



# ***Mycoplasma Genitalium***

***Presented by:***

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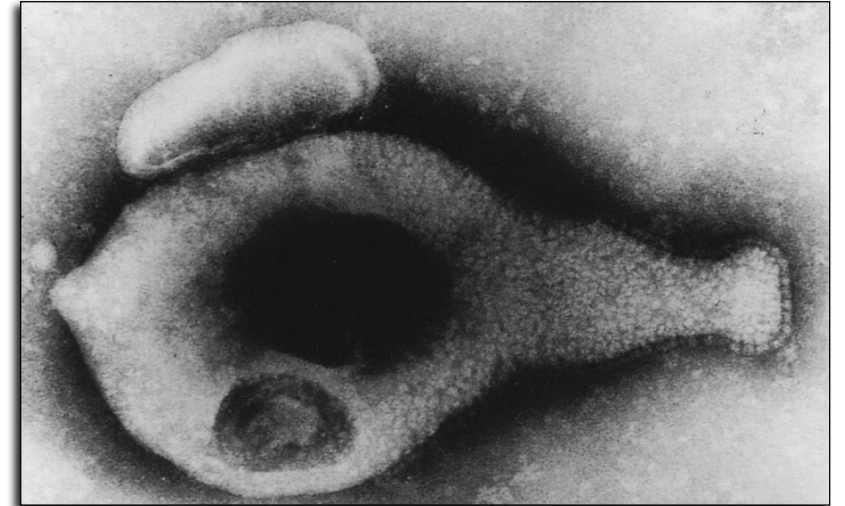
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**Medical and Laboratory Director,**

**Durham County Department of Public Health**

# History of *M. genitalium*

- Smallest genome of any free-living organism (~480 genes), no cell wall.<sup>1</sup>
- Very similar to other Mycoplasma spp. (*M. pneumoniae*, *Ureaplasma urealyticum*).<sup>1</sup>
- Immunodominant adhesion protein is MgPa, contributes to pathogenesis.
- Lives on and in the epithelial cells of the urinary and genital tracts.<sup>1</sup>
- First identified in 2 male cases of non-gonococcal urethritis in 1981.<sup>1</sup>

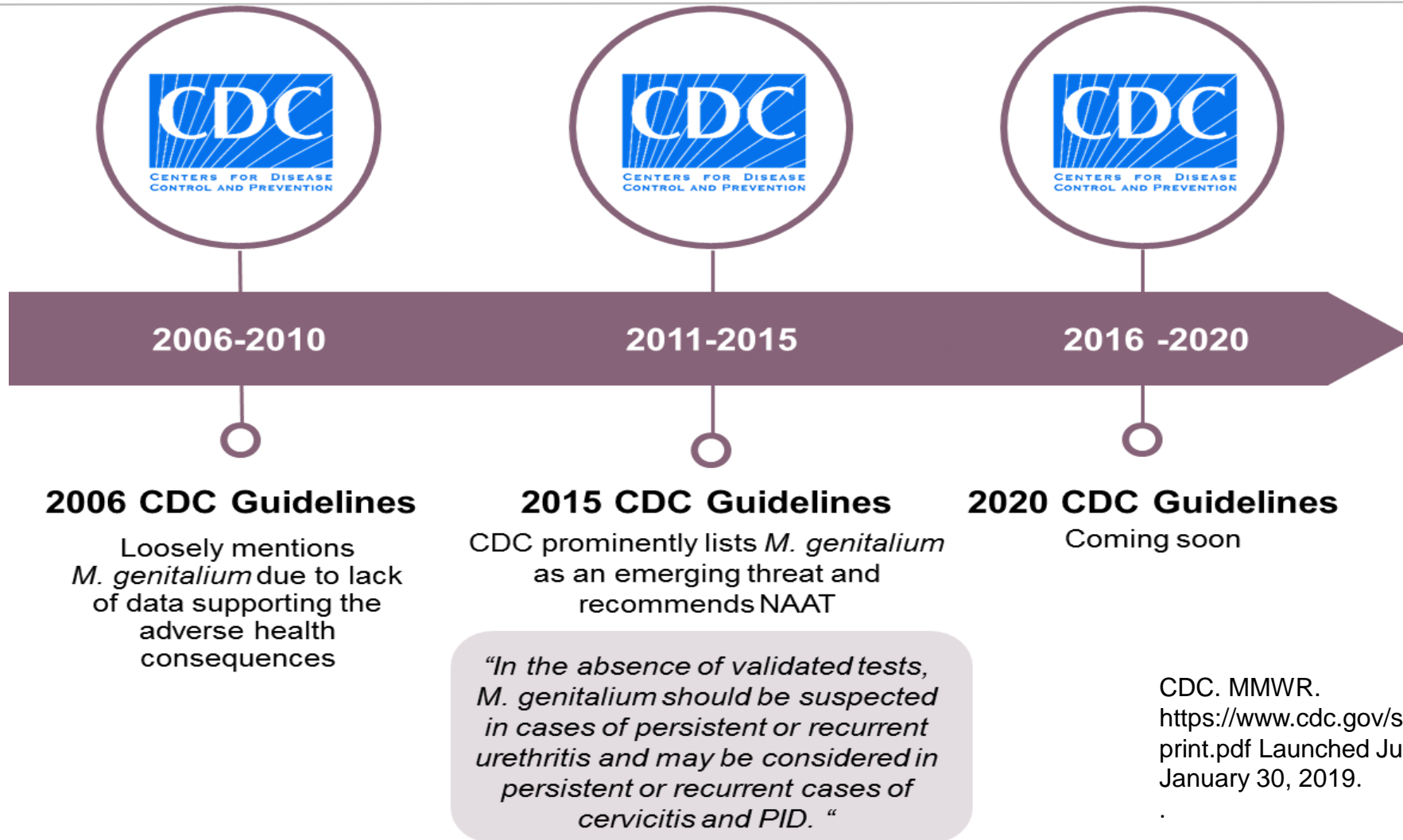


Lind, Lancet 1982

1. Tully, et al. *Lancet*. 1981;1(8233):1288-91.

2. Taylor-Robinson and Jensen. *Clin Microbiol Rev* 2011; 24:498-514.

# *M. genitalium* as an Sexually Transmitted Infection (STI)



# Population Prevalence

***M. genitalium* infection is more common than *Neisseria gonorrhoeae*, and has similar prevalence as *Chlamydia trachomatis* in most settings.<sup>1</sup>**

Low Risk Populations<sup>2</sup>  
1% - 3%

High Risk Populations<sup>3-6</sup>  
7.3% - 14%

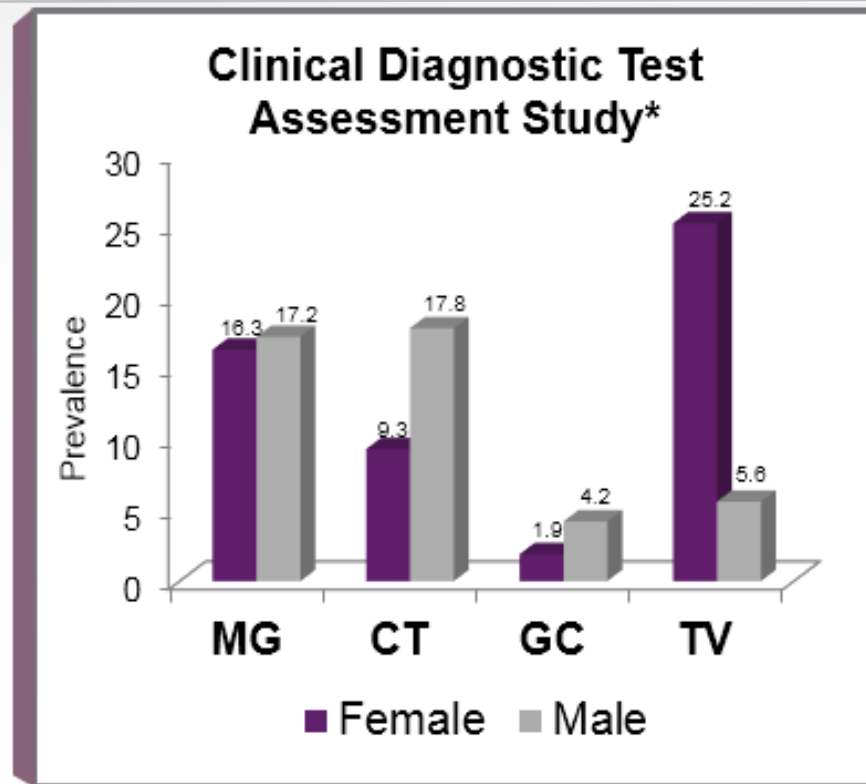


Low Risk Populations<sup>2</sup>  
1% - 3%

High Risk Populations<sup>3-6</sup>  
10% - 41%

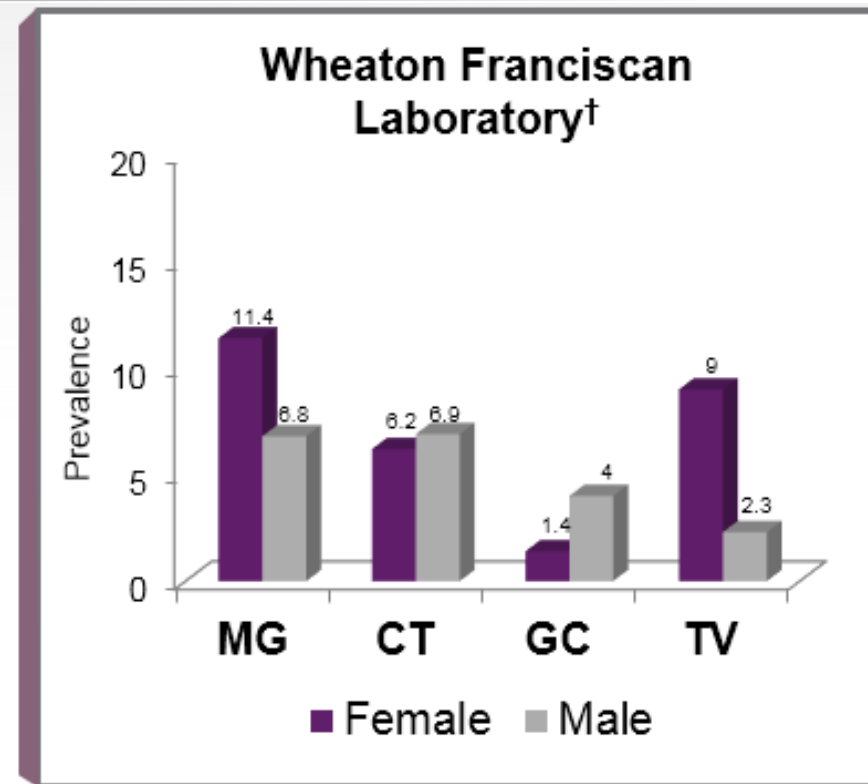
1. CDC. 2015 Sexually Transmitted Diseases and Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>. Accessed January 30, 2019.
2. Anagnius C, et al. *PLoS One*. 2013 Apr 8;8(4):e61481.
3. Hilton J, et al. *Sex Health*. 2010;7(1):77-81.
4. Wikstrøm, et al. *Sex Transm Infect*. 2006; 82:276-279.
5. McGowin CL, et al. *PLoS Pathog*. 2011;7(5):e1001324.
6. Wroblewski, et al. *J Clin Microbiol*. 2006; 44:3306-12. doi:10.1128/JCM.00553-06.

# Clinic Prevalence in the United States



\* Symptomatic & asymptomatic individuals from family medicine, OBGYN, family planning, public health and STD clinics (n=7 sites)

Getman et. al. *J Clin Micro* 2016; 54(9):2278-83



† Female specimens from > 50 healthcare locations; male specimens from STI clinic

Napierala et. al. *Diag Micro Inf Dis* 2015; 82 (2015) 194–198

Munson et al. *J Clin Micro* 2016; 54(2):432-8

# Clinical Presentations



Frequently asymptomatic.<sup>1</sup>  
Detected in **10-30%** of women with clinical cervicitis.<sup>1</sup>  
Identified in up to **22%** of pelvic inflammatory disease (PID) cases.<sup>1</sup>  
Untreated PID can lead to adverse pregnancy outcomes.<sup>1</sup>



May also increase the risk of HIV acquisition and transmission.<sup>2,3</sup>



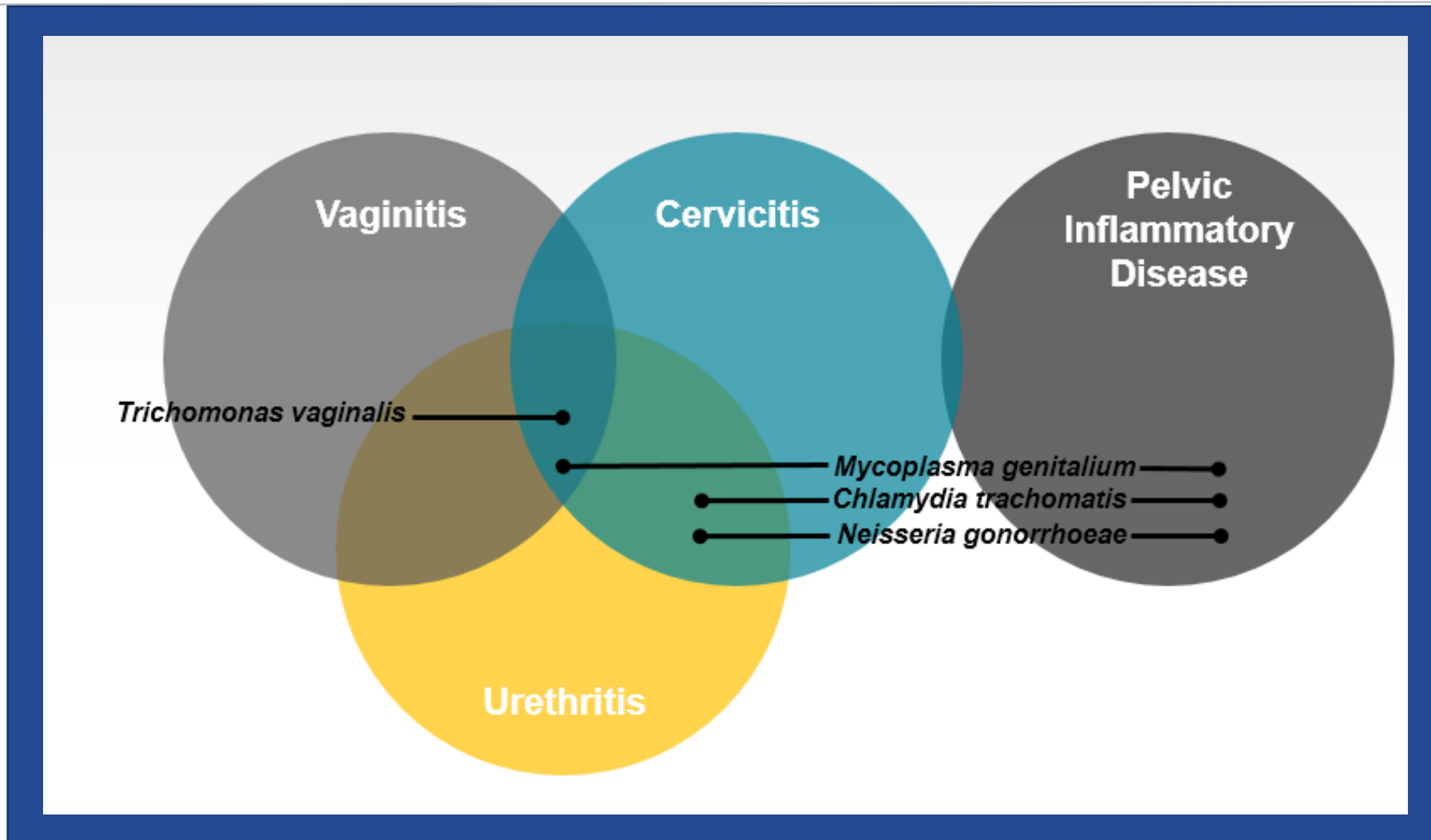
More likely to exhibit symptoms of an *M. genitalium* infection.<sup>1</sup>  
Responsible for **30%** of persistent or recurrent urethritis in men.<sup>2</sup>



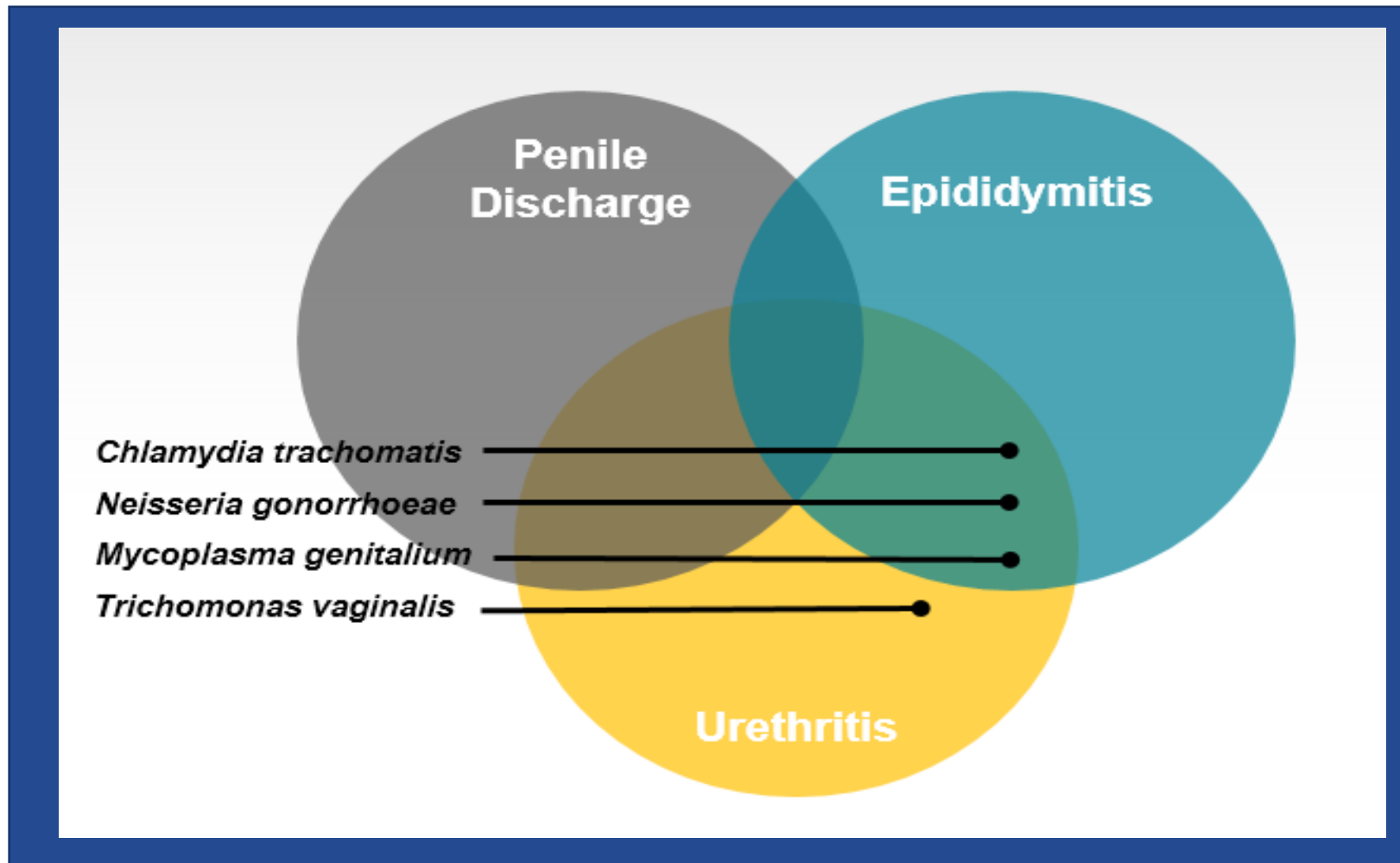
When patients do experience symptoms, they are similar to those associated with other urogenital tract bacterial infections.<sup>4</sup>

1. Taylor-Robinson D, et al. *Clin Microbiol Rev.* 2011;24(3):498-514.
2. CDC. 2015 STD Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>. Accessed January 30, 2019.
3. Lis R, et al. *Clin Infect Dis.* 2015;61(3):418-26.
4. Vandepitte J, et al. *Sex Transm Infect.* 2014;90(7):545-9.

# STI Syndromes in Women



# STI Syndromes in Men





# Complications from *M. genitalium* Infections

- Strongly associated with reproductive sequelae in women similar to chlamydia<sup>1,2</sup>
  - Pelvic inflammatory disease (PID), infertility, preterm birth, spontaneous abortion<sup>3</sup>
- Associated with chronic urethritis, balanoposthitis in men; possibly prostatitis, epididymitis<sup>1</sup>
- Over 2-fold increased risk for HIV-1 acquisition<sup>4</sup>

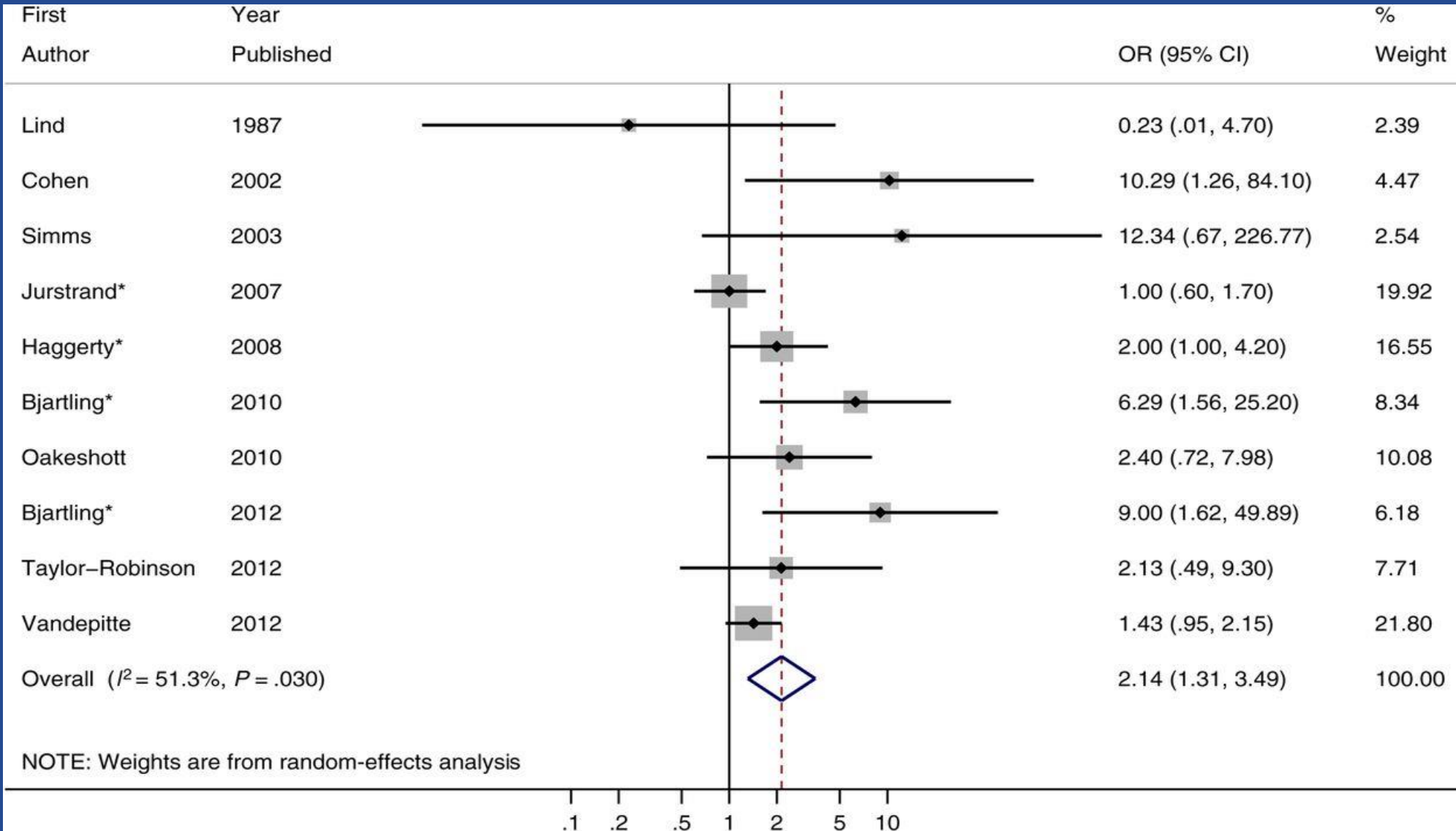
1. Taylor-Robinson D et al. *Clin Microbiol Rev* 2011; 24:498-514.

2. CDC. 2015 Sexually Transmitted Diseases and Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>.

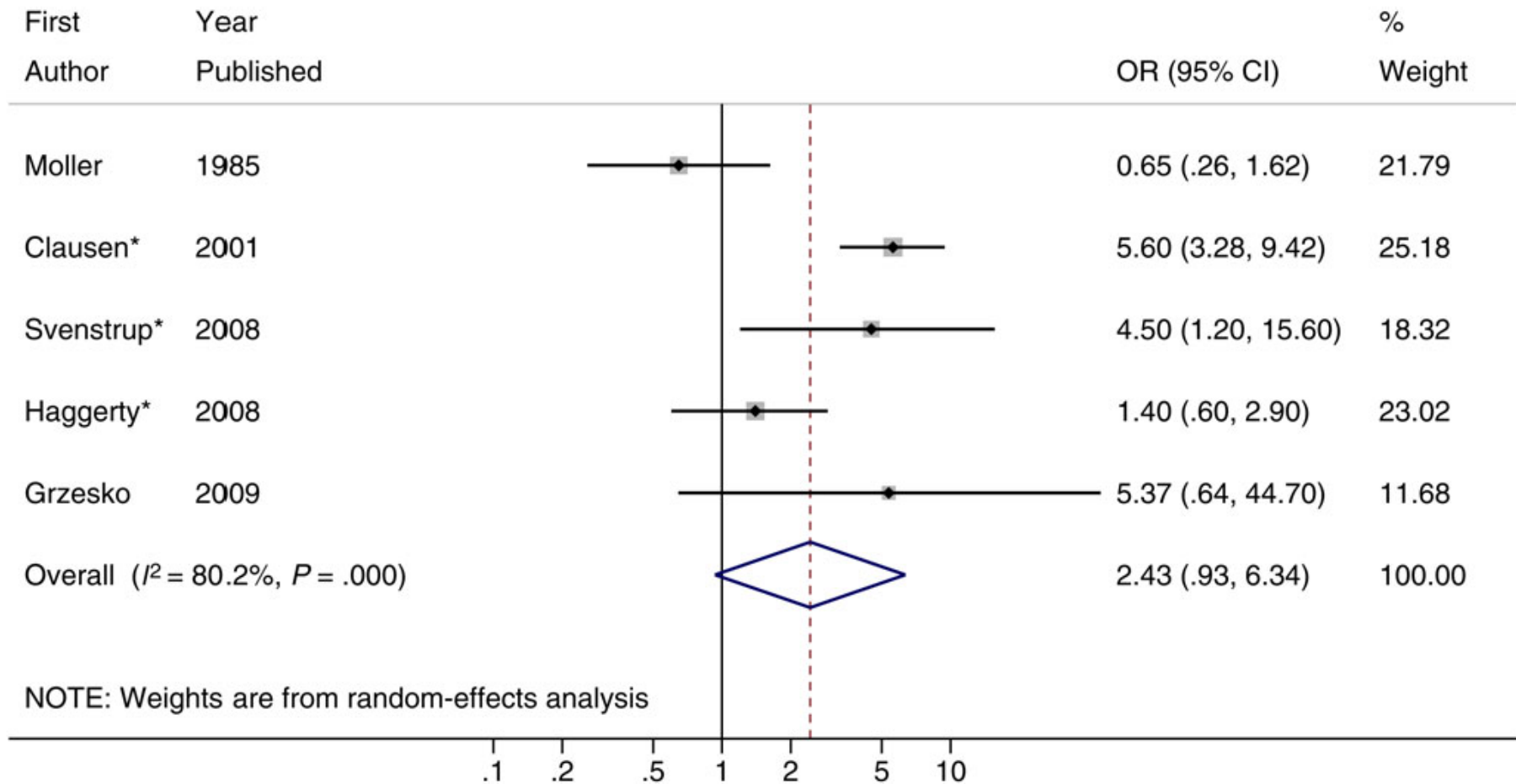
3. Lis et al. *Clin Infect Dis* 2015 Aug 1; 61:418-426.

4. Mavedzenge SN et al. *AIDS* 2012 Mar 13; 26(5): 617-24.

# *M. genitalium* Association with PID



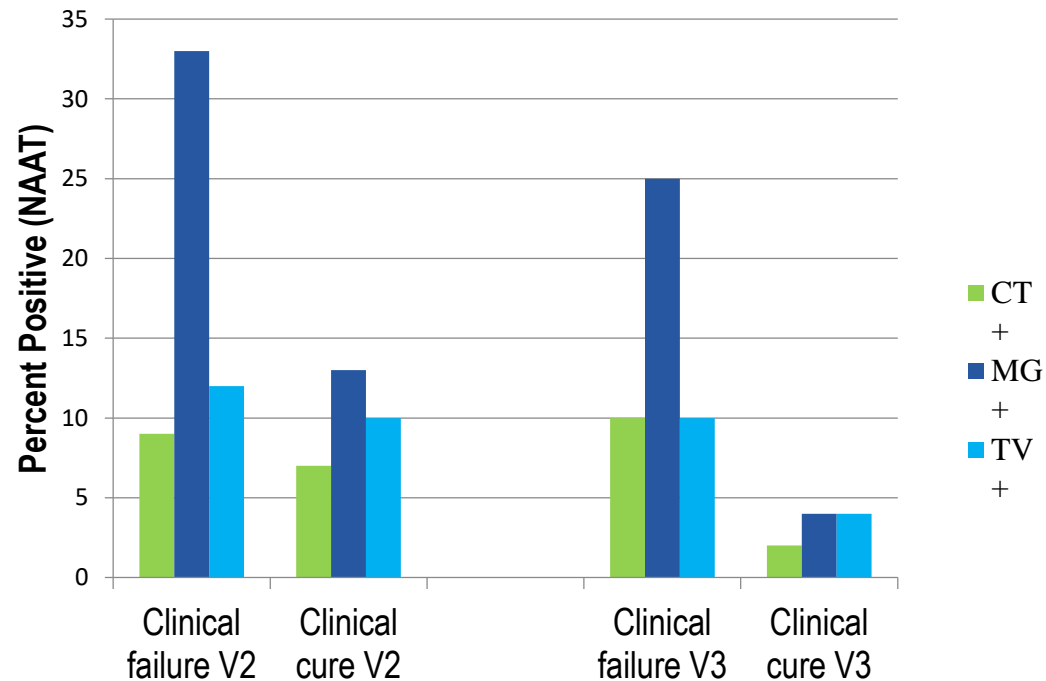
# *M. genitalium* Association with Infertility



Lis et al. *Clin Infect Dis* 2015 Aug 1;  
61:418-426.

# Persistence of *M. genitalium*

## Persistence in men (18-45 yo) with NGU following treatment (1 week, 3 weeks)<sup>1</sup>



## Persistence in asymptomatic women (15-25 yrs of age) with bacterial vaginosis<sup>2</sup>

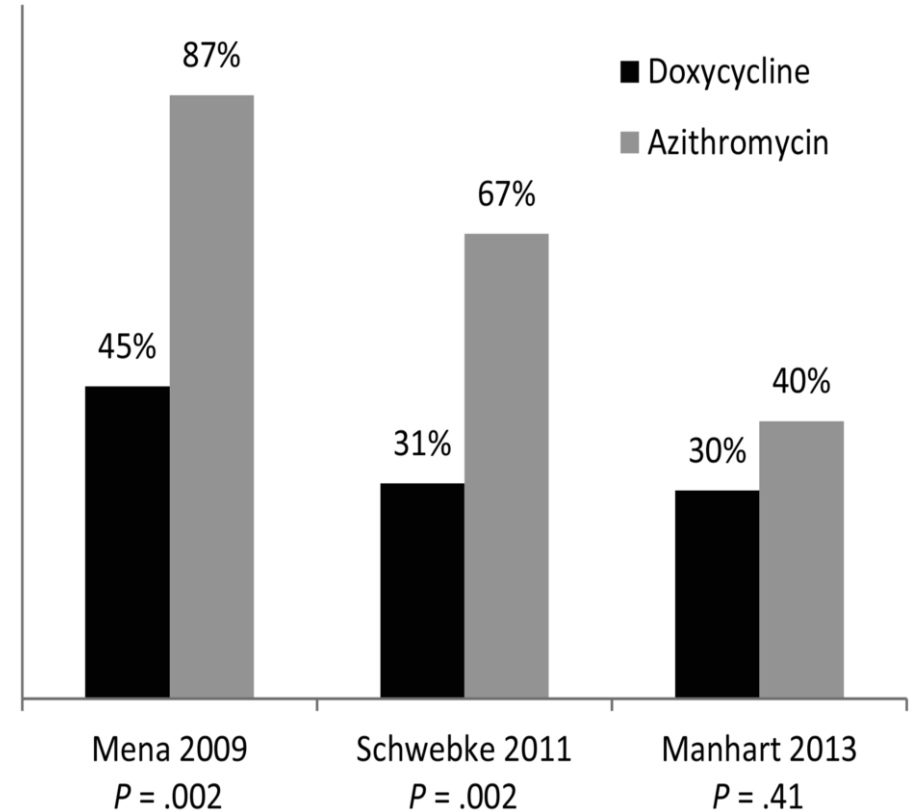
Follow-up Status	N (%)
Persistent MG (all follow-up results are positive)	42 (20.6)
Cleared after baseline (no + test results after baseline)	50 (24.5)
Cleared after 2 months (no + test results after 2 months)	13 (6.4)
Cleared after 4 months (no + test results after 4 months)	11 (5.4)
Cleared after 6 months (no + test results after 6 months)	11 (5.4)
Mixed (both + and – results throughout follow-up)	77 (37.8)

1. Seña, AC, et al. *J Infect Dis.* 2012 Aug 1;206(3):357-65.

2. Seña, AC, et al. *Clin Infect Dis.* 2018;67(1):73-79

# Therapies for *M. genitalium*

- Doxycycline for 7 days has poor cure rates.<sup>1</sup>
- **Azithromycin 1.0 gram in single dose** is recommended therapy.<sup>2</sup>
  - Decline in cure rates from 85% to 67% before and after 2009, respectively.<sup>3</sup>
  - Azithromycin 1.5g over 5 days not more effective than single dose.<sup>4</sup>



1. Manhart LE, et al. *Clin Infect Dis*. 2015 Dec 15;61 Suppl 8:S802-17.

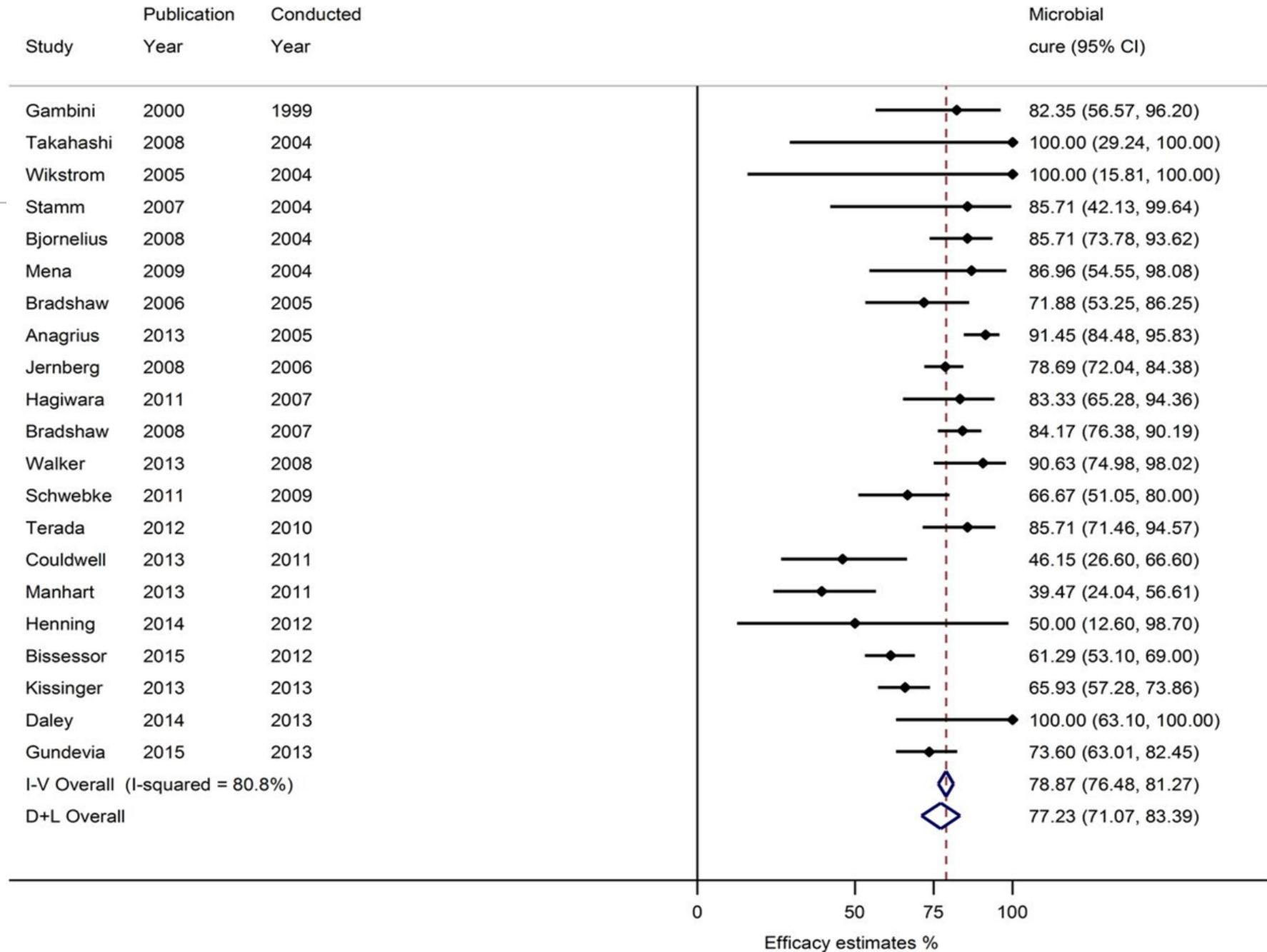
2. CDC. 2015 STD Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>. Accessed January 30, 2019

3. Lau A, et al. *Clin Infect Dis* 2015;61(9):1389–9.

4. Read TR, et al. *Clin Infect Dis*. 2017 Feb 1;64(3):250-256

# Pooled Cure Rates with Azithromycin

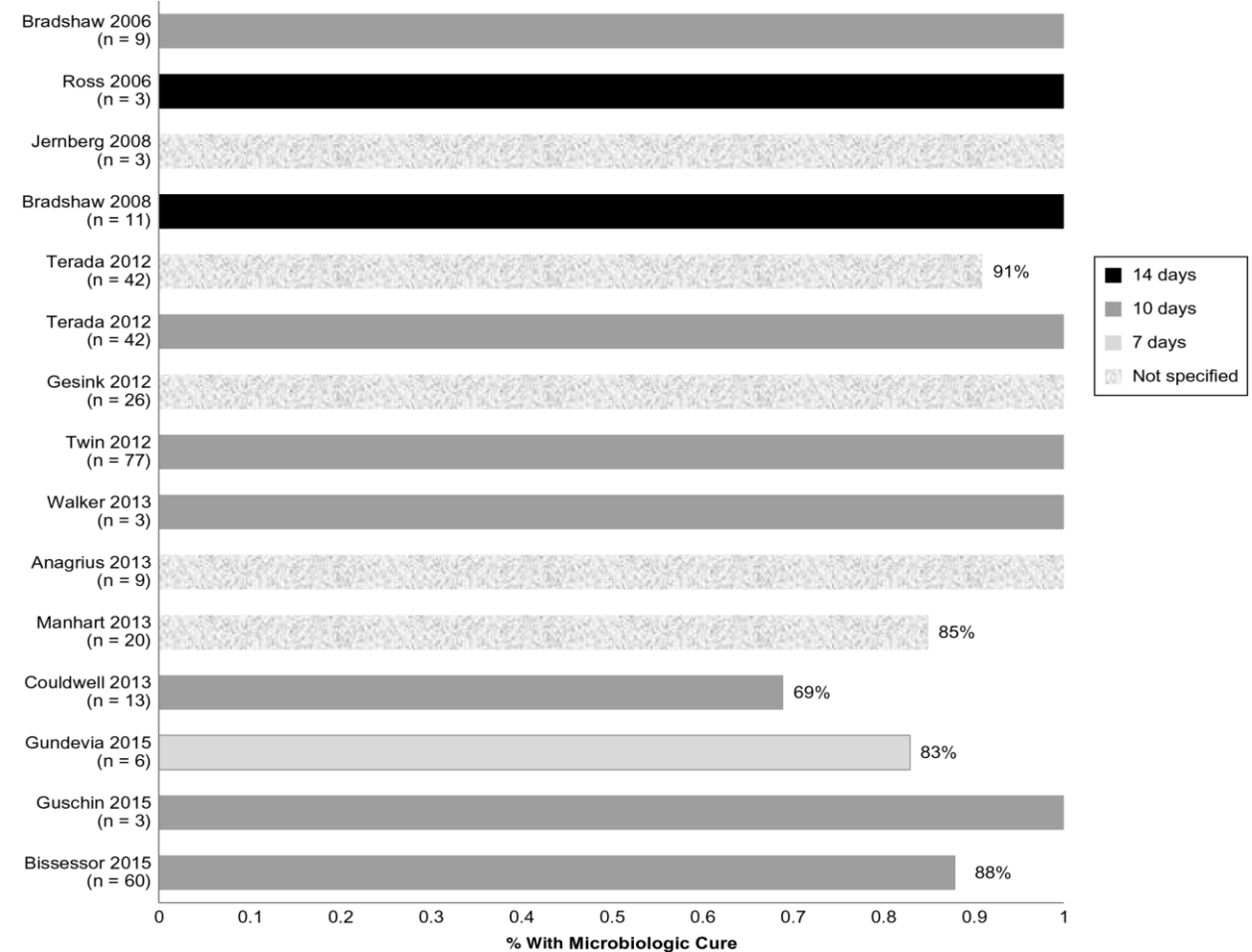
Lau A et al. *Clin Infect Dis* 2015 Nov 1; 61(9):1389-99.



# Therapies for *M. genitalium*

- Moxifloxacin 400 mg daily for 7–14 days is preferred second-line agent.<sup>1</sup>
- Duration of moxifloxacin does not significantly affect cure rates.<sup>2</sup>
- Decline in cure rates from 100% to 89% before and after 2010, respectively.<sup>3</sup>

1. CDC. 2015 STD Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>. Accessed January 30, 2019.
2. Manhart LE, et al. *Clin Infect Dis* 2015 Dec 15;61 Suppl 8:S802-17.
3. Li Y, et. al. *Int J STD AIDS*. 2017 Oct; 28(11):1106-1114



# Increasing Antibiotic Resistance

- Azithromycin -Single-nucleotide polymorphisms in region V of the 23S ribosomal RNA gene of *M. genitalium* can prevent macrolide binding.
- Moxifloxacin - Presence of mutations in *gyrA* and *parC* in the quinolone resistance-determining region of *M. genitalium* correlated with treatment failures.
- Macrolide resistance is now reported in >50% of diagnosed infections in many countries, and multi-drug resistant *M. genitalium* in Australia and Japan.

To effectively target therapy against *M. genitalium*,  
**accurate and sensitive tests are essential for clinical diagnosis.**



# *M. genitalium* Diagnosis



## Clinical Presentation



## Microscopy

As the bacterium has no cell wall, Gram stain cannot be used to detect *M. genitalium*.



## Culture

The organism is extremely fastidious and only a few laboratories worldwide have successfully cultured *M. genitalium* from patient specimens.



## NAATs

NAAT is the recommended method of detection.<sup>1,2</sup>

1. Frolund, 2016. Urethritis-associated Pathogens in Urine from Men with Nongonococcal Urethritis: A Case-control Study. *Acta Dermatol* 96, 689 2. CDC. Sexually Transmitted Diseases and Treatment Guidelines: *Mycoplasma genitalium*. <http://www.cdc.gov/std/tg2015/emerging.htm>. Updated June 4, 2015. Accessed January 30, 2019.

# *M. genitalium* Detection

- Nucleic acid amplification tests (NAATs) have been in use since the early 1990s for research purposes.
- Early polymerase chain reaction (PCR) tests focused on the MPa adhesion gene and the 16S ribosomal RNA gene.<sup>1,2</sup>
- Transcription-mediated amplification (TMA) assays targets the 23S rRNA.<sup>3</sup>
- Multiplex tests have been developed for detection of multiple pathogens (e.g. *C. trachomatis*, *Neisseria gonorrhoeae*, and *M. genitalium*).








1. Jensen JS, et. al. *J Clin Microbiol* 1991; 29:46–50.

2. Jensen JS, et. al. *J Clin Microbiol* 2003; 41:261–6.

3. Gaydos CA. *J Infect Dis* 2017; 216(Suppl 2): S406–S411.

# *M. genitalium* TMA Assay

First FDA-approved assay for detection of *M. genitalium* in the US (Hologic, Inc)

Sample Type	Clinician-collected vaginal swab	Patient-collected vaginal swab	Endocervical swab	Female urine	Patient-collected penile meatal swab	Male urethral swab	Male urine
							
Sensitivity	92.0%	98.9%	81.5%	77.8%	88.4%	98.2%	90.9%
Specificity	98.0%	98.5%	98.3%	99.0%	97.8%	99.6%	99.4%

# Key Questions

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- ❖ Which patients with specific STI syndromes (e.g. cervicitis, persistent NGU, PID) should undergo testing for *M. genitalium*?
- ❖ Should screening programs be developed for *M. genitalium* to avoid complications, especially in women?
- ❖ What should be the recommended first-line treatment for *M. genitalium*?
  - Are there novel agents in the US that are promising as future therapies?
- ❖ In addition to NAATs for diagnosis, do we also need molecular based assays for prediction of antimicrobial resistance in *M. genitalium*?



# Case Study

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Courtesy of William Geisler, MD, MPH

Professor, Division of Infectious Diseases

University of Alabama at Birmingham

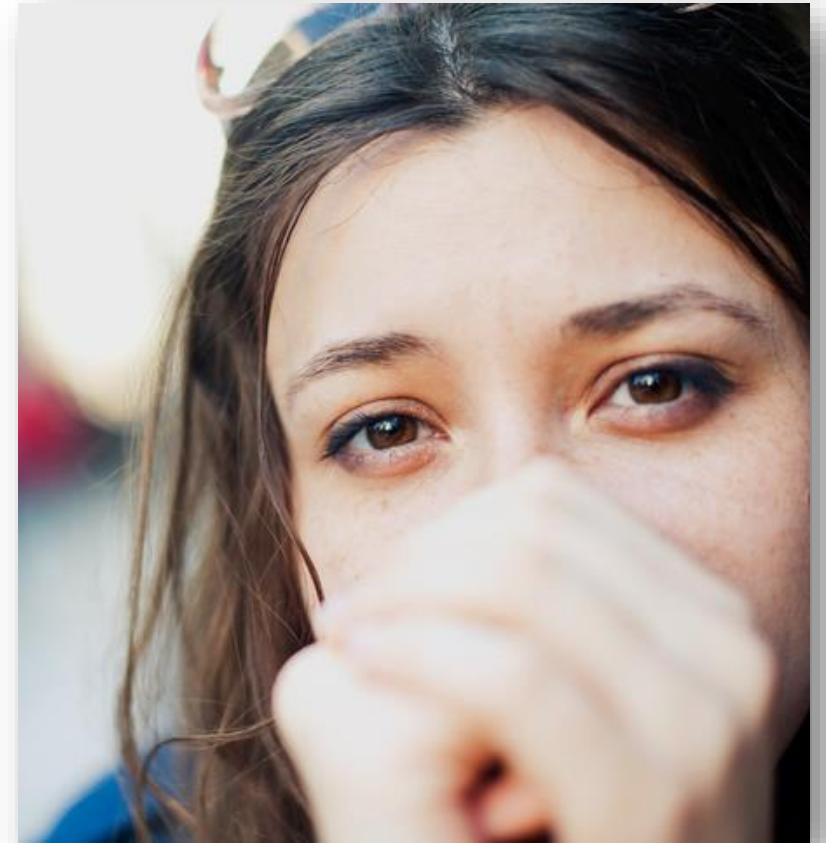


## • Case Description

### • The Patient:

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- A 21-year-old sexually active white female, gravida 0, para 0, comes to the office complaining of mild vaginal discharge. You take a history and find that she has had three male sexual partners over the past year, and that she uses oral contraceptives and condoms for birth control. Pelvic examination reveals cervicitis.





## • Decision Point

How would you manage this patient?

*(More than one answer may be correct)*

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- Order chlamydia and gonorrhea tests
- Order a trichomoniasis test, if available
- Evaluate for bacterial vaginosis (BV)
- All of the above



## • Case Continued



- Since the patient has cervicitis, you prescribe presumptive antibiotic therapy prior to confirmation of infection. You also instruct her to abstain from intercourse until the results of her STI tests come back and her recent partner(s) have received empiric treatment.<sup>1</sup>





## • Decision Point

Which antibiotic regimen do you prescribe?

*.....(More than one answer may be correct).....*

- a) Azithromycin 1 g by mouth
- b) Doxycycline 100 mg by mouth twice daily for 7 days
- c) Ceftriaxone 250 mg intramuscular injection
- Both a and c
- Both b and c



## • Case Continued



- You administer a ceftriaxone 250-mg intramuscular injection and give the patient azithromycin 1 g to take by mouth.<sup>1,2</sup>
- NAAT returned positive for chlamydia. Despite tolerating antibiotics, the patient returns in 3 weeks with persistent vaginal discharge. The patient was abstinent after treatment and her partner was also treated. A repeat pelvic examination reveals cervicitis.

1. CDC. 2015 STD Treatment Guidelines: Gonococcal Infections. 2016. [www.cdc.gov/std/tg2015/gonorrhea.htm](http://www.cdc.gov/std/tg2015/gonorrhea.htm). Updated July 27, 2016. Accessed March 4, 2019.
2. American College of Obstetricians and Gynecologists. Dual Therapy for Gonococcal Infections. Committee Opinion No. 645. Published November 2015. Accessed March 4, 2019.



## • Decision Point

How do you further manage this patient?

*(More than one answer may be correct.)*

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- Retest for chlamydia
- Retest for gonorrhea
- Test for *M. genitalium*
- Consider treatment with doxycycline 100 mg twice daily for 7-days
- All of the above



## • Case Continued



- The patient does not improve with doxycycline and the *M. genitalium* test is returned positive, while the chlamydia and gonorrhea tests are negative.



## • Decision Point

What antibiotic regimen would you choose to resolve the *M. genitalium* infection? *(More than one answer may be correct.)*

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- Repeat doxycycline for 7 days at a dose of 100 mg twice daily by mouth
- Repeat azithromycin 1 g by mouth
- Prescribe moxifloxacin 400 mg daily for 7, 10, or 14 days by mouth
- Prescribe erythromycin base 500 mg QID for 7 days by mouth



## Case Conclusion

### Summary

- It is prudent to be suspicious for *M. genitalium* infection in women with cervicitis, particularly if the condition persists despite initial antibiotic treatment for other STIs.
- Azithromycin is the first-line treatment for *M. genitalium* infection, but it is increasingly ineffective due to developing antibiotic resistance.
- Moxifloxacin is the second-line treatment for *M. genitalium* infection, but it has also been associated with treatment failure.

# Prevalence of Mycoplasma genitalium in Clinical Specimens

The Use of Nucleic Acid Amplified Test (NAAT)

**KnowledgeLab 2017**

March 26-29, 2017  
Gaylord Opryland  
Resort & Convention Center  
Nashville, Tenn.

# Mycoplasma genitalium

- First identified in 1980's
- Cause of nongonococcal urethritis in men (NGU)
- Inhabits the epithelial cells of the urinary tract
- Considered to be an STD in men and women
- Is thought to be more common than gonorrhoea



# Mycoplasma genitalium

- Fastidious organism
- Takes 6 months to grow in a culture
- Not feasible for diagnosing this STD bacterium
- NAAT test of choice
- Not FDA approved yet

# Mycoplasma genitalium

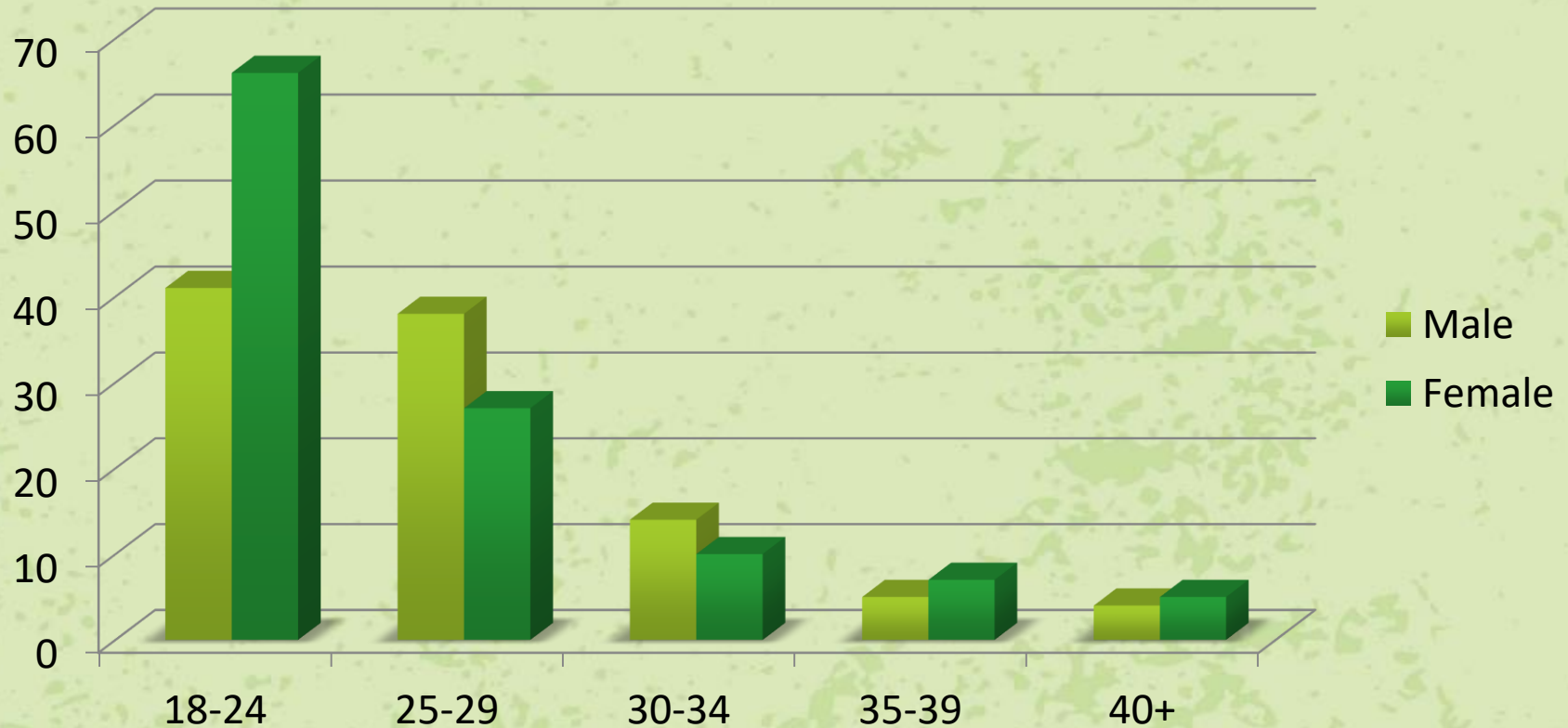
- Started validation studies in October, 2015
- Went live with testing on January 4, 2016
- Test performed on urines, urethral/cervical swabs, vaginal swabs
- Also testing rectal and throat swabs

# Mycoplasma genitalium

- Insight to Springfield-Greene Co Health Department
- 3 STD nurses
- Express Clinic
- Went from 100 patients per month to currently over 700 patients per month

# Mycoplasma genitalium

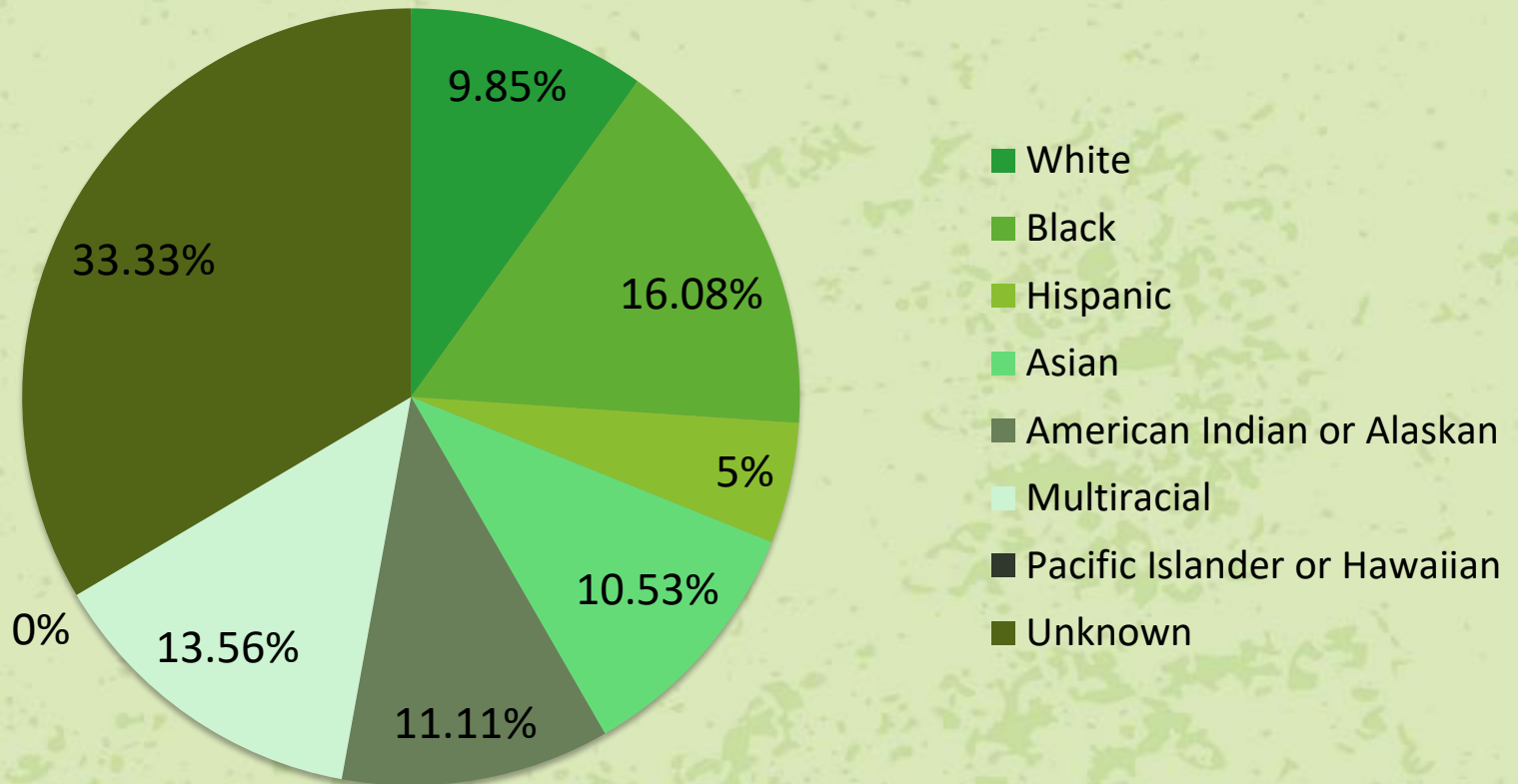
*M. genitalium* results by gender



*Age group calculation based on current year and year of birth provided. Age group may not be accurate if only year of birth was provided.*

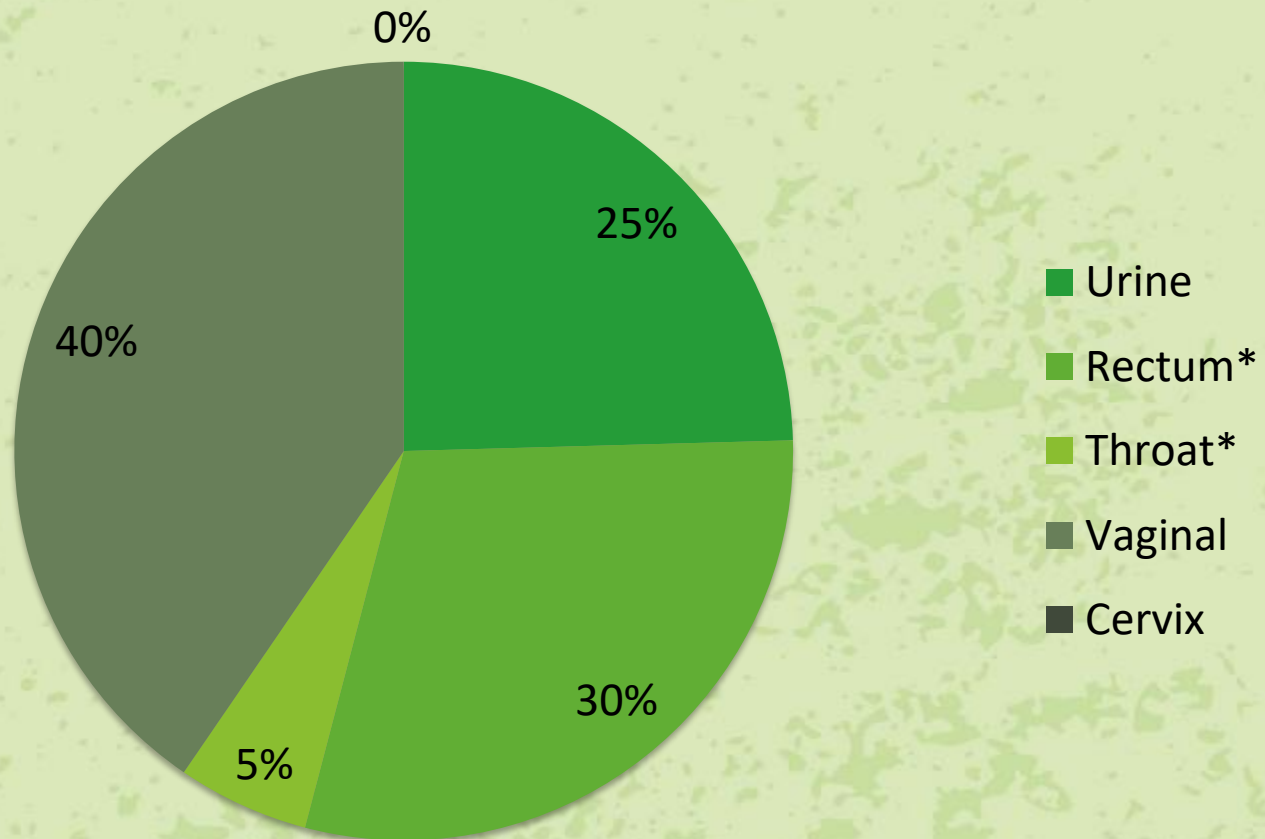
# Mycoplasma genitalium

*M. genitalium* percentages based on reported race of clinic patients



# Mycoplasma genitalium

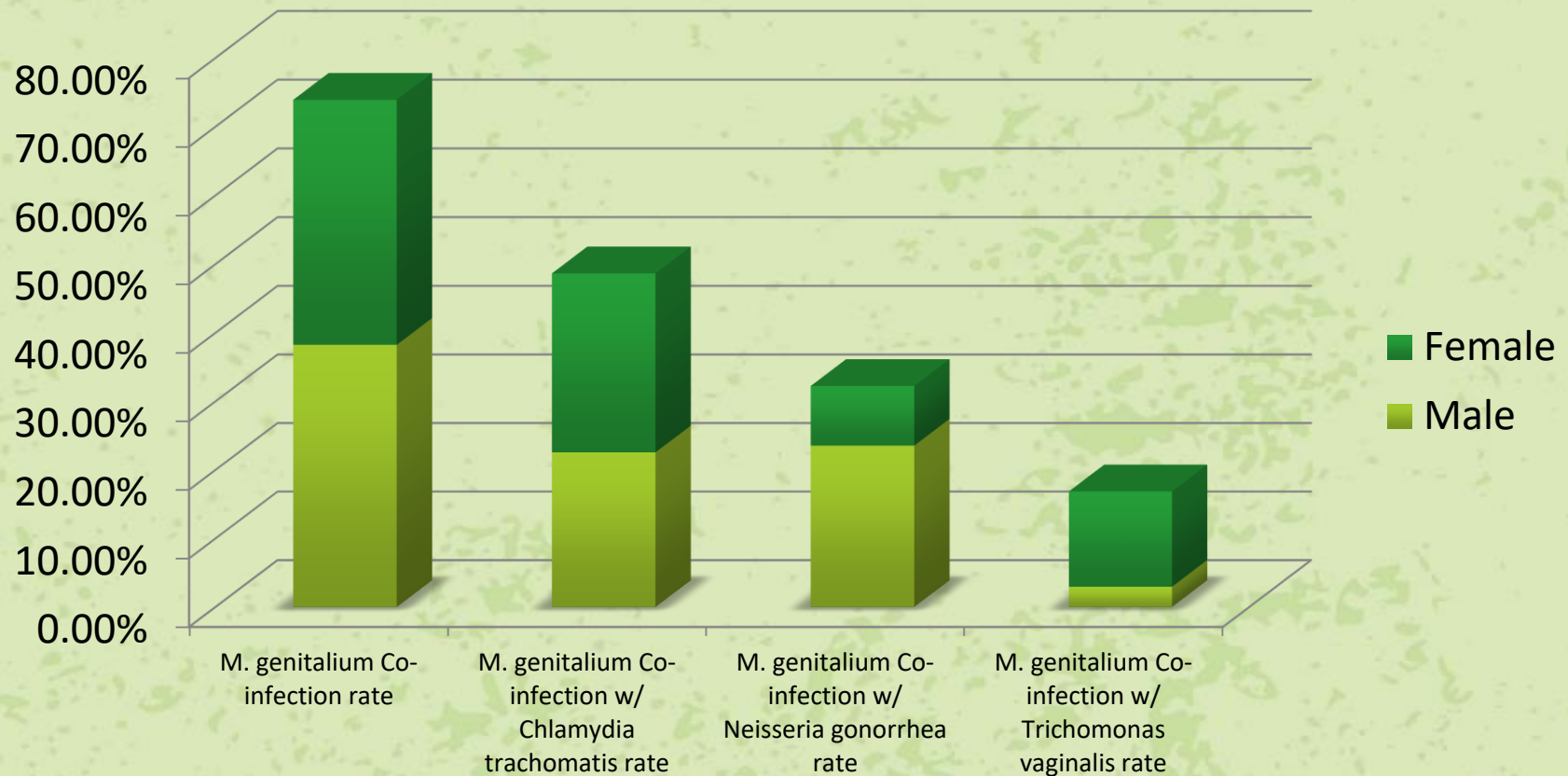
*M. genitalium* results for sample source data – % Positive



\* Rectal and throat samples only collected from MSMs (men who sleep with men).

# Mycoplasma genitalium

Co-infection percentages of *M. genitalium* with *Chlamydia trachomatis*, *Neisseria gonorrhoea*, or *Trichomonas vaginalis*



# Mycoplasma genitalium

- Case study of NGU patients
- 51 NGU treatments
- 6 positive for Mycoplasma genitalium Only
- 4 positive for Chlamydia trachomatis and Mycoplasma genitalium
- 2 positive for Neisseria gonorrhoea and Mycoplasma genitalium
- 23.5% positivity rate



# Mycoplasma genitalium

- Case study of reoccurring bacterial vaginosis
- 41 cases
- 11 Positive for Mycoplasma genitalium
- 27% positivity rate
- 5 of those cases had no history of other STD's

# Why all labs should add *Mycoplasma genitalium* to their STD Panel

- 21 year old female presented with sore throat for a few days
- Had been tested for strep with a negative result
- Swabbed throat
- Positive for *Mycoplasma genitalium*

# Why all labs should add *Mycoplasma genitalium* to their STD Panel

- 32 year old black male presented with burning with urination
- Dysuria for 5 years
- Same partner for 8 years
- Never been tested
- Positive for *Mycoplasma genitalium*

# Mycoplasma genitalium

- Conclusion
- Overall positivity rate is 10.75%
- Females slightly higher than men 12.67% vs. 9.18%
- Age range of 18-34
- Mycoplasma genitalium is a good addition to our STD panel

# Mycoplasma genitalium Report January - December 2016

Mycoplasma genitalium <sup>5</sup> Positives				
Source	Negative	Positive	TOTAL TESTED	% Positive
Urine	3313	453	3766	12.03%
Rectum <sup>1</sup>	220	31	251	12.35%
Throat <sup>1</sup>	263	6	269	2.23%
Vaginal	48	10	58	17.24%
Cervix	2	0	2	0%
TOTALS	3846	500	4346	11.50%

Mycoplasma genitalium positive - Race and Age <sup>2</sup>								
Age	18-24	25-29	30-34	35-39	40+	TOTAL +	TOTAL Samples <sup>3</sup>	% +
White	185	100	38	16	16	355	3325	10.68%
Black	43	30	10	8	5	96	604	15.90%
Hispanic	4	3	0	2	0	9	128	7%
Asian	2	1	1	0	0	4	44	9.10%
American Indian or Alaskan	12	2	0	0	0	14	86	16.28%
Multiracial	15	3	1	1	1	21	132	15.91%
Pacific Islander or Hawaiian	0	0	0	0	0	0	14	0%
Unknown	0	0	1	0	0	1	13	7.70%
TOTAL	261	139	51	27	22	500	4346	11.50%

# Mycoplasma genitalium Report January - December 2016

Mycoplasma genitalium Positive - Gender & Age <sup>2</sup>								
Age	18-24	25-29	30-34	35-39	40+	TOTAL +	TOTAL Samples <sup>3</sup>	% +
Male	93	72	35	14	11	225	2357	9.55%
Female	168	66	17	13	11	275	1989	13.83%
TOTALS	261	138	52	27	22	500	4346	11.50%

M. Gen + Co-infection <sup>4</sup> rate			
Age	TOTAL Co-infected	TOTAL M.gen +	% co-infected
Male	40	225	17.78%
Female	48	275	17.45%
TOTALS	88	500	17.60%

# Mycoplasma genitalium

- Different types of specimen collection and transport media
- Why it is important to collect specimens appropriately

# Mycoplasma genitalium

