Incubation period = 6 days

Baczynska et al, *Hum Reprod* 2007

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M. genitalium & Disease – Meta-Analyses

Syndrome	Summary risk estimate	Studies accounting for CT *(subset)*
NGU	5.5 (4.3 – 7.0)	-
Female Urethritis	2.2 (1.6 – 2.9)	2.1 (1.5 – 2.9)
Cervicitis	1.6 (1.4 – 2.0)	1.9 (1.4 – 2.8)
PID / Endometritis	1.9 (1.3 – 3.5)	2.0 (0.95 – 4.0)
Preterm Delivery	1.9 (1.2 – 2.9)	2.3 (1.1 – 5.0)
Spontaneous Abortion	1.8 (1.1 – 3.0)	2.3 (1.0 – 4.9)
Infertility	3.0 (1.3 – 6.7)	3.7 (1.7 – 8.1)
HIV	2.0 (1.4 – 2.8)	-

Taylor-Robinson & Jensen, *Clin Microbiol* Rev 2011; Lis et al., *CID* 2015 – updated; Mavedzenge, AIDS 2009

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M. genitalium & Disease – Meta-Analyses

Syndrome	Summary risk estimate	Studies accounting for CT *(subset)*
NGU	**5.5**-fold increased risk	
Female Urethritis	**2**-fold increased risk (Stronger when accounting for other causes of the syndromes)	
Cervicitis		
PID / Endometritis		
Preterm Delivery		
Spontaneous Abortion		
Infertility		
HIV		

Taylor-Robinson & Jensen, *Clin Microbiol* Rev 2011; Lis et al., *CID* 2015 – updated; Mavedzenge, AIDS 2009

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Who should be tested?

M. genitalium

***Mycoplasma genitalium* Testing Recommendations**		
Type of Test	Definition	Recommendation
Screening Test	Testing of asymptomatic people with the goal of preventing disease sequelae and prevent transmission to others	Routine testing of asymptomatic persons is NOT recommended.
Diagnostic Test	Testing of symptomatic persons to direct treatment decisions	Testing recommended for: •Men with persistent or recurrent urethritis •Women with persistent or recurrent cervicitis Testing should be considered for: •Women with pelvic inflammatory disease

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FDA-approved Diagnostic tests

M. genitalium

	Aptima TMA test[1]		Cobas TV/MG test[2]	
	Sensitivity	Specificity	Sensitivity	Specificity
Vaginal Swab	98.9	98.5	96.6	97.0
Endocervical Swab	81.5	98.3	83.1	98.4
Female Urine	77.8	99.0	86.4	97.0
Male Urine	90.9	99.4	100.0	97.6
Male Urethral Swab	98.2	99.6	-	-
Male Penile Meatal Swab	88.4	97.8	85.0	97.9
Resistance Detection	None		None	
FDA approval	January 2019		May 2019	

[1]Hologic package insert (https://www.hologic.com/sites/default/files/2019-01/AW-17946_001_01.pdf); [2] Roche Cobas TV/MG spec sheet (courtesy of Chris McGowin, Roche, Inc.)

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Antibiotic Therapy
M. genitalium

Recommended Regimens if *M. genitalium* Resistance Testing is Available

If *macrolide sensitive:* Doxycycline 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days (2.5 g total)

If macrolide resistant: Doxycycline 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days

Recommended Regimens if *M. genitalium* Resistance Testing is Not Available

If *M. genitalium* is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

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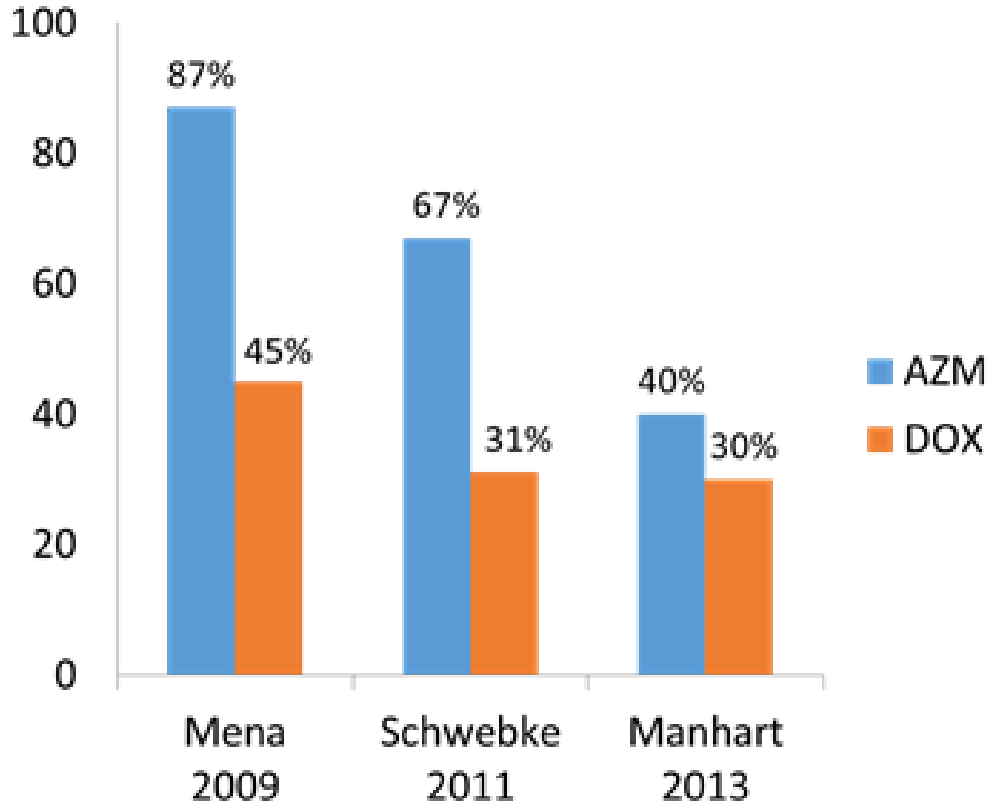
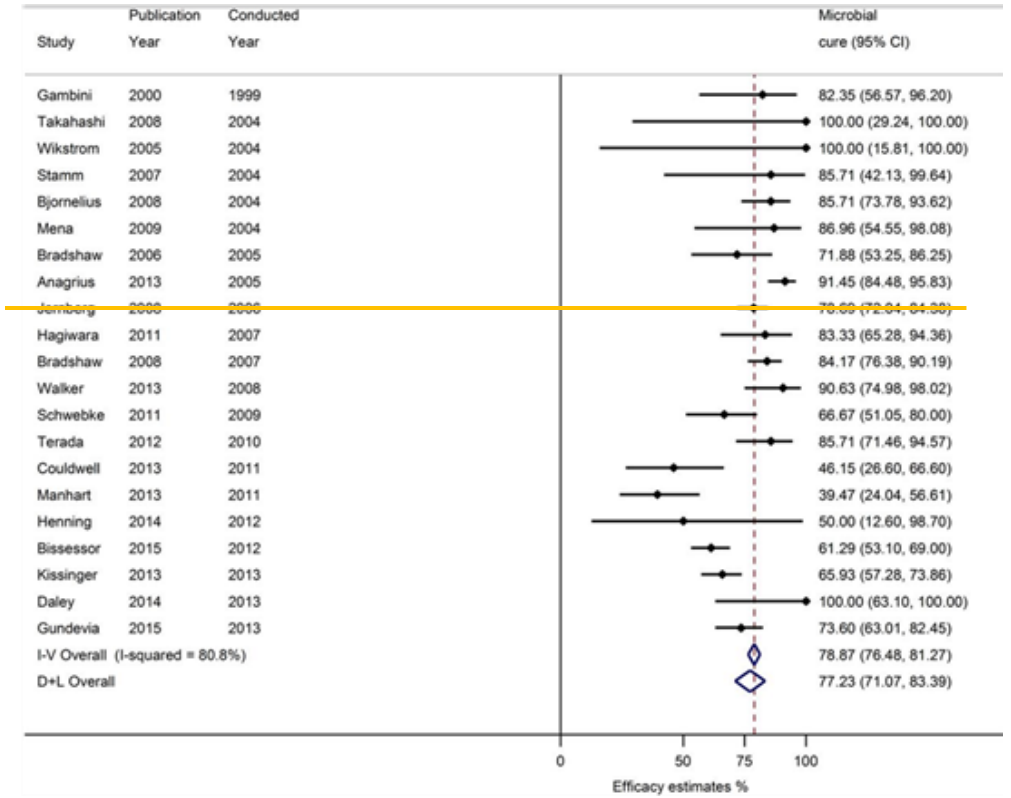
Treatment of *M. genitalium*

Low efficacy of syndromic therapies in U.S. trials



Azithromycin 1g efficacy declined from 86% pre-2009 to 67% post-2009[1]



[1]Lau et al. *Clin Infect Dis*. 2015

Macrolide Resistance Mutations in US (44 - 90%)

M. genitalium

Seattle, WA
62% (MSW)[1]
69% (men w/urethritis)[2]
90% (MSM)[3]

7 cities
48% (clinic attendees)[5]

Pittsburgh, PA
58% (men w/urethritis)[2]

Durham & Greensboro, NC
61% & 64% (men w/urethritis)[2]

Los Angeles, CA
80% (clinic attendees)[4]

Birmingham, AL
44% (STD Clinic)[6]
61% (heterosexual couples)[7]
61% (men w/urethritis)[2]
74% (HIV+ MSM)[8]

New Orleans, LA
60% (men w/urethritis)[2]

[1]Romano 2018; [2]Bachmann 2019; [3]Chambers 2019; [4]Allan-Blitz 2018; [5]Getman 2016; [6]Xiao 2018; [7]Xiao 2019; [8]Dionne-Odom 2018

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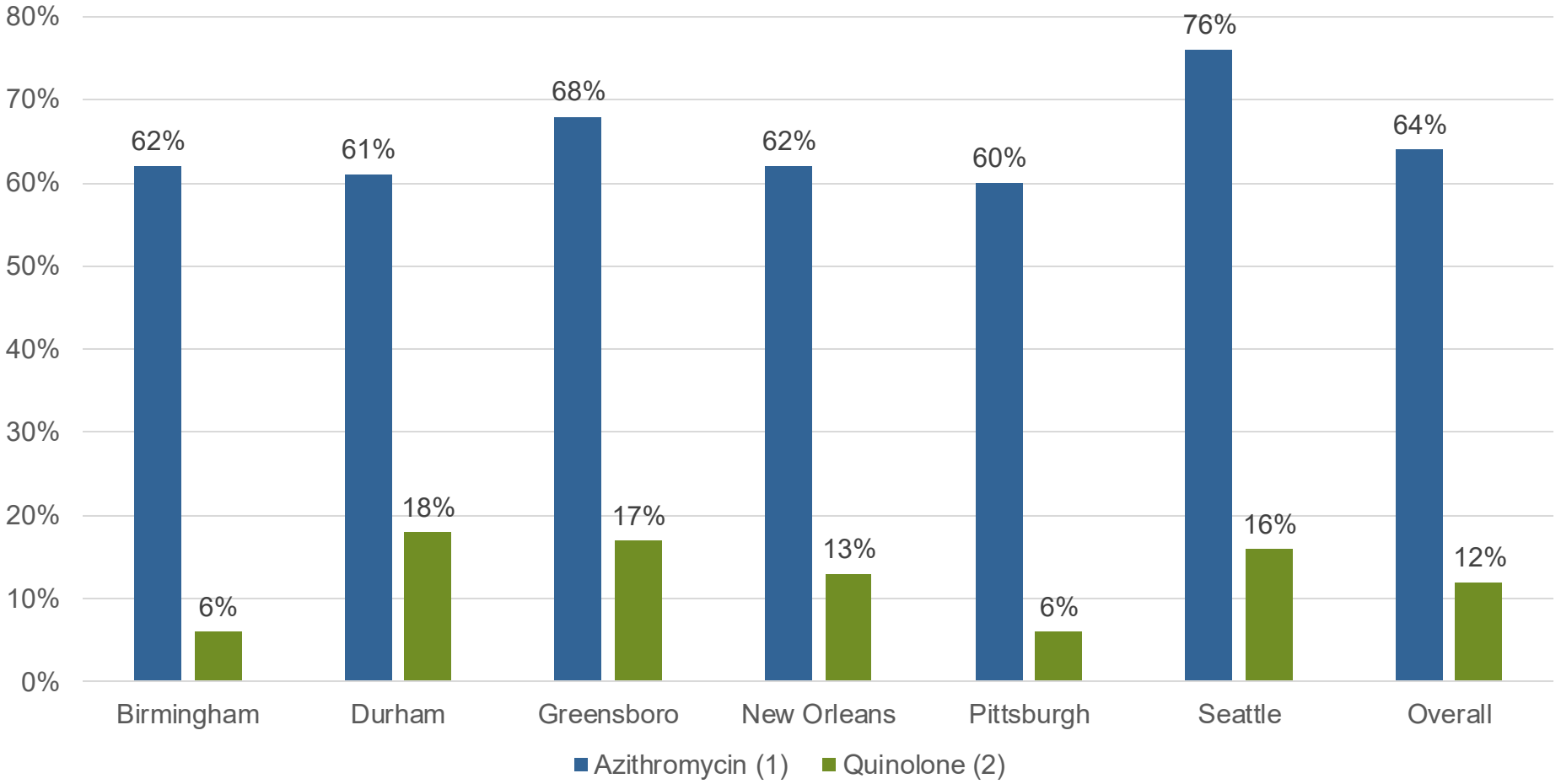
Prevalence of Resistance Mutations in *M. genitalium* among Men with Urethritis



1. 23S rRNA mutation, among those with evaluable results
2. *parC* mutation, among those with evaluable results

Bachmann LH, *CID* 2020

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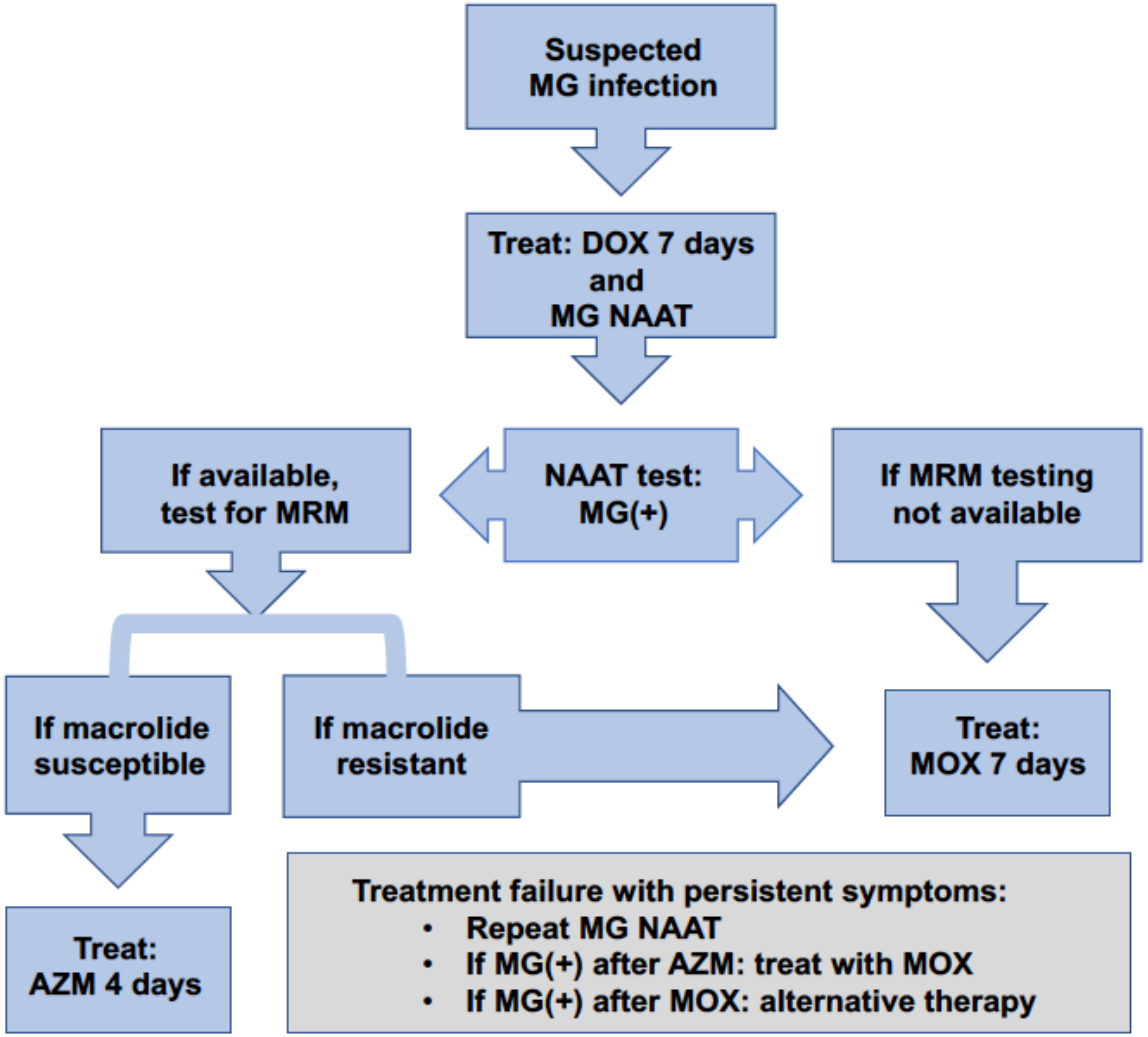
Review of MG Treatment



Wood GE, Bradshaw CS, Manhart LE. Update in Epidemiology and Management of *Mycoplasma genitalium* Infections. *Infect Dis Clin North Am*. 2023 Jun;37(2):311-333.

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Summary

What we know:

- MG prevalence higher than gonorrhea; sometimes higher than chlamydia
- MG elicits inflammation and causes tubal damage *in vitro*
- Most genital tract syndromes are associated with MG
- Antibiotic resistance rapidly emerges to each new agent

What we still don't know:

- How frequently *M. genitalium* results in PID & infertility
- Can early detection & treatment prevent PID & infertility
- What are the implications of asymptomatic MG infection

Summary

What should you do if you suspect a patient has MG:

Order a test

- Multiple FDA-approved tests available
- Resistance testing not widely available in the US

Treat sequentially

- Empiric treatment for non-pregnant patients: Doxycyline 100mg BID x7d→ Moxifloxacin 400mg x 7d
- Encourage patients to return if symptoms recur

If you suspect MG treatment failure:

- Minocycline 100mg bid x 14d
- Tinidazole may be effective
- Omadacycline may be effective
- Get an expert consult

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Summary

- Infection most common in women <25
- Screening asymptomatic patients not recommended
- Treatment in pregnancy is challenging
  - Best empiric treatment: High dose azithromycin (1g on d1 → 500mg d2-4) with TOC on d21
- TOC only recommended in those treated with azithromycin in the absence of resistance testing
- Include Moxifloxacin for PID if MG+
- Ongoing sex partners should be tested and treated if
  - Same regimen as partner (index patient)
  - Presumptive treatment only when testing not possible
- Expert consultation for pregnancy and treatment failures

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THANK YOU!

Acknowledgment

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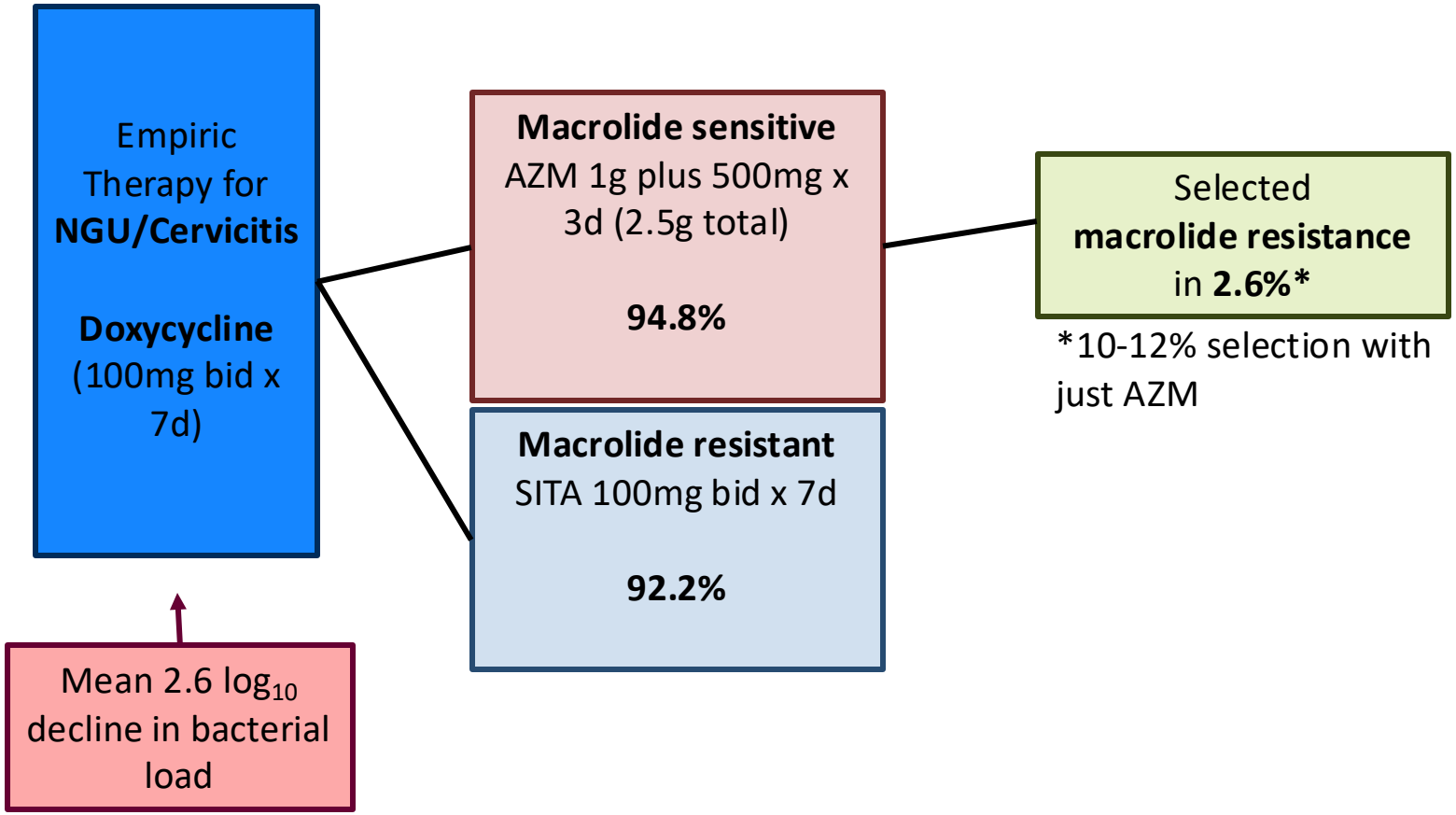
Resistance guided therapy
M. genitalium



Read et al., 2018

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Antimicrobials for treatment failures
M. genitalium

ANTIMICROBIAL	EFFICACY
Pristinamycin 1g qid x 10d 1g bid x 10d 1g tid x 10d + DOX (7d)	100% in 6 AZM/MOX failures[1] 75% efficacy in larger study; no difference by dose[2]
Minocycline 100mg bid x 14d	4 of 6 case reports[3-5]
Spectinomycin 2g IM x 7d	One case report [6]

[1]Bissessor 2015; [2]Read 2018; [3]Deguchi 2017; [4]Glaser 2019; [5]Bradshaw (personal communication); [6]Falk 2017; [7]Mondeja 2018

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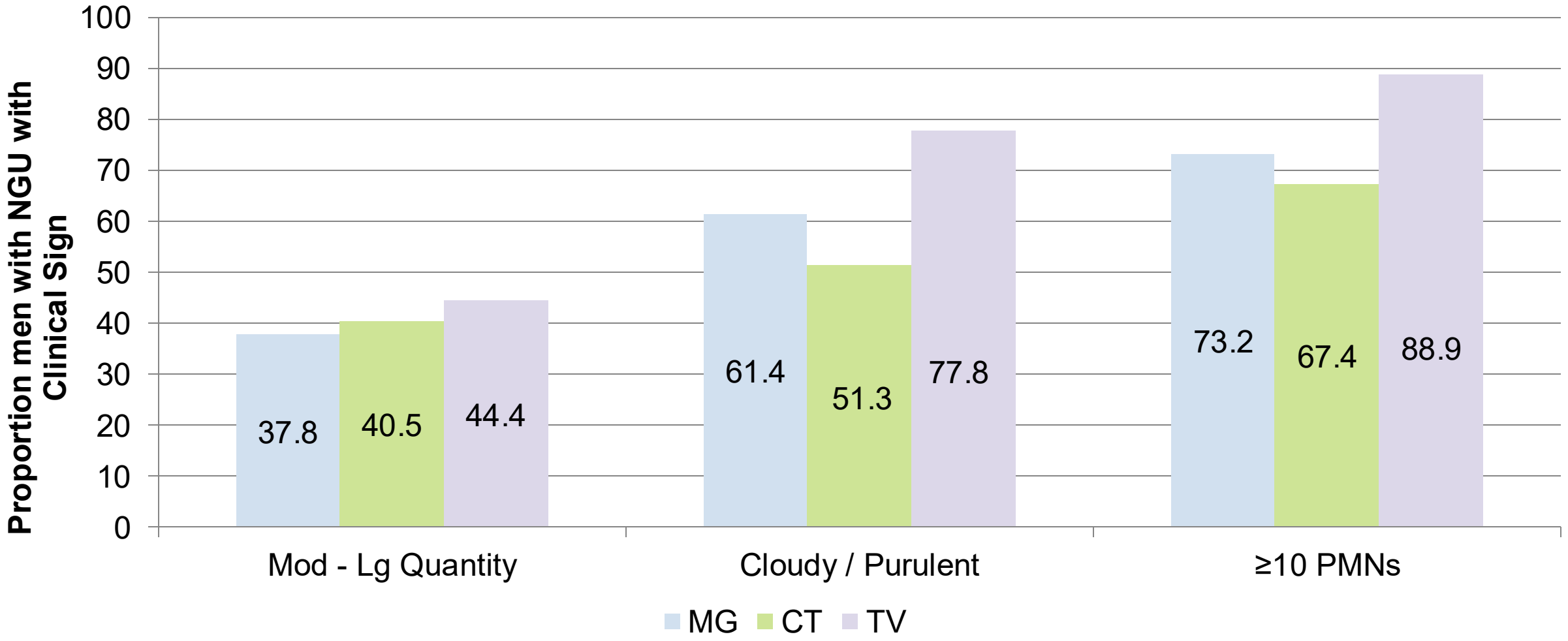
M. genitalium-associated NGU
Clinical signs



Wetmore et al, *Sex Transm Dis* 2011

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