# Laboratory Services for STI Testing –

## What should your lab be offering and How should it be offered?

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# Disclosures

(Research Support, Consulting or Honorarium)

**Research Grants to my Institution**

- NIH
- Abbott Molecular
- BD Diagnostics
- BioFire
- Cepheid
- Cue
- FIND
- Hologic
- Rheonix
- Roche Molecular

**Salary/Consulting Honoraria**

- UAB
- FDA
- Abbott Molecular
- BD Diagnostics
- Preventx
- Roche Molecular

*It is a duty of academicians and experienced scientists paid using tax-payer dollars to advise industry in bringing forward new technologies to advance medicine and public health. Not doing so would be detrimental to the public interest by limiting access to expertise. I have several disclosures, but none represents a conflict of interest as my primary interest is public health.*

# Topics

- Pathogens
- Sample Types
- Sample Collection Options

# THE MENU

# STI that can be Detected using NAATs

- Chlamydia (CT) and gonorrhea (GC)
  - *account for >80% of all non-CoVID notifiable infections*
  - *CT predominately asymptomatic*
- Trichomonas (TV)
  - *Often more prevalent that CT & GC **combined**!*
  - *Asymptomatic in up to 50% of women*
- *Mycoplasma genitalium* (MG)
  - *? Similar to chlamydia?*
  - *40-80% are macrolide resistant*
- Causes of Vaginitis (BV and *Candida spp.*)
  - *Symptomatic women only*

www.cdc.gov

# CDC Guidelines

"For Cause"

- In high prevalence setting
- New partner
- Infected partner
- On PrEP

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- *Chlamydia trachomatis*
  - *Screen asymptomatic women under 25 & "for cause"*
  - *Test anyone with discharge, dysuria, or other symptoms*

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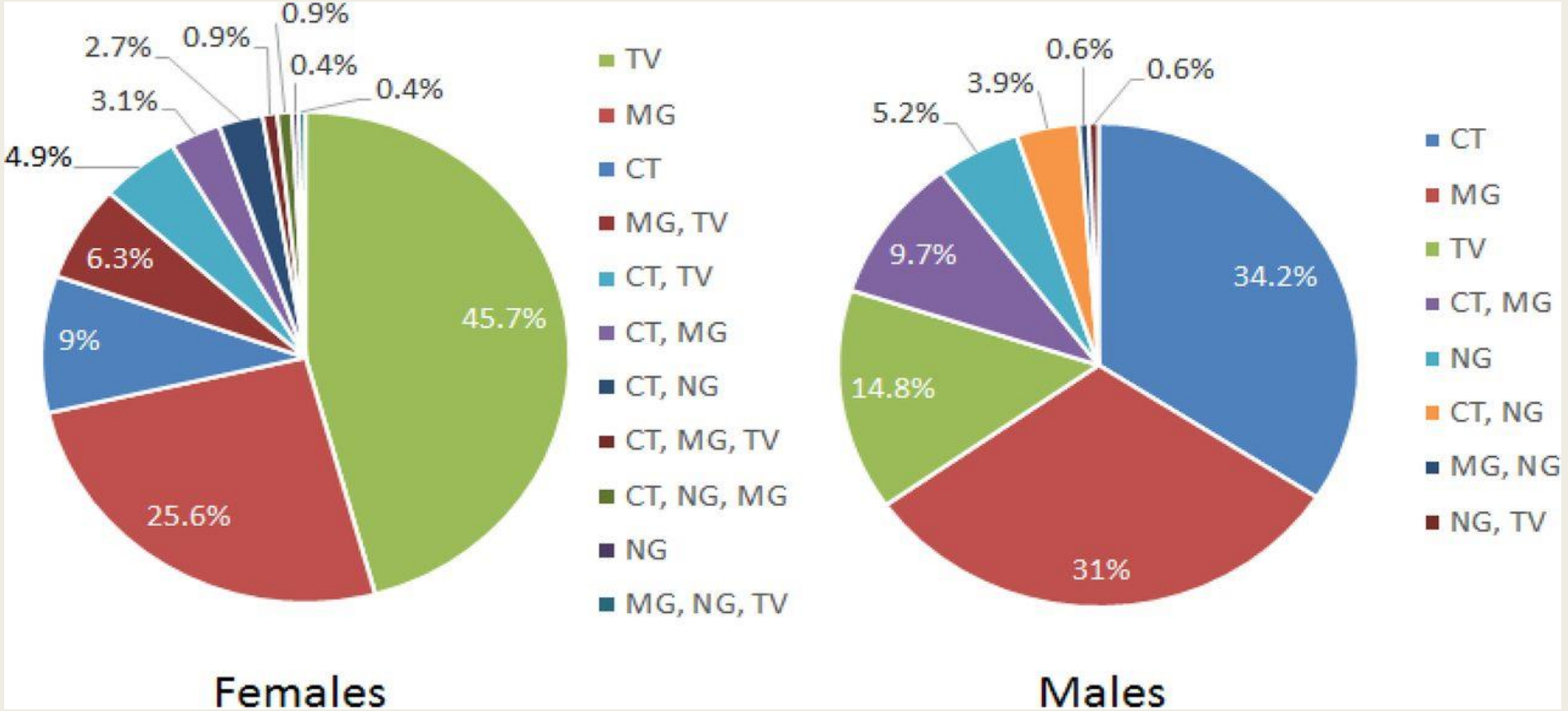
- *Trichomonas vaginalis*
  - *Screen women "for cause"*
  - *Test anyone with discharge, dysuria, or other symptoms w/o CT/GC*
- *Mycoplasma genitalium*
  - ***Screening NOT recommended***
  - *Test those with **recurrent urethritis or cervicitis or PID***
  - *AMR marker detection recommended*

# Co-Infections in Symptomatic Patients




Getman et al. J Clin Microbiol 2016

# Prevalence of STI based on Vaginitis Diagnosis

| STI | BV Only | Candida Only | BV + Candida | No Vaginitis | Overall |
|---|---|---|---|---|---|
| Chlamydia | 6.0%* | 6.1% | 12.8%* | 1.8% | 6.2% |
| Gonorrhea | 2.5% | 1.5% | 1.0% | 1.2% | 1.7% |
| Trichomonas | 11.4%* | 1.6%* | 8.6% | 8.0% | 8.3% |
| Any STI | 17.4%* | 9.2% | 20.8%* | 10.9% | 14.9% |

*p<0.5 compared to No Vaginitis category)

Van Der Pol et al. C. Inf. Dis. 2018; doi:10..1093/cid/ciy504

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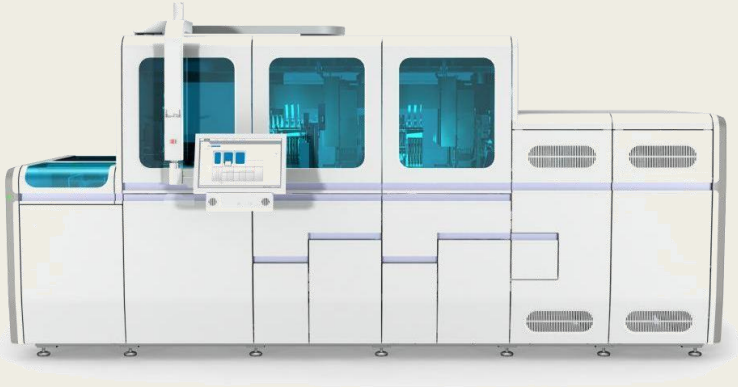
  - *Responds to therapy for Gardnerella*
- *Ureaplasma spp.*
  - *Data lacking regarding disease outcomes*

# A Solution for Every Setting!

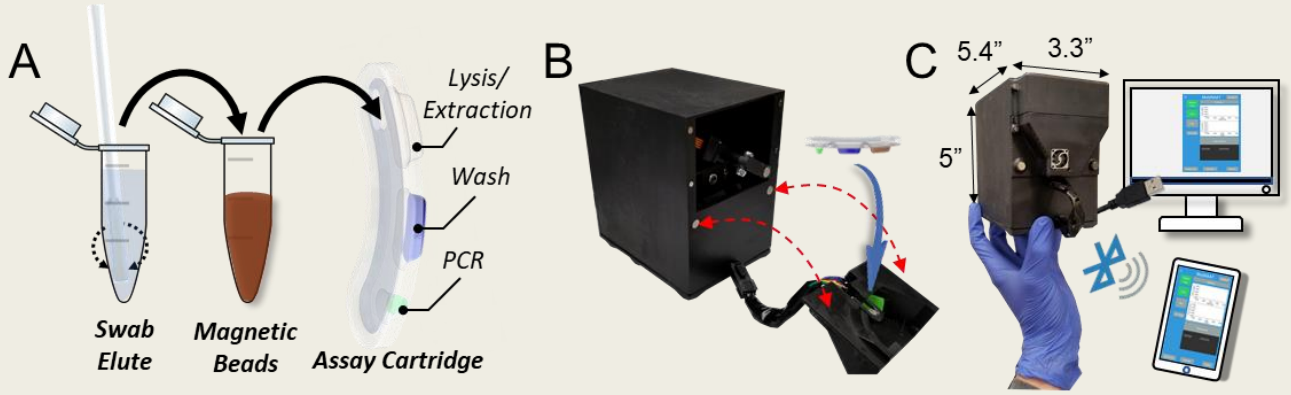




# A Word About AMR

- Does AMR marker testing need to be point-of-care (POC) ONLY?
- In clinic decision making for GC
  - *If gyrA wild type, Cipro can be used rather than ceftriaxone*

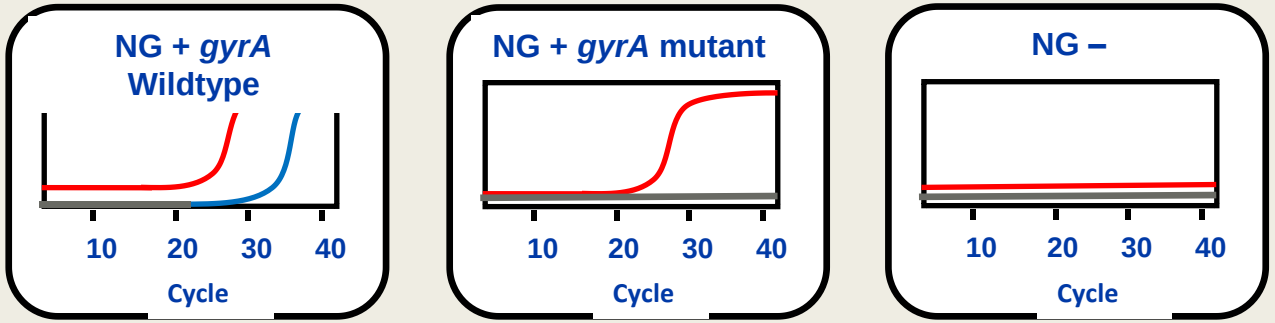
# MobiNAAT Gonorrhea ID and Ciprofloxacin Resistance Testing




**Duplexed FRET Probes:** *opa* *gyrA*

***gyrA* wildtype**
ciprofloxacin susceptible

***gyrA* mutant**
ciprofloxacin resistant

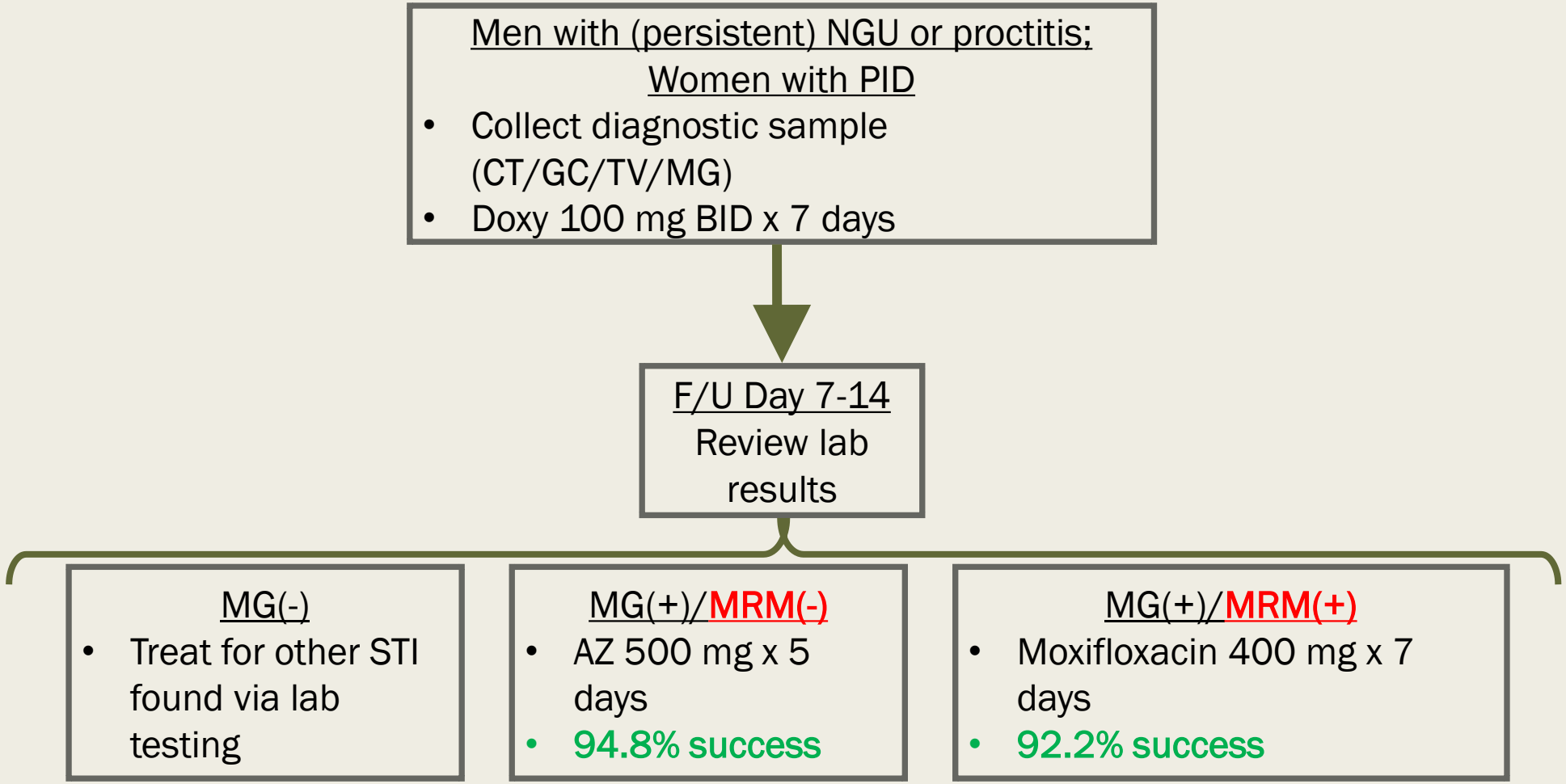



Slide courtesy of Charlotte Gaydos

# A Word About AMR

- Does AMR marker testing need to be point-of-care (POC) ONLY?
- In-clinic decision making for symptomatic GC
  - *If gyrA wild type, Cipro can be used rather than ceftriaxone [Klausner, CID 2021]*
- Lab-based testing for asymptomatic GC and all MG

# Two-Stage RGT for *M. genitalium*




Read, et al. CID 2019

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  - *Reverse or traditional algorithm ($)*
- Hepatitis (B & C)
- Herpes
  - *HSV-2 only?*
  - *Confirmation REQUIRED*
  - *What does HSV antibody testing tell the clinician???*

# What's the Answer?

- Disentangle screening and diagnostic testing
  - *MG only in rare cases*
- Have a full menu
  - *Don't bundle!*
- Consider patient outcomes (e.g. Herpes) when deciding to offer a test
  - *You may need to work with your clients*

# SAMPLE TYPES

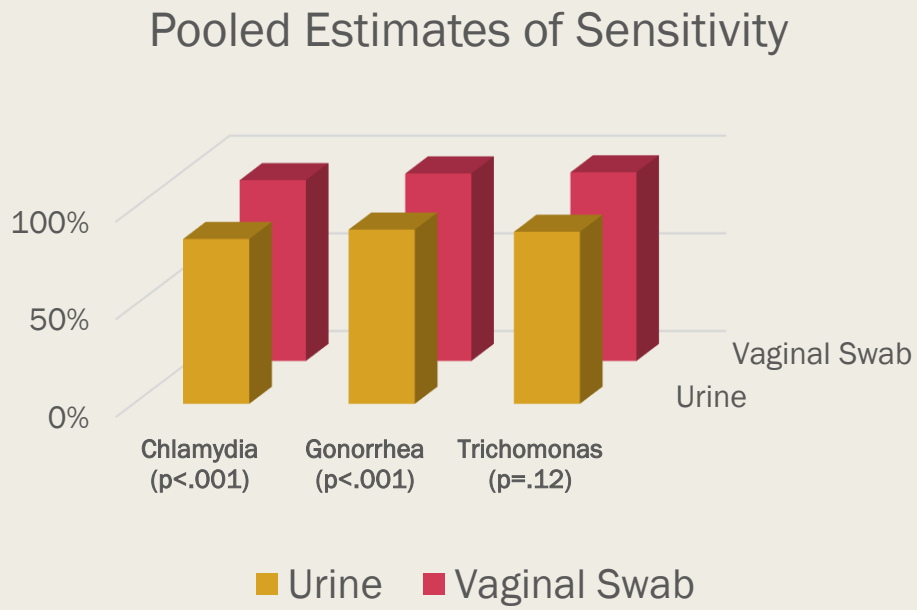
# 2014 CDC Laboratory Diagnostic Recommendations (from 2009)

- Vaginal swabs
  - *great for vaginitis testing too!*
- Male urine
  - *Meatal swabs are approved for 1 assay, 1 pathogen*
- Anorectal
- Oropharyngeal (not buccal!)
- **Need data on trans anatomical sites!!**

Papp, et al. MMWR 2014

# Not All Samples are Created Equal

- >50% of samples from women tested in PH Labs are urine*




*Davis et al, STD 2020
**Figure adapted from Van Der Pol, et al, 2013 STD

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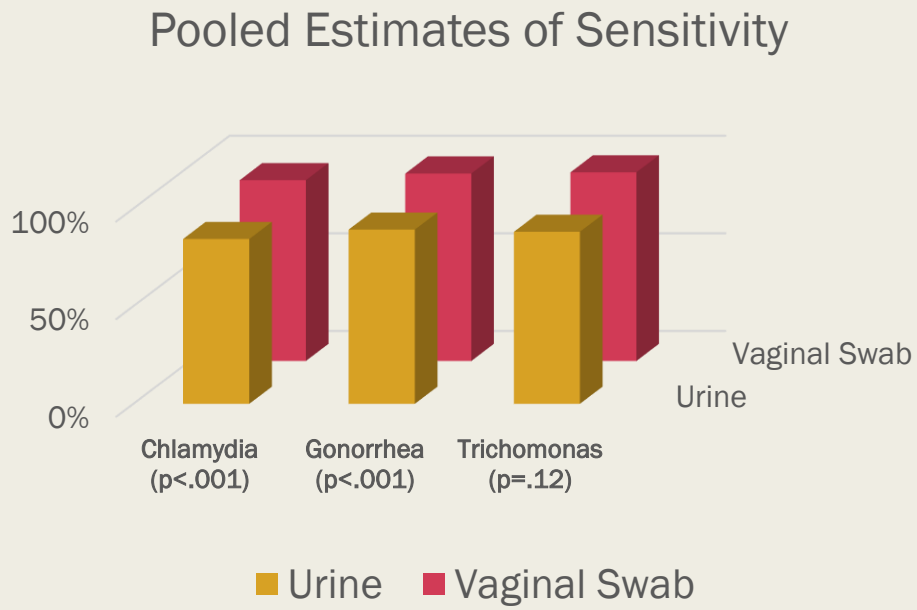
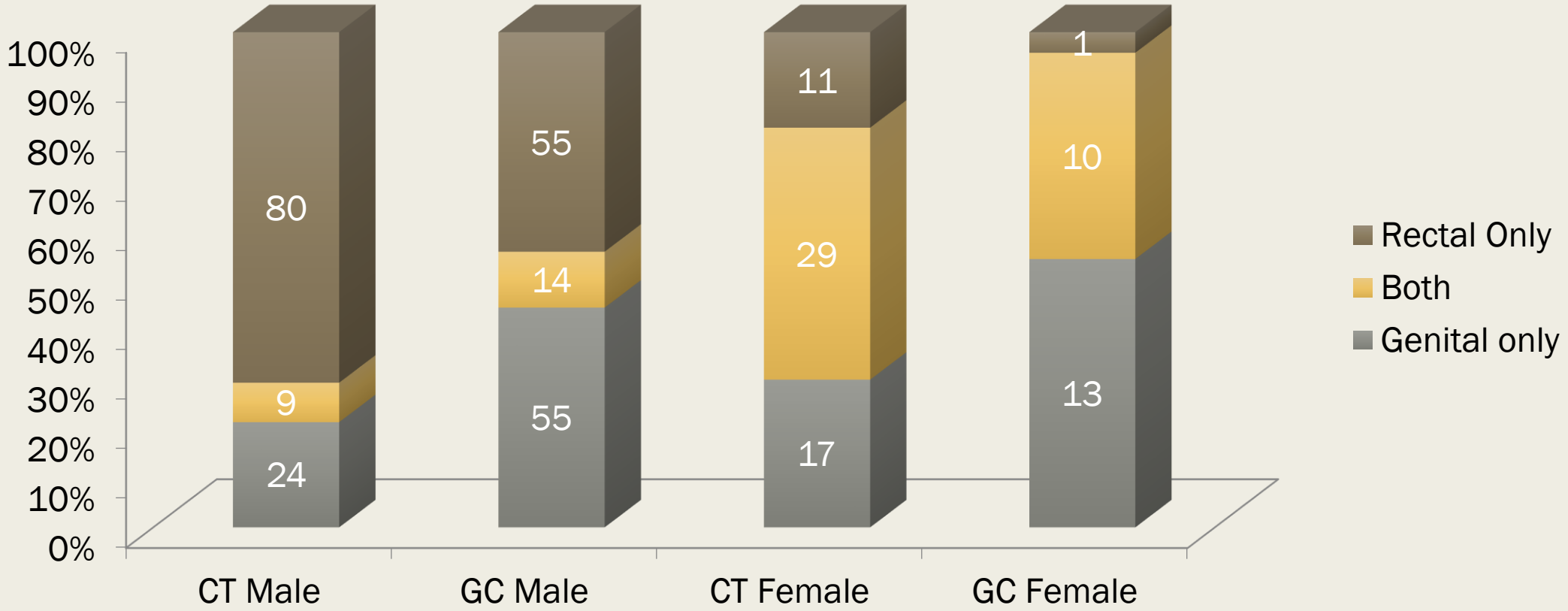
Can a **Clean Catch Urine** Sample Be Used to Diagnose Chlamydia and Gonorrhea in Adolescent Females?
*Pickett L. 2021 J Adol H*

*86.2% (64.8-93.1%) compared to vaginal swab=**80.5%***




*Davis et al, STD 2020
**Figure adapted from Van Der Pol, et al, 2013 STD

# Proportion of Infections Detected by Rectal or Genital Sampling




Marion Co, IN Health Department, 2011

# Avoid the Bundle (again)!

- CT and GC are easy
  - *3 site testing is helpful (in some populations)*
- TV: benefits to testing in men and women
  - *Genital only*
- MG:
  - *Genital (when recommended)*
  - *What about anal??*
    - No claims
    - **Need  antimicrobial resistance marker detection!**

# SELF-COLLECTION

For Remote Testing

# Definitions

- Self-collection
  - *In a clinical setting*
  - *In any non-clinical setting*

- Self-testing
  - *End user*
    - Collects sample,
    - Performs, and
    - Interprets test

  *with no interaction with a healthcare professional*

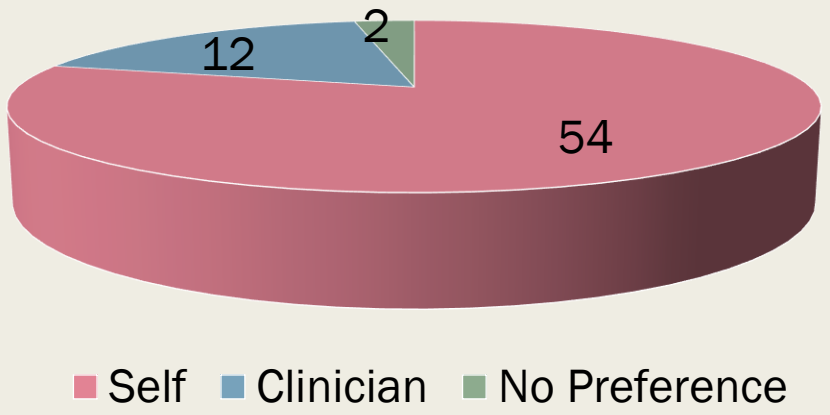
# Not a New Concept

- Started adolescent in-home self-sampling in 1999
  - *No AEs in 10 years!*
- Recommended for CT/GC by CDC since 2009*
- Recommend by WHO**
- Shown to be cost effective***
  - *Lower clinical costs/improved clinic flow*
  - *Equal or better case finding*

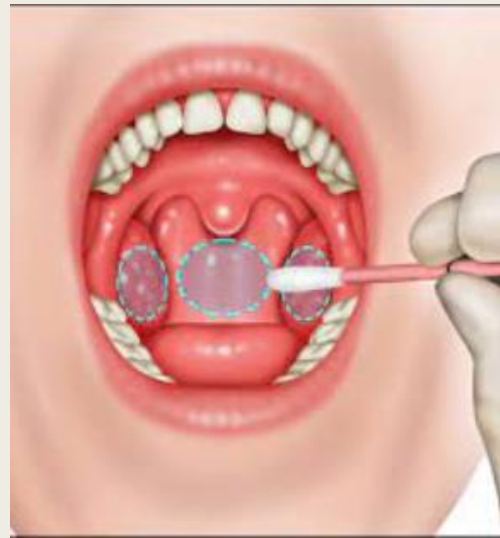
*Papp et al, MMWR 2014
**WHO/SRH/20.10. World Health Organization, 2020.
***Blake, et al. Sexually Transmitted Diseases, 2008

# Extra-Genital

- Rectal self-sampling is great!*
  - *And is acceptable/preferred*




- Throat self-sampling requires more instruction
  - *Works well at Dean Street Express*



*Dodge, et al. Int J STD AIDS 2010
Image from Aptima instructions for use

# Knowledge Gaps for Non-Clinical Settings

- Claims only for "…in a clinical setting"
  - *Devices are NOT assays and CANNOT be validated*
- Samples collected in preservative
  - *Exposure to buffer needs safety evaluation*
- Need stability data
  - *How long, at what temperature/s, in what medium?*

# Applications of Remote Self-Sampling

- Telemedicine is distinct from Direct to Consumer
  - *The first is well controlled while the latter is largely unregulated*
- Useful for screening in key populations(e.g. People on PrEP)
- Useful for people concerned about exposures with no symptoms
- Useful for people with barriers to access ??

# What Can Go Wrong?

- Case 1
  - *Positive for syphilis*
    - Treponemal specific test only – no confirmation
  - *Notification received by PHD **8 weeks** later*
    - No provider name or contact
  - ***3 months** later re-tested and found to be negative*
- Case 2
  - *Person attended to initiate HIV care (no linkage) with printed report*
    - Confirmatory testing unclear
  - *No PH notification from testing lab or provider*
- Case 3
  - *Positive for syphilis (confirmed with high titre)*
  - *Lab in different state (reported in lab's state)*
    - **30 days later** patient's home state was notified
  - *Prescribed **14 days of Doxy  1 week** after signing off on lab result*
  - *Lab and provider unavailable for follow-up*

Cannon, et al. STD 2021.

# Follow-up appointment for interpretation of results (THIS IMPACTS THE LAB)

- Be cautious when interpreting results unless access to performance data is available.

- **Additional screening and counseling should be provided as needed.**
  - ***Confirmatory testing may be offered but testing should not be a barrier to treatment.***

- Verify that all reporting of infections identified by DTC testing has been performed.

- Ascertain the treatment prescribed to ensure appropriate treatment for any potentially identified pathogens.

See Exten, et al. STD 2021
https://journals.lww.com/stdjournal/Abstract/9000/Direct_to_Consumer_STI_Testing_Services__A.97656.aspx

# What to Do With Confirmatory Testing

- Will the lab have any way to know that it IS confirmatory?
- Why we dropped confirmatory GC testing in 2009
- Who is liable for untreated infections?
  - *The provider*
  - *The lab if based on a “false negative”*

# SUMMARY

# No One-Size-Fits-All Test Menu

- Give the people what they want?
  - *Depends on your client base.*
  - *Work with providers to educate them about guidelines and interpretation of results*

- Avoid bundling even if your platform does it
  - *TV should be encouraged*
  - *Vaginitis causes should be encouraged in Sx Women*
  - *MG should be discouraged as routine (until AMR)*

# Offer All Sample Types Possible

- Discourage routine use of female urine
- Sexual routes of exposure vary
  - *Testing of all potential exposures is warranted (for CT/GC)*
- Among men who report receptive anal intercourse
  - *>60-70% of CT/GC infections are ONLY in the rectal compartment*
  - *Oropharyngeal testing? It will be requested*

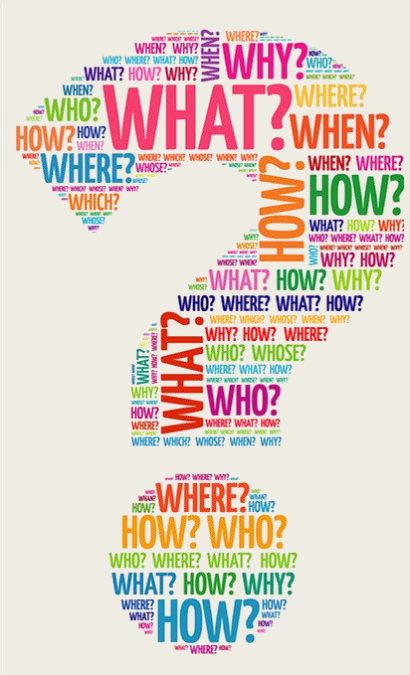
# Remote Collection

- Can your lab support this?
  - *No claims exist*
  - *Devices are not LDTs (can't be "validated")*

- Confirmation testing of previously tested people
  - *How will you flag these requests?*
  - *What do negative results mean?*
  - *What disclaimers on results make sense?*

# A Brave New World

- Change is constant and exciting
- The lab needs to be aware of developments and how to capitalize on opportunities
- Beware of some of the pitfalls of new technology
  - *Just because we CAN doesn't mean we SHOULD test anything/everything!*




# I'M ALWAYS HAPPY TO ANSWER QUESTIONS!

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# Testing Methods

**Obiageli Okafor, MD, DrPH**
Sr. Manager, Product Applications
Global Health Equity
Thermo Fisher Scientific

# *Chlamydia trachomatis (CT)* Testing Methods

**NAAT**

Good sensitivity and specificity ((more sensitive than culture)

Expensive

Fast results

Not test-of-cure ( detects DNA/RNA not live pathogen)

**Culture**

Sample can be difficult to obtain

Many false negatives

Expensive (lab resources).

Required for legal situations* (100% sensitivity)

**Rapid tests** –

Molecular tests

Direct fluorescent antibody (DFA), Enzyme-linked immunosorbent assay (ELISA)

Sensitivity mixed, good specificity

Fast and cheap

Common in outpatient and ED

**Serology**

Sensitivity and specificity not high enough to diagnose active infection

*Clinical practice today might deviate

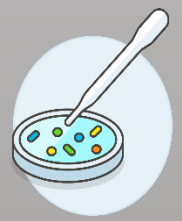
https://emedicine.medscape.com/article/214823-workup#c9

# *CT* Testing Methods

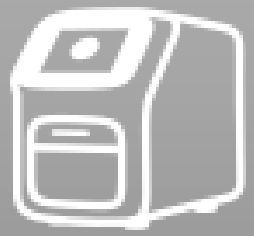
- **CDC STI guidelines**- NAATs are the most sensitive tests for these specimens and are the recommended test for detecting *C. trachomatis* infection
- **EU STI guidelines** NAATs are recommended due to their superior sensitivity, specificity, and speed of diagnosis of both symptomatic and symptomatic chlamydial infections compared to all other diagnostic techniques

https://www.cdc.gov/std/treatment-guidelines/chlamydia.htm
https://iusti.org/wp-content/uploads/2019/12/Chlamydia2015.pdf

# *Neisseria gonorrhoeae* (*NG*) Testing



**Culture** – reference test, less sensitive than NAAT, may detect other Neisseria species, good for antibiotic resistance, preferred for legal cases



**NAAT -** more sensitive, faster, expensive

https://www.aphl.org/aboutAPHL/publications/Documents/ID-2019Mar-GC-Fact-Sheet.pdf

# *NG* Testing Methods

- **CDC STI guidelines -** Laboratories should use NAATs to detect chlamydia and gonorrhea except in cases of child sexual assault. *N. gonorrhoeae* culture is required to evaluate suspected cases of gonorrhea treatment failure and to monitor developing resistance to current treatment regimens.
- **EU STI guidelines -** N. gonorrhoeae can be detected by nucleic acid amplification tests (NAATs) or culture. NAATs are the recommended diagnostic tests for symptomatic and asymptomatic individuals, however, culture of individuals with urogenital symptoms and in gonococcal NAAT-positive individuals prior to treatment to obtain isolates for AMR testing is also encouraged. NAATs are more sensitive than culture

https://www.cdc.gov/std/laboratory/2014labrec/default.htm

https://iusti.org/wp-content/uploads/2020/10/IUSTI-Gonorrhoea-2020.pdf

# *Mycoplasma genitalium (Mgen)* Testing Methods

**NAAT** - good sensitivity and specificity, fast

**Culture** – hard to culture, fastidious and takes week or months to grow

**Serology** – enzyme immunoassay - issues with cross reactivity to M. pneumoniae. Microimmunofluorescence tests show better performance compared to other serology tests but none have gained widespread use and none FDA cleared

https://journals.asm.org/doi/10.1128/JCM.01125-19
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3193707/

https://journals.asm.org/doi/10.1128/jcm.00790-21

# *Mgen* Testing Methods

- **CDC STI Guidelines -** *M. genitalium* is an extremely slow-growing organism. Culture can take up to 6 months, and technical laboratory capacity is limited to research settings. NAAT for *M. genitalium* is FDA cleared for use with urine and urethral, penile meatal, endocervical, and vaginal swab samples

- **EU STI Guidelines** - Nucleic acid amplification tests (NAATs) identifying M. genitalium-specific nucleic acid (DNA or RNA) in clinical specimens are the only useful methods for diagnosis

https://www.cdc.gov/std/treatment-guidelines/mycoplasmagenitalium.htm

https://iusti.org/wp-content/uploads/2022/03/Jensen-et-al_Published.pdf

# *Trichomonas vaginalis* Testing Methods

**Clinical Diagnosis -** symptoms and wet preparation microscopy – cheap, fast, low sensitivity

**Culture -** results can take up to 7 days, moderate sensitivity

**NAAT -** rapid, best sensitivity, expensive

**Rapid Tests –** Several FDA approved tests approved for POC, time to result as low as 10mins, cheap, good sensitivity

https://journals.asm.org/doi/10.1128/JCM.02025-15

# *TV* Testing Methods

- **CDC STI Guidelines** - More highly sensitive and specific molecular diagnostic options are available, which should be used in conjunction with a negative wet mount when possible. NAATs are highly sensitive, detecting more *T. vaginalis* infections than wet-mount microscopy among women. Multiple FDA-cleared rapid tests are available for detecting *T. vaginalis* with improved sensitivities and specificities, compared with wet mount.
- **EU STI Guidelines -** (NAATs) offer the highest sensitivity for the detection of TV in comparison to both microscopy and culture. They should be the test of choice where resources allow.

https://www.cdc.gov/std/treatment-guidelines/trichomoniasis.htm
https://iusti.org/wp-content/uploads/2023/04/IUSTI-vaginal-discharge-guidelines_2023.pdf

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