Gonorrhea:
What's the Evidence and Why Things Changed

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Pediatric Infectious Diseases
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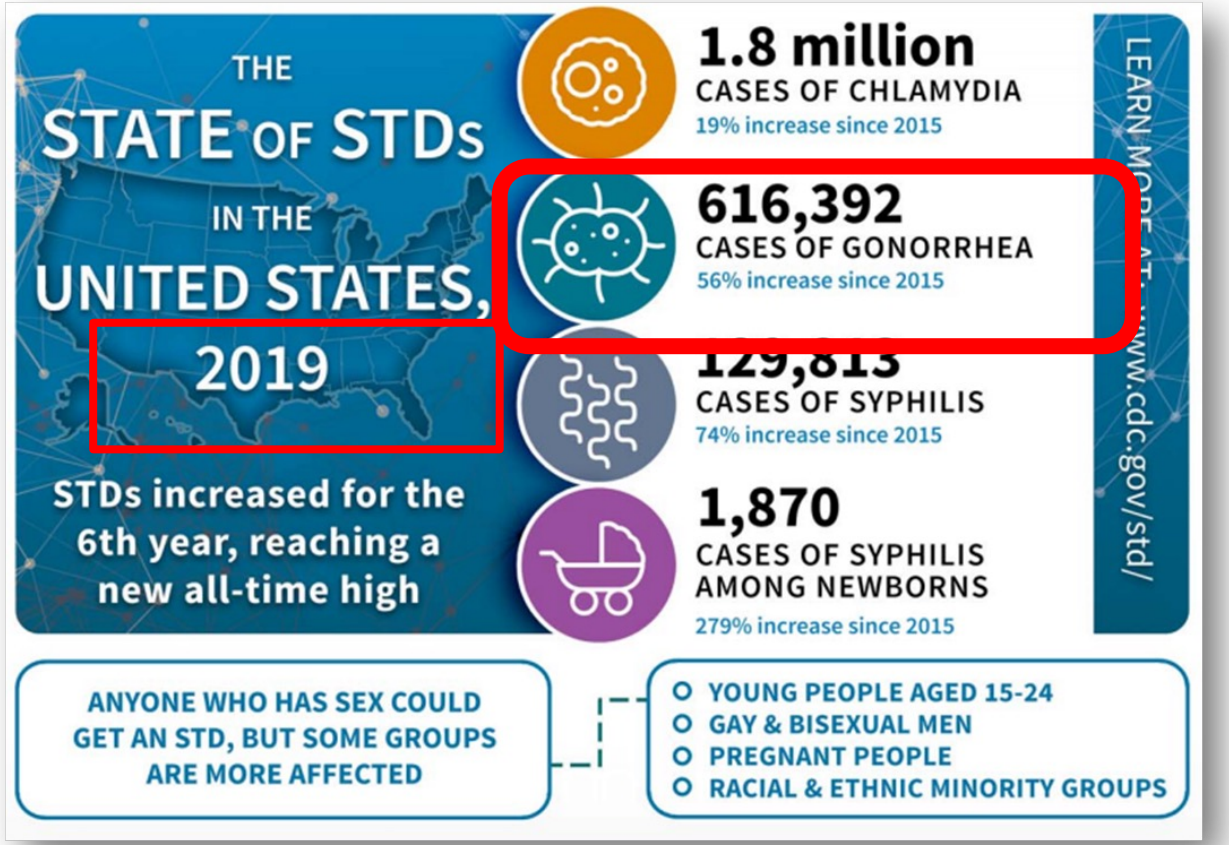
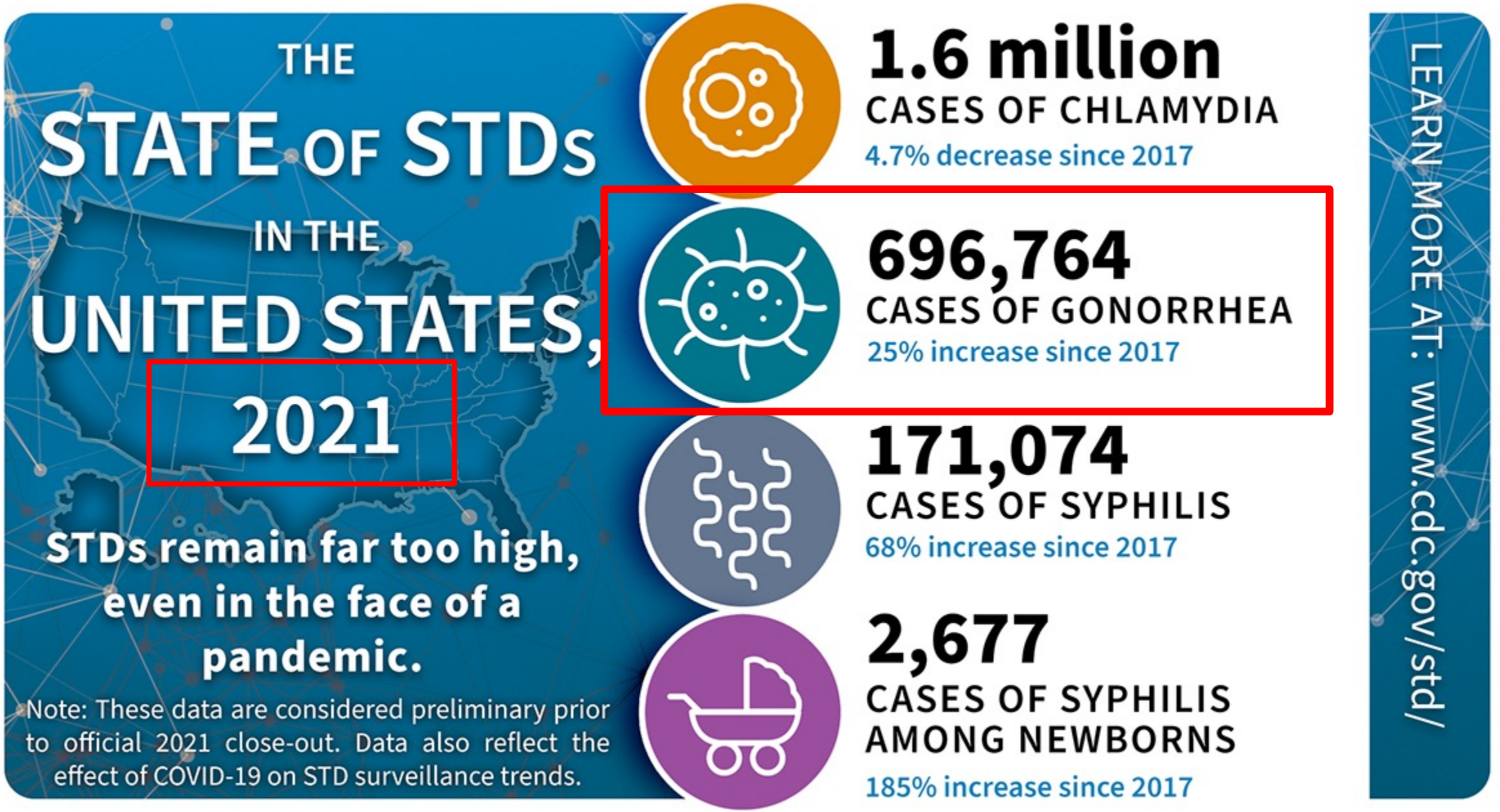
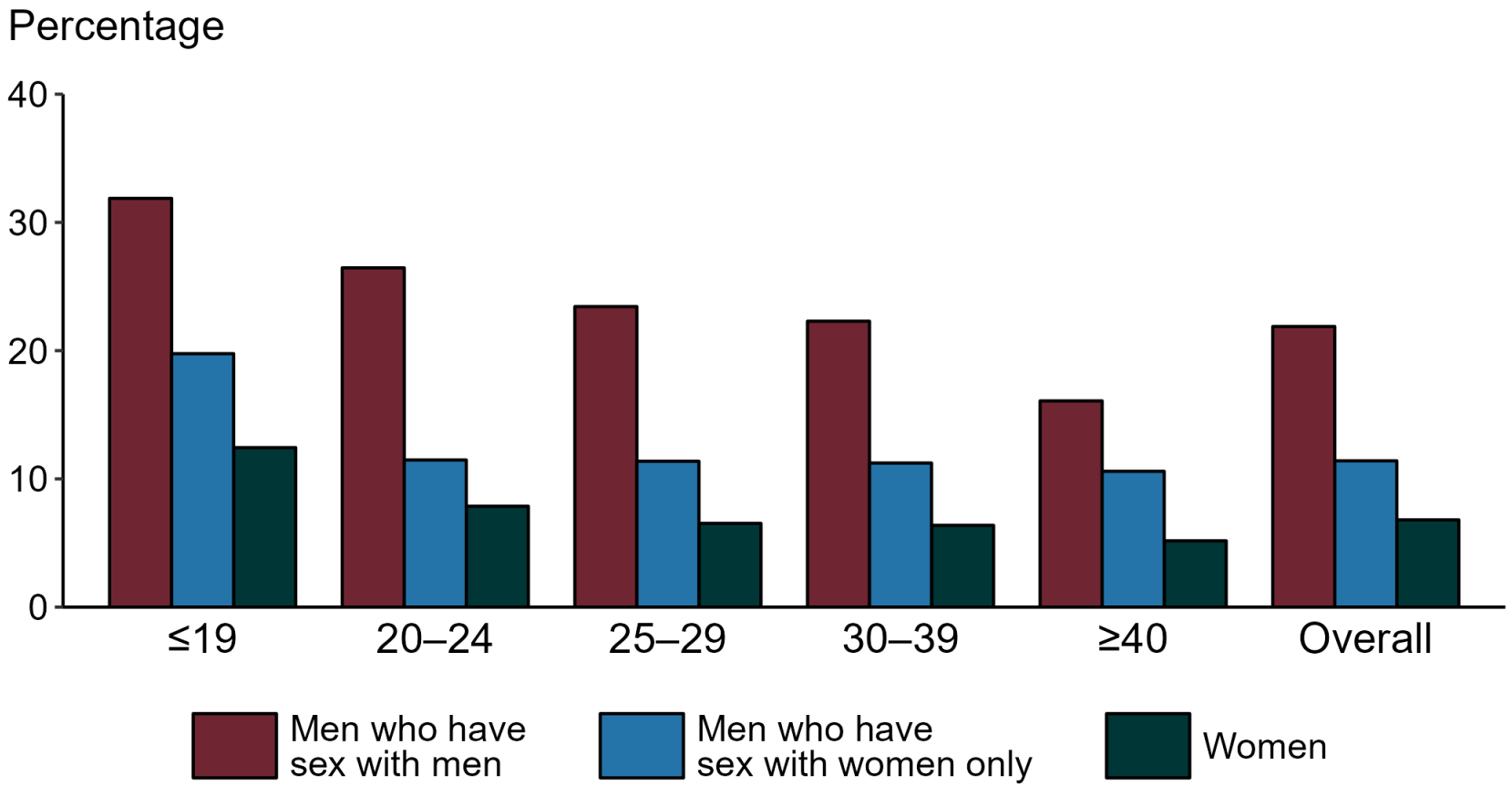
11.8.22

Sexually Transmitted Infections




THE
STATE OF STDs
IN THE
UNITED STATES,
2021
STDs remain far too high, even in the face of a pandemic.
Note: These data are considered preliminary prior to official 2021 close-out. Data also reflect the effect of COVID-19 on STD surveillance trends.
1.6 million
CASES OF CHLAMYDIA
4.7% decrease since 2017
696,764
CASES OF GONORRHEA
25% increase since 2017
171,074
CASES OF SYPHILIS
68% increase since 2017
2,677
CASES OF SYPHILIS AMONG NEWBORNS
185% increase since 2017
LEARN MORE AT: www.cdc.gov/std/

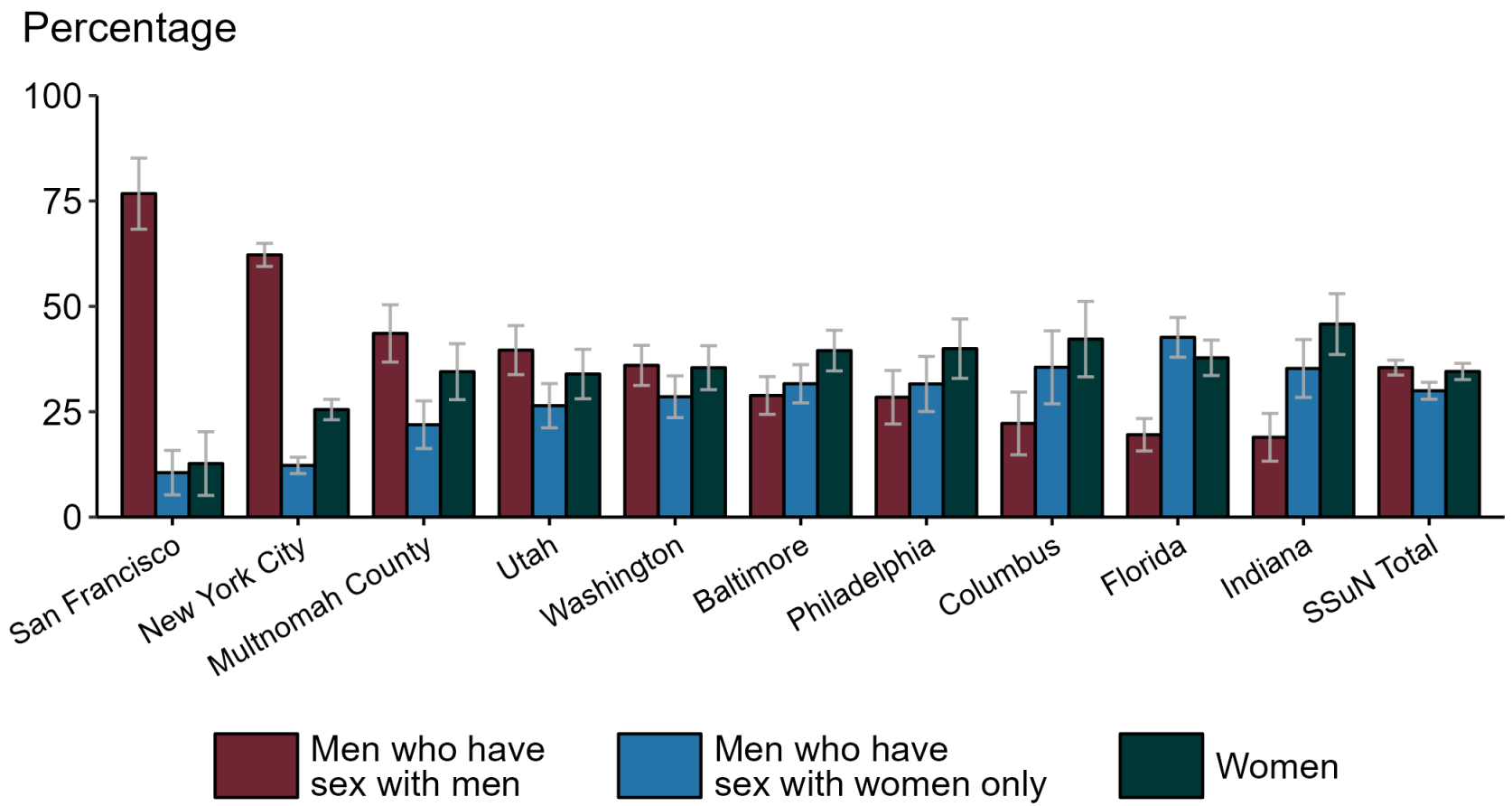
Gonorrhea — Proportion of STD Clinic Patients Testing Positive by Age Group, Sex, and Sex of Sex Partners, STD Surveillance Network (SSuN), 2021*



* Reported 2021 data are preliminary as of June 15, 2022

NOTE: Results are based on data obtained from unique patients in participating sites with known sex of sex partners attending SSuN STD clinics who were tested ≥1 times for gonorrhea in 2021 (n = 41,017).

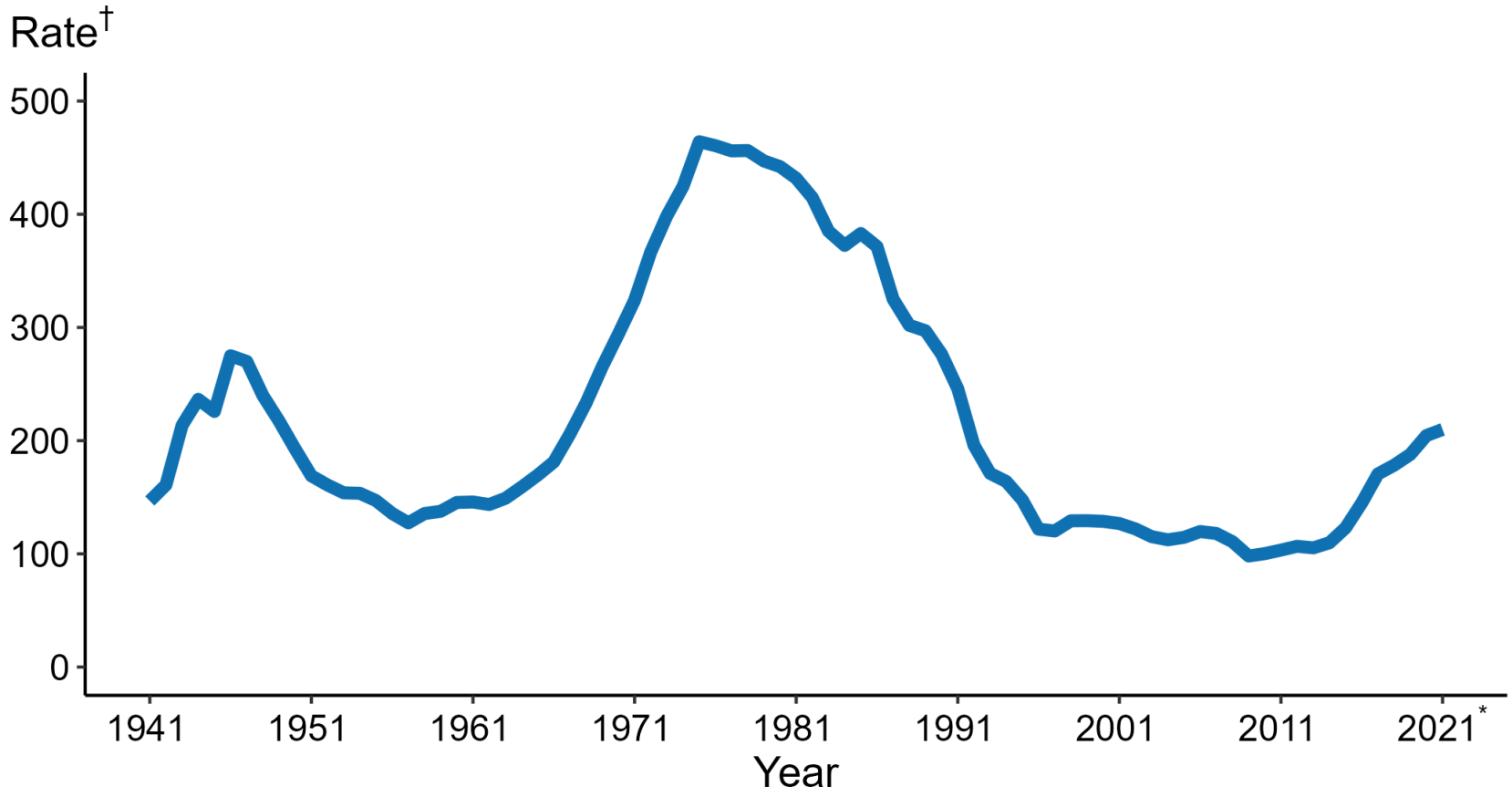
Network (SSuN), Estimated Proportion of Gonorrhea Cases by Sex and Sex of Sex Partners and Jurisdiction, STD Surveillance 2021*



* Reported 2021 data are preliminary as of June 15, 2022

NOTE: Estimate based on weighted analysis of data on sex of sex partners obtained from interviews (n = 5,312) conducted among a random sample of gonorrhea cases reported January to December 2021. Includes ten SSuN sites reporting completed case investigations in 2021 for at least 2% of all reported gonorrhea cases.

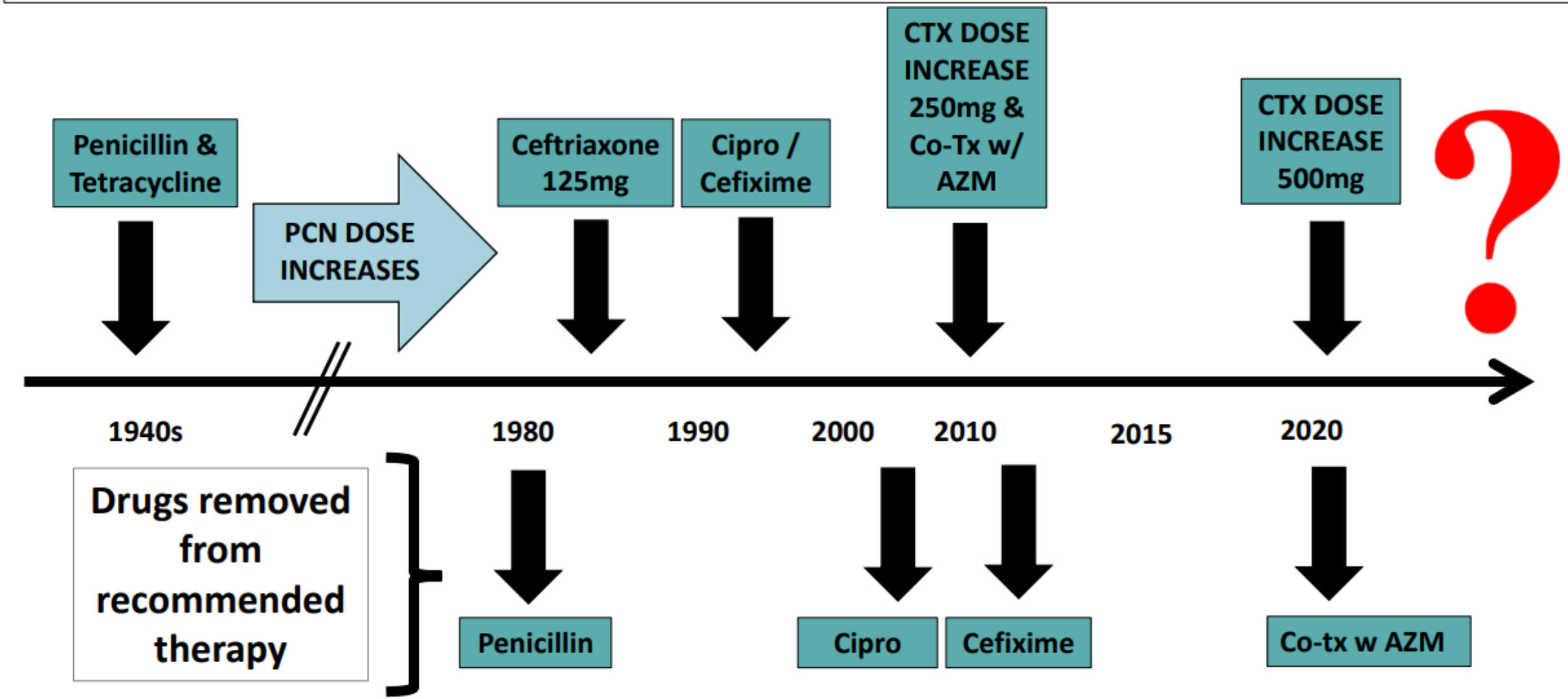
Gonorrhea — Rates of Reported Cases by Year, United States, 1941–2021*



* Reported 2021 data are preliminary as of July 7, 2022
† Per 100,000
CDC statistical data 2021

Antimicrobials for Gonorrhea

HISTORICAL PERSPECTIVE : CDC Recommended Gonococcal Treatments



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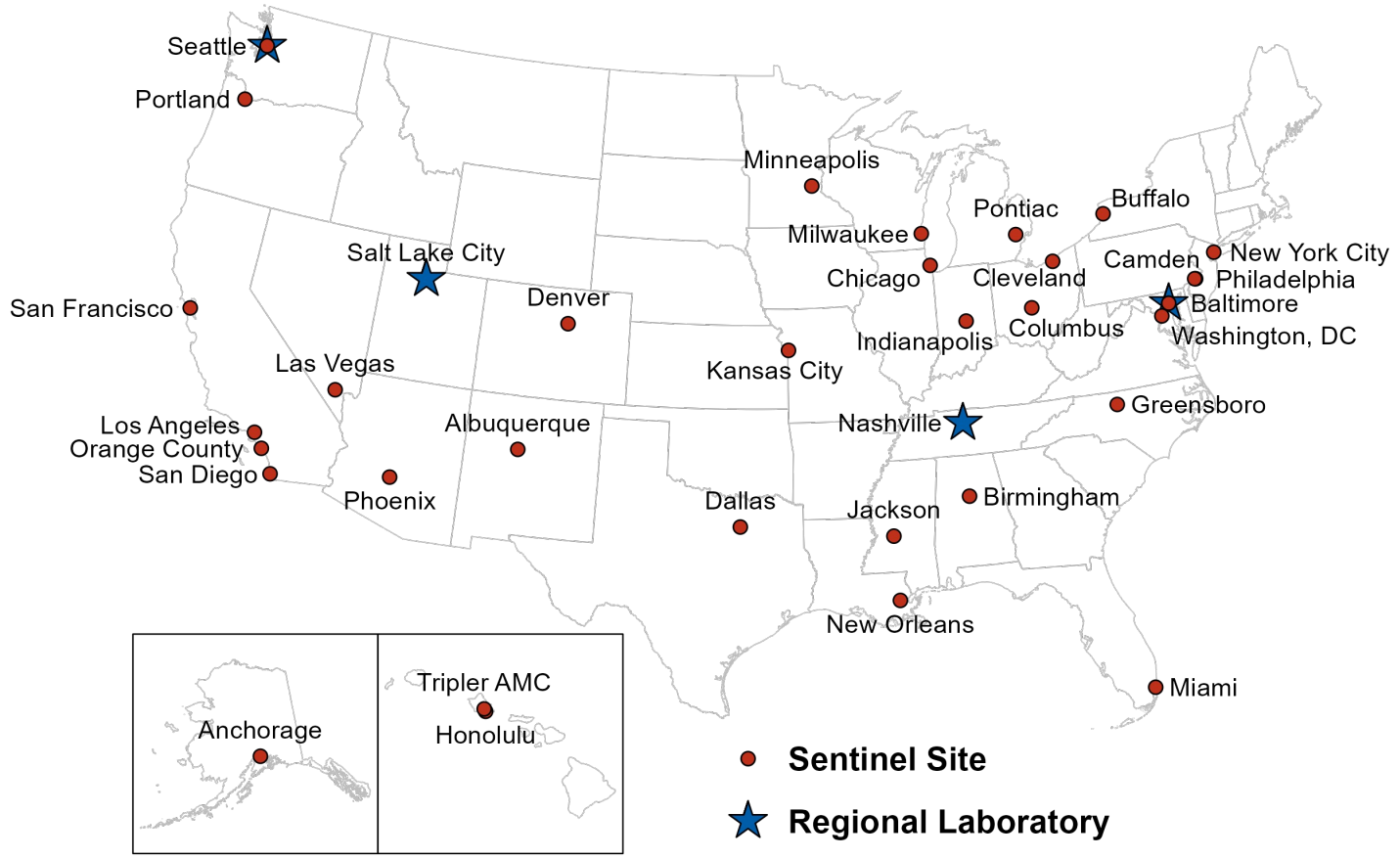
Location of Participating Sentinel Sites and Regional Laboratories, Gonococcal Isolate Surveillance Project (GISP), 2021



NOTE: Baltimore and Seattle are both sentinel sites and regional laboratories.

GISP Data on Susceptibility

Antimicrobial susceptibility criteria used in GISP in 2020

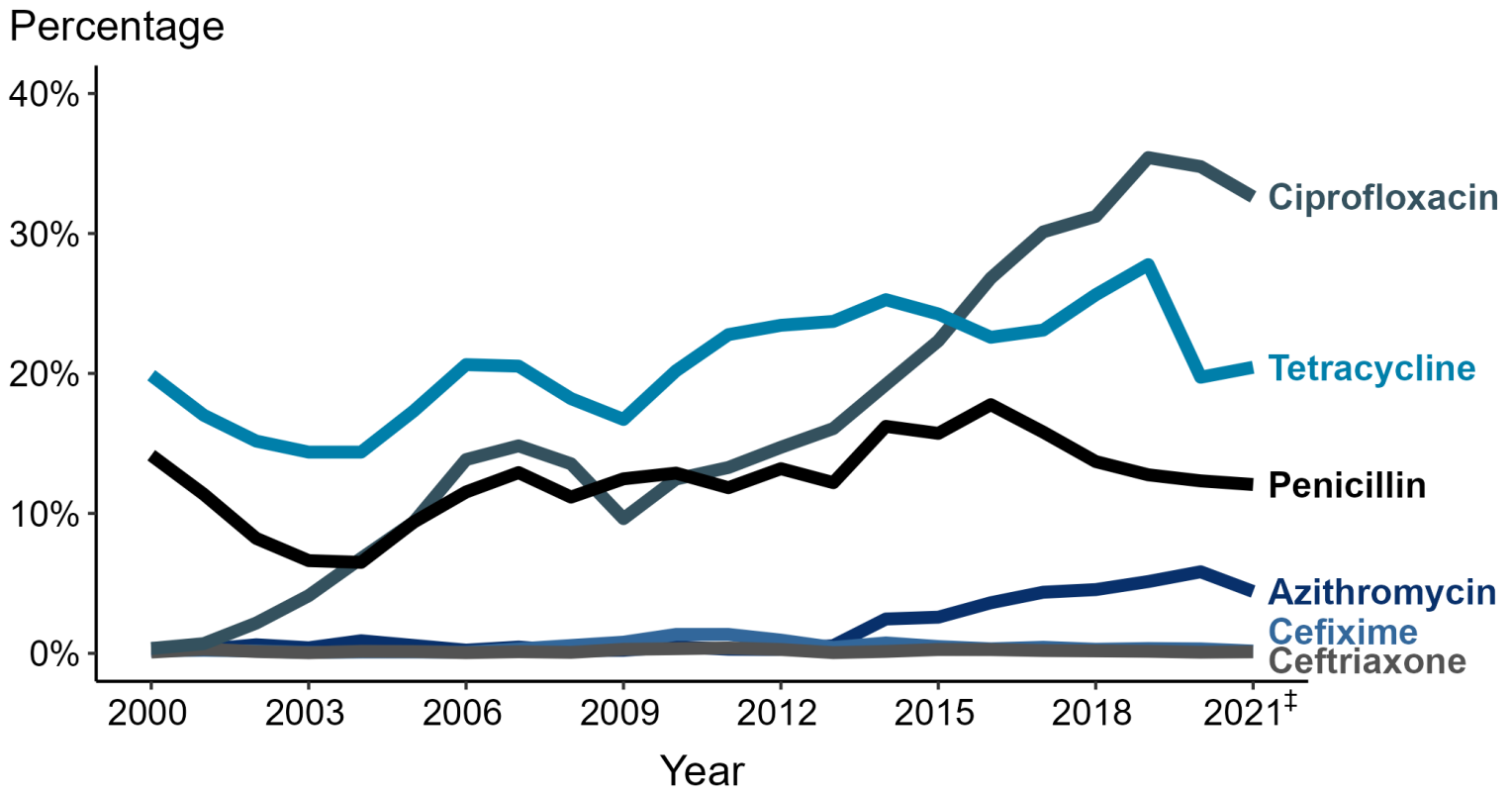
Antimicrobial	MIC Value	MIC Interpretation
Ceftriaxone	MIC ≥0.125 µg/ml	Elevated MIC*
Cefixime	MIC ≥0.25 µg/ml	Elevated MIC*
Azithromycin	MIC ≥2.0 µg/ml	Elevated MIC*
Ciprofloxacin	MIC ≥1.0 µg/ml	Resistance
Penicillin	MIC ≥2.0 µg/ml or Beta lactamase positive	Resistance
Tetracycline	MIC ≥2.0 µg/ml	Resistance
Gentamicin		MIC values correlated with susceptibility and resistance have not been established*

The majority of these criteria are consistent with Clinical and Laboratory Standards Institute (CLSI) criteria.

* As of December 2020, the CLSI criteria for resistance to ceftriaxone, cefixime, gentamicin, and azithromycin and for susceptibility to gentamicin have not been established for *N. gonorrhoeae*.

CDC - GISP Profiles - 2020

Neisseria gonorrhoeae — Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2021‡



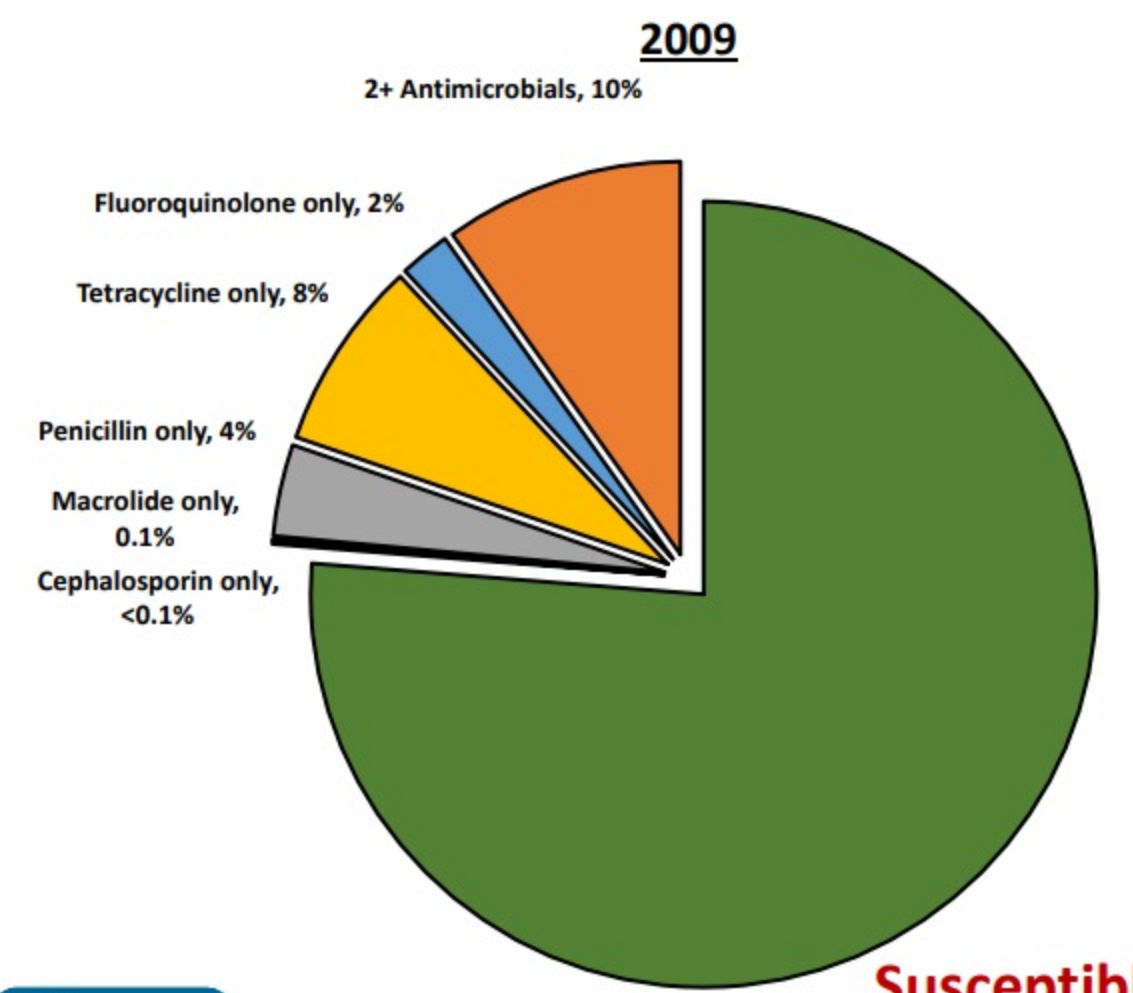
* Resistance: Ciprofloxacin: MIC ≥ 1.0 µg/mL; Penicillin: MIC ≥ 2.0 µg/mL or Beta-lactamase positive; Tetracycline: MIC ≥ 2.0 µg/mL

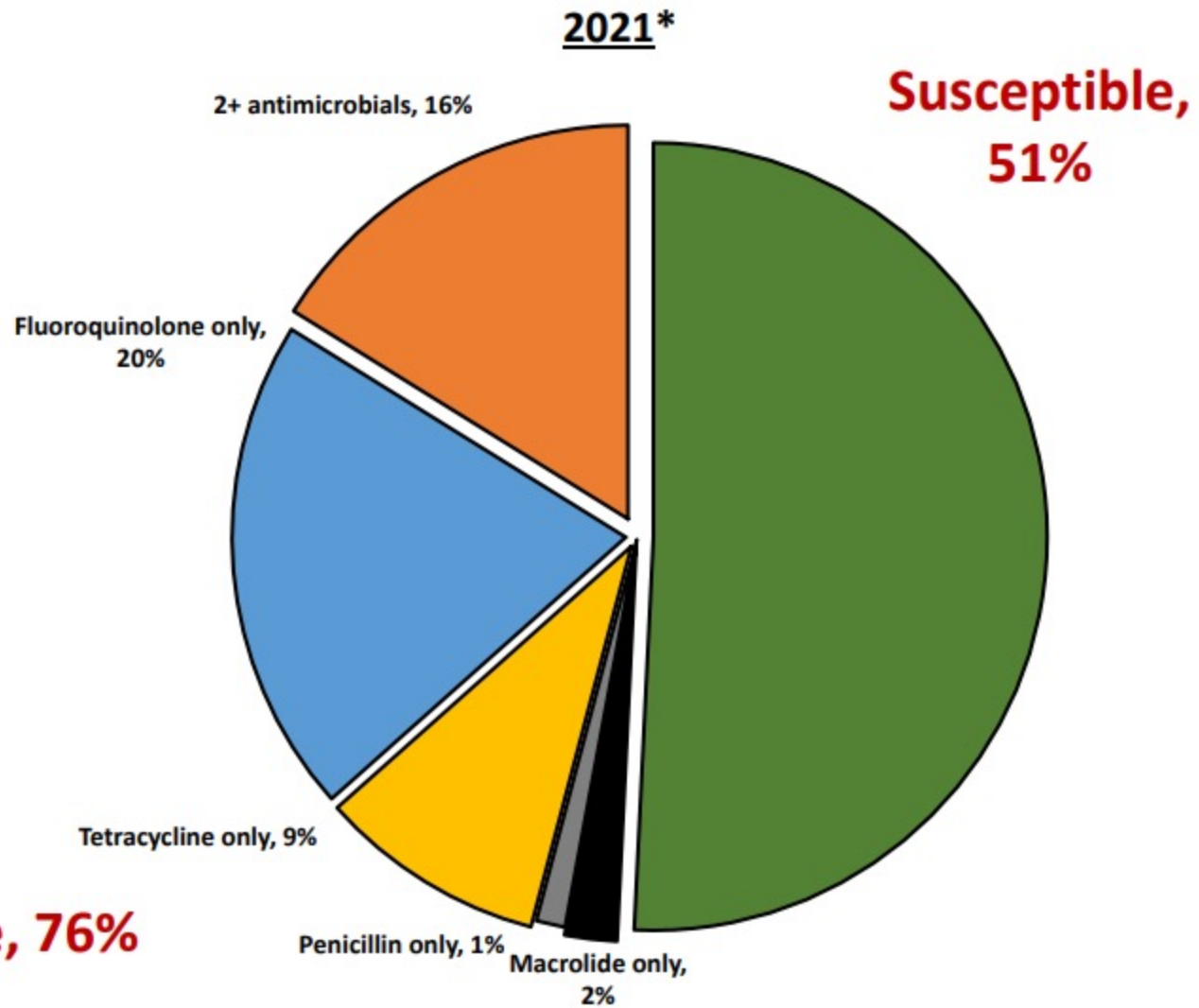
† Elevated MICs: Azithromycin: MIC ≥ 1.0 µg/mL (2000–2004); ≥ 2.0 µg/mL (2005–2021); Ceftriaxone: MIC ≥ 0.125 µg/mL; Cefixime: MIC ≥ 0.25 µg/mL

‡ Reported 2021 data are preliminary as of June 23, 2022

NOTE: Cefixime susceptibility was not tested in 2007 and 2008.

Prevalence of Resistant or Reduced Susceptibility of *N. gonorrhoeae* Isolates to Antimicrobials, GISP, 2009 and 2021*





* Reported 2021 data are preliminary as of July 2022

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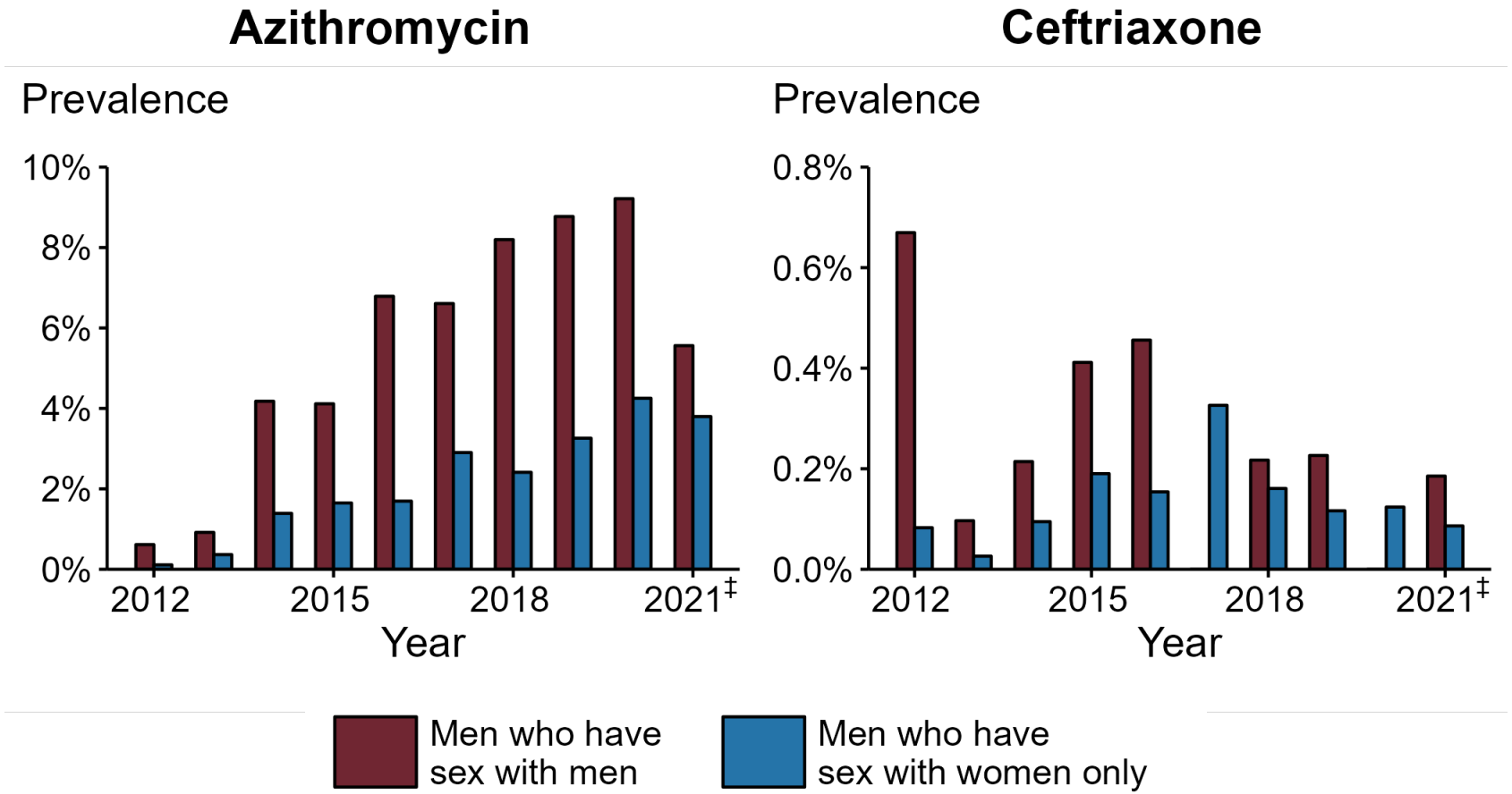
Neisseria gonorrhoeae — Percentage of Urethral Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin* and Ceftriaxone† by Sex and Sex of Sex Partners, Gonococcal Isolate Surveillance Project (GISP), 2012–2021‡



* Elevated Azithromycin MIC: ≥ 2.0 µg/mL

† Elevated Ceftriaxone MIC: ≥ 0.125 µg/mL

‡ Reported 2021 data are preliminary as of June 23, 2022

2021 Treatment Guidelines for Gonorrhea

NEW Treatments

Ceftriaxone **500** mg IM x 1
for persons weighing <150kg*

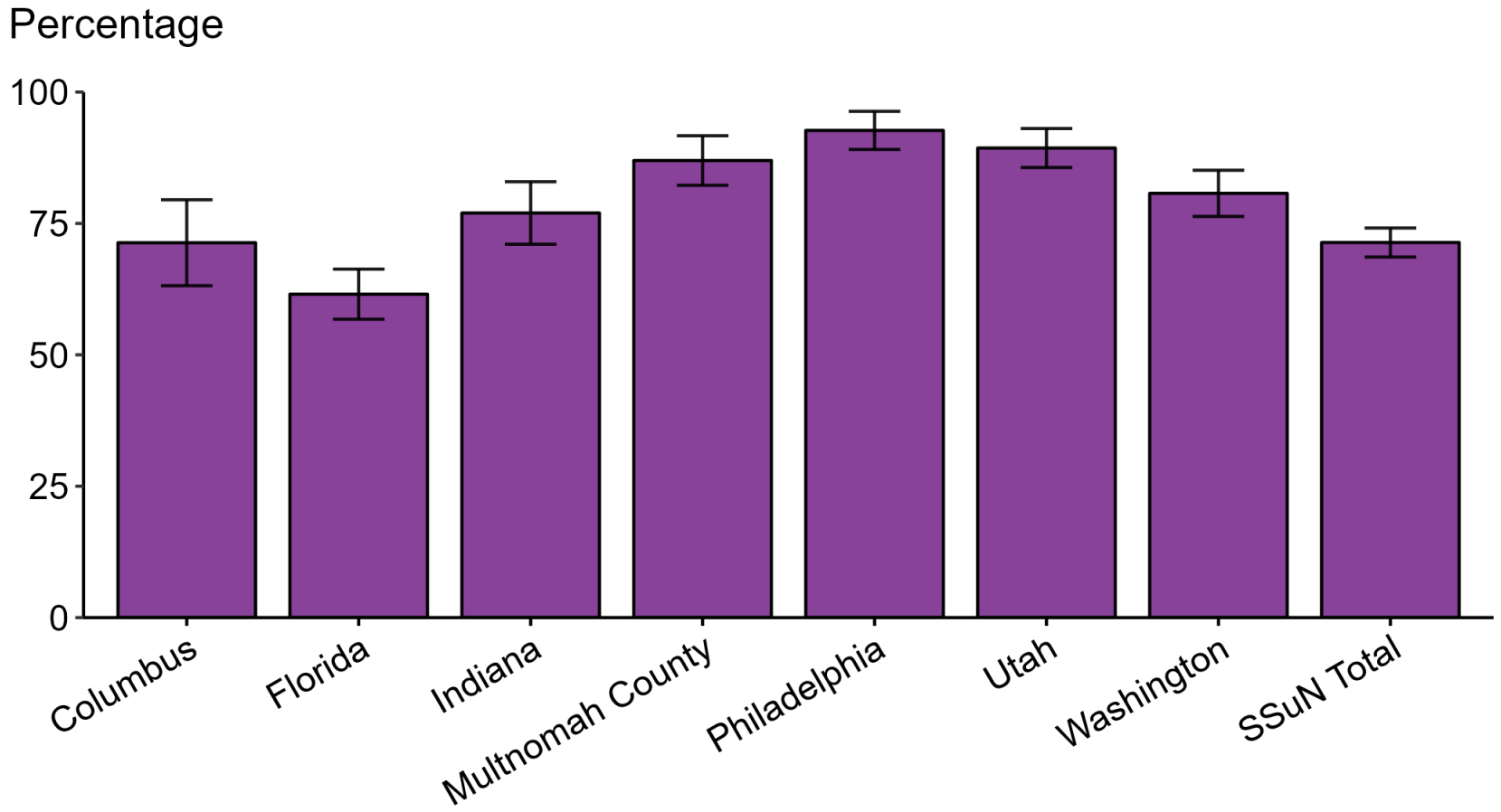
*For persons weighing ≥ 150kg, 1 g of IM ceftriaxone should be administered

If chlamydia has **not** been excluded, treat for chlamydia with:

Doxycycline 100 mg PO twice daily x 7 days

*For pregnancy, allergy, or concern for non-adherence 1g PO Azithromycin can be used

Gonorrhea — Estimated Proportion of Cases Treated with Recommended Regimen by Jurisdiction, STD Surveillance Network (SSuN), 2021*



* Reported 2021 data are preliminary as of June 15, 2022

NOTE: Includes only SSuN jurisdictions with treatment and dosage data ascertained for at least 80% of sampled, investigated cases. In 2021, the recommended treatment for uncomplicated gonorrhea was monotherapy with 500 mg ceftriaxone intramuscular. Data in this figure reflect patients treated in compliance with the current treatment recommendations. N = 3,462 completed investigations among randomly selected cases.

Why Increase the Dose and Change the Regimen?

- Concern about resistance increasing with azithromycin use
  - Empiric treatments for STIs
  - Other uses e.g. bronchitis, *Mycoplasma genitalium*, etc
- PK/PD of beta-lactam antibiotics
  - fT (free time) >MIC, needs 20 hours above MIC
  - MIC creep for many antibiotics
- Preserving antibiotics in general for the future with lack of antibiotics in the pipeline

Why increase the CTX dose? -- PK/PD

PK/PD Target:

fT>MIC >20 hours

Time Above MIC with Different Ceftriaxone Doses (95% CI)

	Ceftriaxone Dose		
MIC	**250mg**	**500mg**	**1g**
0.015	49.9 (23.8->90)	58.7	65.4 (33->90)
0.03	41.4 (20-86)	49.9	56.9 (28->90)
0.06	32.8 (15-69)	41.3 (20-60)	48.5 (24->90)
0.125	24.1 (10-52)	32.8 (16-46)	40.3 (19.6-83)
0.25	15.4 (5-34)	24.3	31.6 (15-66)

Current MIC_{90} →

"Resistant" →
Max MIC in US in 2019

fT>MIC in pharynx is unknown.

Sources: Chishom JAC 2010

GC Treatment Alternatives and Cephalosporin Allergy

Alternative

- Cefixime 800 mg orally as a single dose
- Ciprofloxacin 500mg PO x 1 if resistance testing available
  - gyrA testing

Allergy

- Gentamicin 240mg IM Plus Azithromycin 2g PO x1

*No reliable alternatives for pharyngeal gonorrhea

- https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm

New Treatments: repurposing antibiotics

NABOGO Trial . deVires et al

- New AntiBiotic treatment Options for uncomplicated GOnorrhea
- RCT , double blinded, single center for anal GC
- Evaluating ceftriaxone, ertapenem, gentamicin and fosfomycin
- Outcome: proportion of participants with negative NAAT at 7-14 days after treatment
- Stats: modified intention to treat with lost to follow up was considered failure; all arms compared to ceftriaxone
- Non inferiority- lower Hochberg-corrected 95% CI for difference between experimental and control group was > -10%

NABOGO Design

- September 2017-June 2020
- 2160 patients
- >18 years of age
- Anal GC diagnosed by NAAT or symptomatic with + gram stain
- 1:1:1 arms
- Excluded: complicated infections (PID, epididymitis), other infections, pregnancy, new HIV diagnosis, CD4 <200, known allergy to any of the medications, renal/liver disease, and other conditions
- DSMB: early termination if <60% efficacy which happened in Fosfomycin arm

NABOGO Results and Conclusions

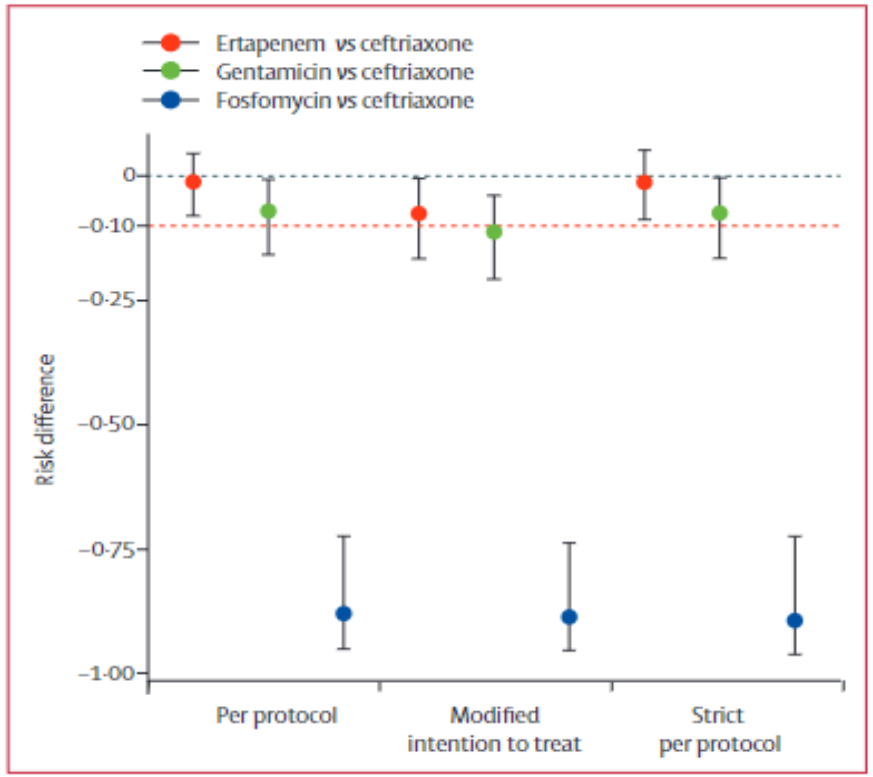
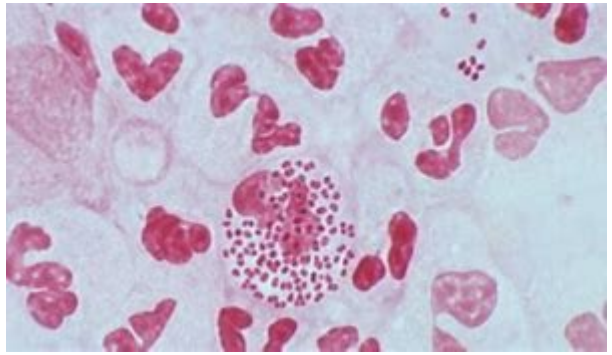


Figure 2: **Risk difference for clearance of *Neisseria gonorrhoeae* at primary infection site 7–14 days after randomisation**
The solid circle shows the risk difference in clearance between ceftriaxone and study treatment. The lines indicate the 97·5% CIs around the risk difference. The red dotted line at −0·10 indicates the predefined non-inferiority margin.

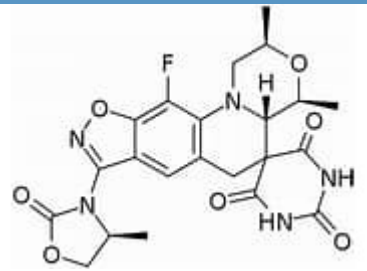
- Single dose of ertapenem 1000mg was non-inferior but in the intention to treat arm (due to lost to follow up), non-inferiority was not established
  - May not be able to use in resistant ceftriaxone organisms- due to volume of distribution and concentrations
  - Costs of ertapenem
  - GI intolerance
  - Risk of carbapenem resistance
- Gentamicin
  - 5mg/kg dose may be higher than the 240 mg IM dose + azithromycin now recommended
  - Frequent pharyngeal failures with single dose; multi-dose may have oto/renal toxicity
- Fosfomycin 6 g oral was inferior; study arm stopped
  - Multiday dosing 3 g days 1,3 5 was non inferior previous studies

New Antimicrobials



Novel Antibiotics in Phase 3 Trials

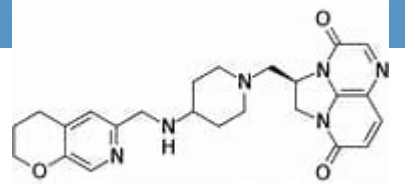
Zoliflodacin



- A novel spiropyrimidinetrione antimicrobial
- Inhibits DNA biosynthesis
- 2gm or 3 gm oral doses
- 96% cure in micro-ITT
- Benefits
  - Maintains efficacy against cipro-resistant strains
- Limitations: few with rectal infections; poor pharyngeal levels→ failures but no resistance detected

Taylor S et al. N Engl J Med 2018; 379:1835-1845

Gepotidacin



- A novel triazaacenaphthylene bacterial type II topoisomerase inhibitor
- Phase 2 study, uncomplicated urogenital GC (originally studied for UTIs)
- Single dose 1500mg or 3000 mg oral
- Micro-ITT eradication was 97%, 95% and 96% for urogenital , pharyngeal and rectal specimen respectively
- Failures occurred in organisms with high MICs and a common gene mutation
- Limitations: small sample size, few patients with pharyngeal or rectal GC enrolled; only 3% evaluated were women

Taylor, S et al. Clin Infect Dis. 2018 Aug 1;67(4):504-512

Changes to GC Screening and Testing

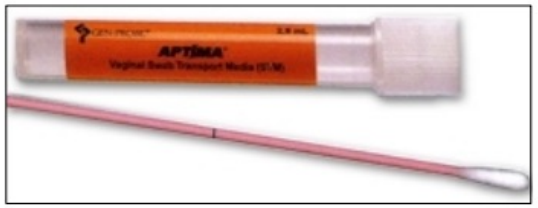
- More frequent screening for populations especially those at risk (sexually active populations)
- Testing at extragenital sites for women (pharyngeal and anal) based on risk for infection and complications
- Offering of self-collected swabs for all anatomic sites provided that the laboratory performing testing has been validated for self-collected specimen types
- NAAT and culture testing at sterile body sites in cases of disseminated gonorrhea (DGI) (limited data on NAAT use) with genital and extra genital testing concurrently to increase yield of diagnosis

What else can we do?

New Factors to Consider for STI Control Strategies

Improved Contact w/ Patients

- EHR with patient portals
- Ubiquity of cell phones



Improved Diagnostics for GC & CT

- Incredibly sensitive and specific
- Patient collected specimens
- Shelf stability
- Faster time to results

Point of Care Tests for GC/CT/TV

- Potential to eliminate overtreatment from:
  - Epidemiologic Treatment
  - Syndromic Management

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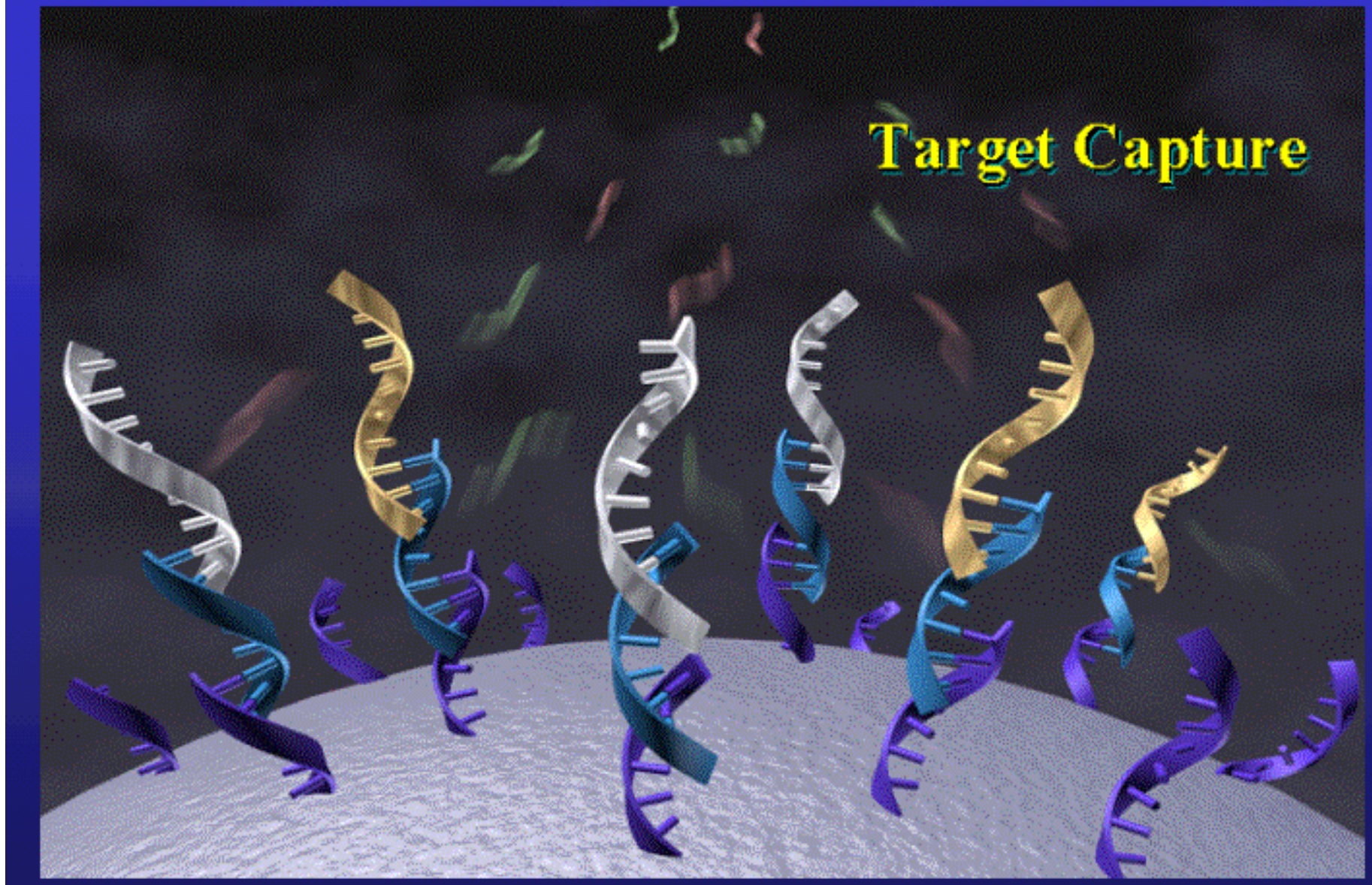
STI Diagnostics: Past, Present, and Future

Gregory J. Berry, Ph.D., D(ABMM)
Associate Professor of Pathology & Cell Biology
Co-Director, Clinical Microbiology Service
Associate Director, Center for Advanced Laboratory Medicine (CALM)
Columbia University Irving Medical Center

Current testing at CUMC

Hologic Aptima Assays

- Aptima Combo assays – utilize TMA and target capture to detect rRNA for the following pathogens:
  - **CT/GC (combo)**
  - **Trichomonas**



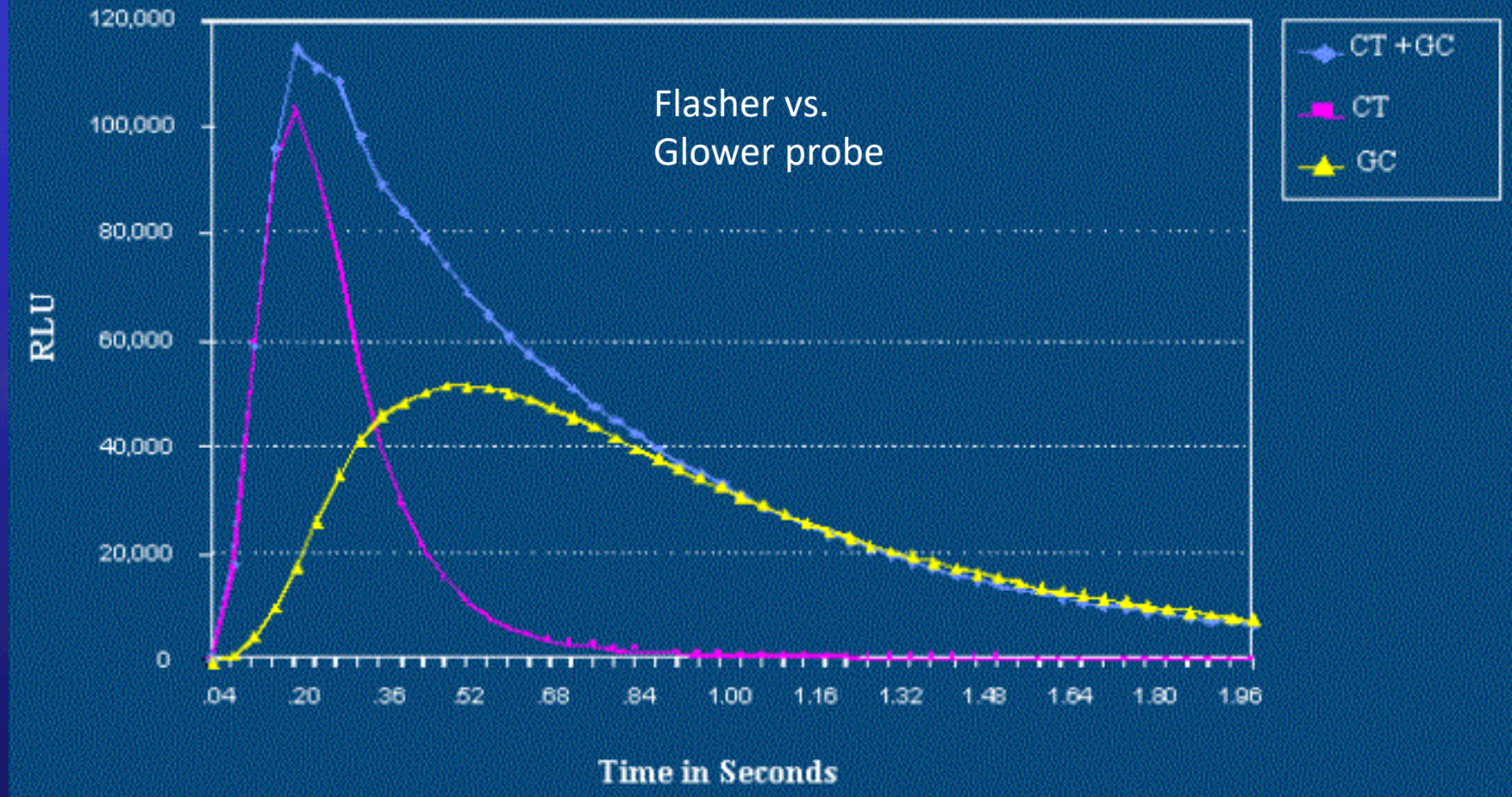
Neisseria gonorrhoeae/*Chlamydia trachomatis* Assay

- Combines target capture, TMA, and DKA
- Cleared for the following specimens on the Panther System:
  - Clinician-collected endocervical, vaginal, and male urethral swab specimens
  - Male urine specimens
  - Clinician-collected PreservCyt Solution liquid Pap specimens
  - Patient-collected vaginal swab specimens

Trichomonas vaginalis Assay

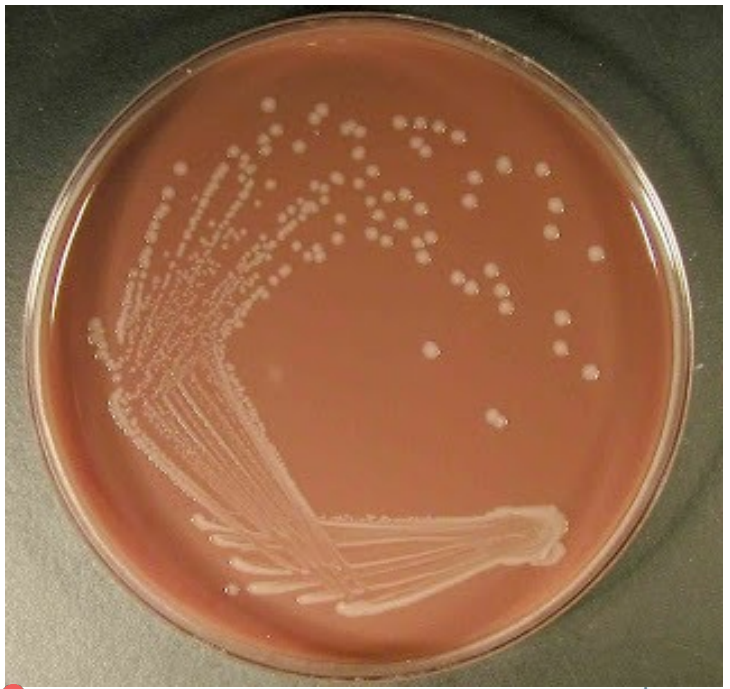
- only female urine, endocervical and vaginal swabs are accepted

Dual Kinetic Assay (DKA)



Neisseria gonorrhoeae Culture

- Fastidious organism and susceptible to cold
  - In general, poor yield
- Requires special media for isolation (e.g. Thayer-Martin agar) and CO2 incubation
- Collection and transport to lab ASAP (<2 hrs ideal)



So why do it at all??

Antibiotic susceptibility results

https://microbeonline.com/chocolate-agar-composition-uses-colony-characteristics/

Point-of-Care Testing for Sexually Transmitted Infections

A Review of Recent Developments

Paul C. Adamson, MD, MPH; Michael J. Loeffelholz, PhD; Jeffrey D. Klausner, MD, MPH

• *Context.*—Sexually transmitted infections (STIs) are among the most common communicable diseases globally and are associated with significant morbidity and mortality worldwide. Point-of-care tests have the potential to revolutionize the prevention and control of STIs by enabling rapid diagnosis and early treatment of infections, thus interrupting transmission and preventing the sequelae of untreated infections. Currently, there are several point-of-care (POC) tests available for the diagnosis of *Treponema pallidum*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* infections, although these tests differ with regard to their performance, turnaround time, and cost.

Objective.—To provide an updated review of the POC tests available and under development for the diagnosis of *T pallidum*, *C trachomatis*, *N gonorrhoeae*, and *T vaginalis* infections, to discuss the context for which these tests might be used, and to highlight future directions for test development.

Data Sources.—We reviewed the literature pertaining to the recent development and performance evaluations of POC tests for the diagnosis of syphilis, chlamydia, gonorrhea, and trichomonas.

Conclusions.—Recently, there has been rapid development of new POC tests for STIs. Although there are inexpensive, rapid, and accurate POC tests available for syphilis, there are few such tests available for the diagnosis of chlamydia, gonorrhea, or trichomonas, and currently none with the ability to detect antimicrobial resistance in *N gonorrhoeae*. Research evaluating implementation strategies for the currently available tests and the development of additional POC tests that are rapid, accurate, and affordable are urgently needed to address the rising number of STIs worldwide.

(*Arch Pathol Lab Med.* 2020;144:1344–1351; doi: 10.5858/arpa.2020-0118-RA)

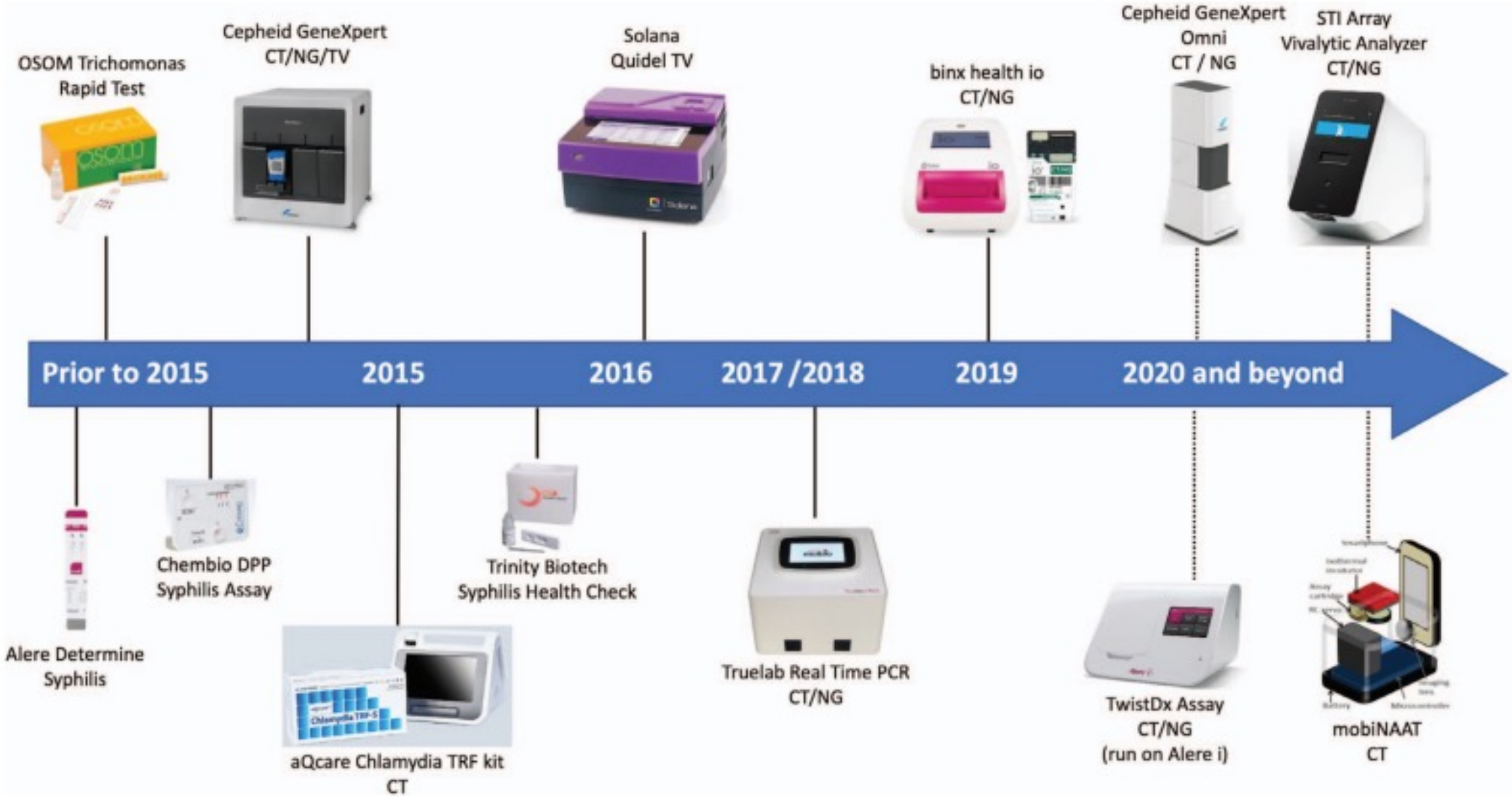


Figure 3. *Point-of-care tests, available and under development, for the diagnosis of syphilis, chlamydia, gonorrhea, and trichomoniasis. Dotted lines indicate tests that are not yet commercially available. Figure adapted from prior report and used with author's permission.*[42] *Abbreviations: CT,* Chlamydia trachomatis*; NG,* Neisseria gonorrhoeae*; PCR, polymerase chain reaction; TV,* Trichomonas vaginalis.

Developments in “Near Patient” Testing

FDA NEWS RELEASE

FDA Allows for First Point-of-Care Chlamydia and Gonorrhea Test to be Used in More Near-Patient Care Settings

Share Tweet Linkedin Email Print

For Immediate Release: March 30, 2021

English

Today, the U.S. Food and Drug Administration announced it is allowing the use of the Binx Health IO CT/NG Assay at point-of-care settings, such as in physician offices, community-based clinics, urgent care settings, outpatient health care facilities and other patient care settings, operating under a CLIA Certificate of Waiver, Certificate of Compliance or Certificate of Accreditation. This action is the result of the FDA granting a waiver under the Clinical Laboratory Improvement Amendments of 1988 ("CLIA") for the Binx Health IO CT/NG Assay.

“The ability to diagnose at a point-of-care setting will help with more quickly and appropriately treating sexually-transmitted infections, which is a major milestone in helping patients,” said Tim Stenzel, M.D., Ph.D., director of the Office of In Vitro Diagnostics and Radiological Health in the FDA’s Center for Devices and Radiological Health. “More convenient testing with quicker results can help patients get access to the most appropriate treatment. According to the CDC, one in five Americans are diagnosed

CLIA Waiver by Application Approval Determination

Decision Summary

A. Document Number

CW200003

B. Parent Document Number

K200748

C. CLIA Waiver Type:

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

D. Applicant

Visby Medical

E. Proprietary and Established Names

Visby Medical Sexual Health Click Test

F. Measurand (analyte)

Chlamydia trachomatis DNA,
Neisseria gonorrhoeae DNA, *and*
Trichomonas vaginalis DNA

G. Sample Type(s)

Female Vaginal Swabs (self-collected in healthcare settings)

H. Type of Test

Qualitative, Polymerase Chain Reaction (PCR)

Original research article

INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
2016, Vol. 27(14) 1275–1282

DOI: 10.1177/0956462415615775
std.sagepub.com
SAGE

Multiplex PCR testing for nine different sexually transmitted infections

John D Kriesel[1], Amiteshwar S Bhatia[1], Cammie Barrus[2], Mike Vaughn[3], Jordan Gardner[4] and Robert J Crisp[3]

Abstract

Current sexually transmitted infection (STI) testing is not optimal due to delays in reporting or missed diagnoses due to a lack of comprehensive testing. The FilmArray® (BioFire Diagnostics, LLC, Salt Lake City, Utah) is a user-friendly, fully automated, multiplex PCR system that is being developed for rapid point-of-care use. A research-use-only STI panel including multiple PCR primer sets for each organism was designed to detect *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, *Trichomonas vaginalis*, *Mycoplasma genitalium*, *Ureaplasma urealyticum*, *Haemophilus ducreyi*, and herpes simplex virus (HSV) types 1 and 2. Standard clinical testing included Gram stain, nucleic acid amplification, wet mount examination, herpes simplex virus culture, and syphilis IgG. Standard clinical tests were not available for all the organisms tested by the FilmArray STI panel. Two hundred and ninety-five clinical specimens from 190 subjects were directly compared to standard testing. Urine ($n = 146$), urethral/cervical swabs (31), oral swabs (60), rectal swabs (43), and ulcer swabs (15) were tested. Among the tested samples, FilmArray detected *C. trachomatis* in 39 (13%), *N. gonorrhoeae* in 20 (7%), *T. vaginalis* in nine (3%), HSV 1 in five (2%), HSV 2 in five (2%), *U. urealyticum* in 36 (12%), *M. genitalium* in eight (3%), and *T. pallidum* in 11 (4%). Concordance between the FilmArray STI panel and standard nucleic acid amplification testing for *C. trachomatis* was 98% and for *N. gonorrhoeae* was 97%. Multiplex PCR STI testing has the potential to improve public health by providing rapid, sensitive, and reliable results within the clinic or nearby laboratory.

Keywords

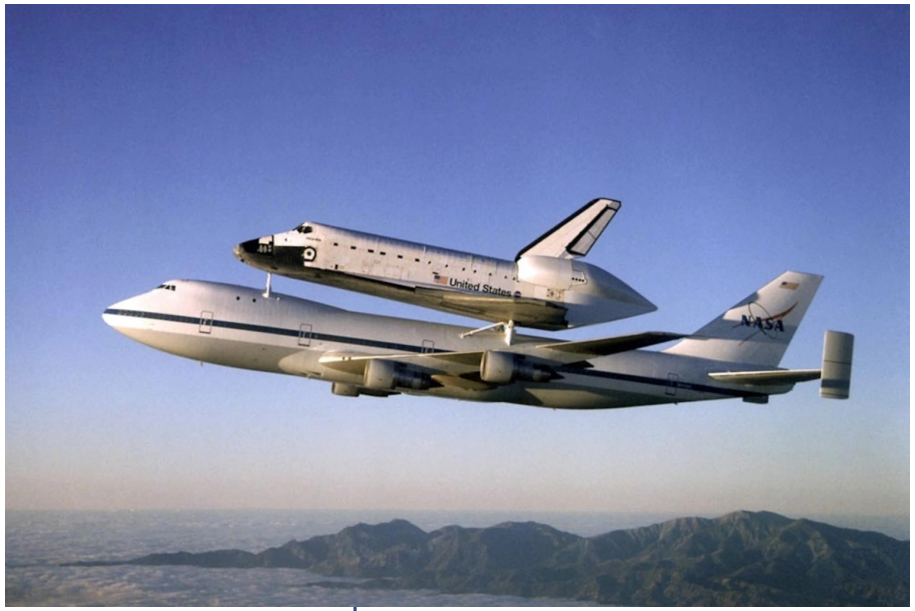
FilmArray, sexually transmitted diseases, sexually transmitted infections, STI, diagnostic test performance, multiplex PCR

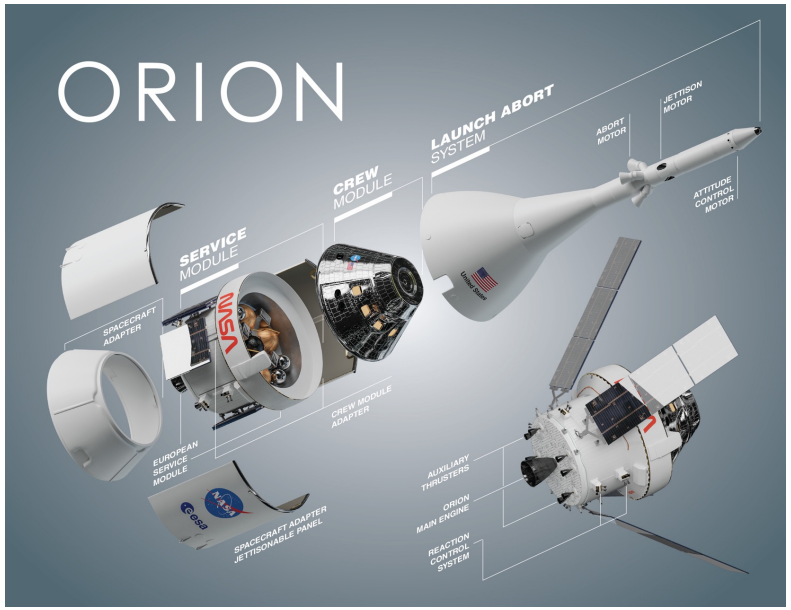
Date received: 24 June 2015; accepted: 14 October 2015

Table 4. Results for specimens (by type) tested by the FilmArray STI panel. Two hundred and ninety-five specimens from 190 subjects were selected for testing on the FilmArray device. The table header shows the total number of samples tested for each specimen type. The table body shows the number of tested specimens that were positive by the FilmArray.

Organism	Urine $n=146$	Urethral	Ulcer swab $n=15$	Total $n=295$
Chlamydia trachomatis	23	5	0	39
Neisseria gonorrhoeae	9	1	0	20
Treponema pallidum	2	0	5	11
Trichomonas vaginalis	5	3	0	9
HSV1 or HSV2	5	1	1	10
Mycoplasma genitalium	5	1	0	8
Ureaplasma urealyticum	9	9	0	36
Haemophilus ducreyi	0	0	0	0
Total	58	20	6	133

CANCELLED





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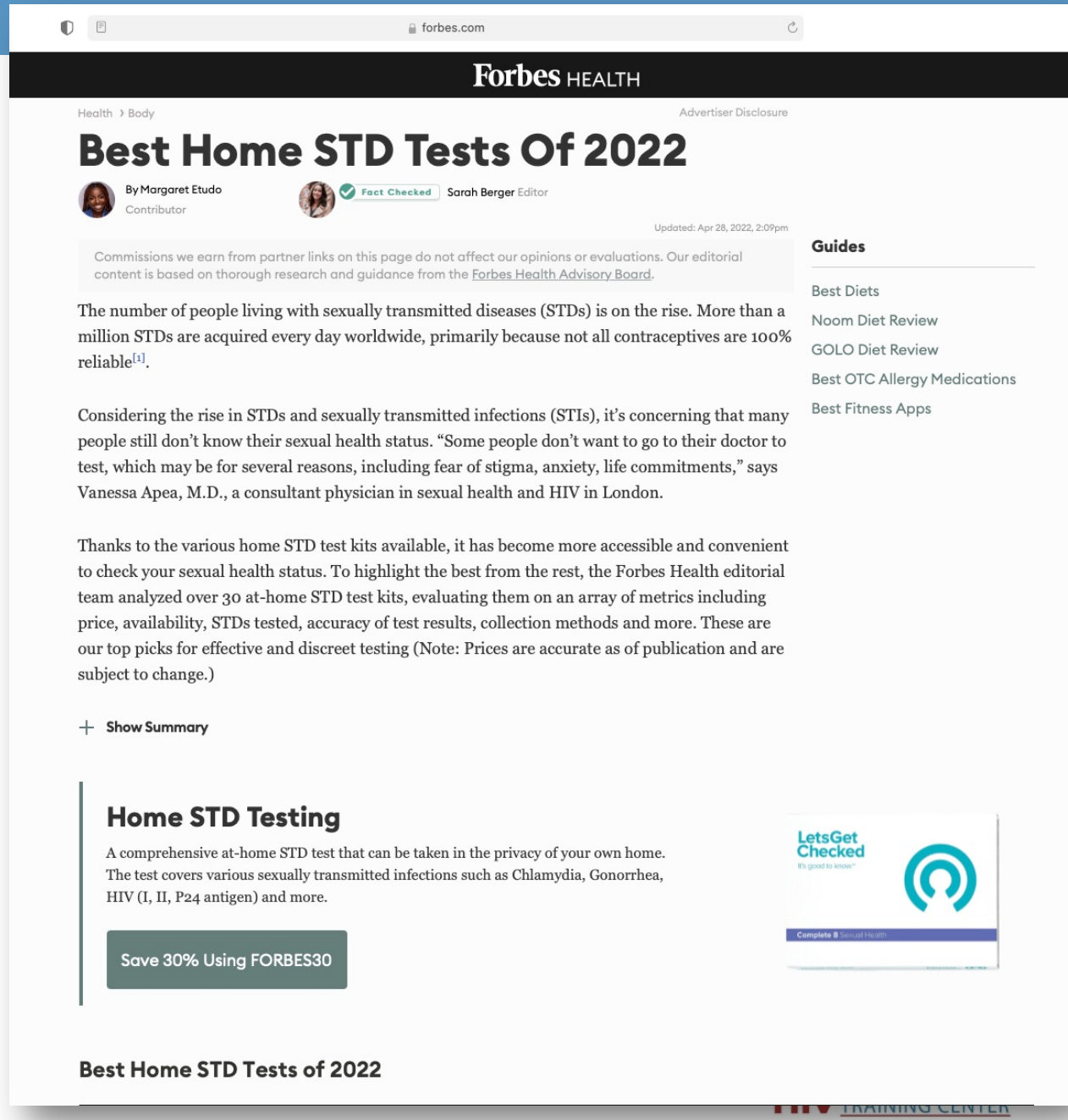
https://www.nationalgeographic.com/science/article/space-shuttle-program
https://www.nasa.gov/feature/meet-nasa-s-orion-spacecraft/

STD HIV PREVENTION TRAINING CENTER

Alternate Future of STI testing?

- Does “Home Testing” mean POC,or something else??
- Convenient (and discreet) vs. Rapid



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What's Missing?

These assays all give an ID, but where's my AST result??

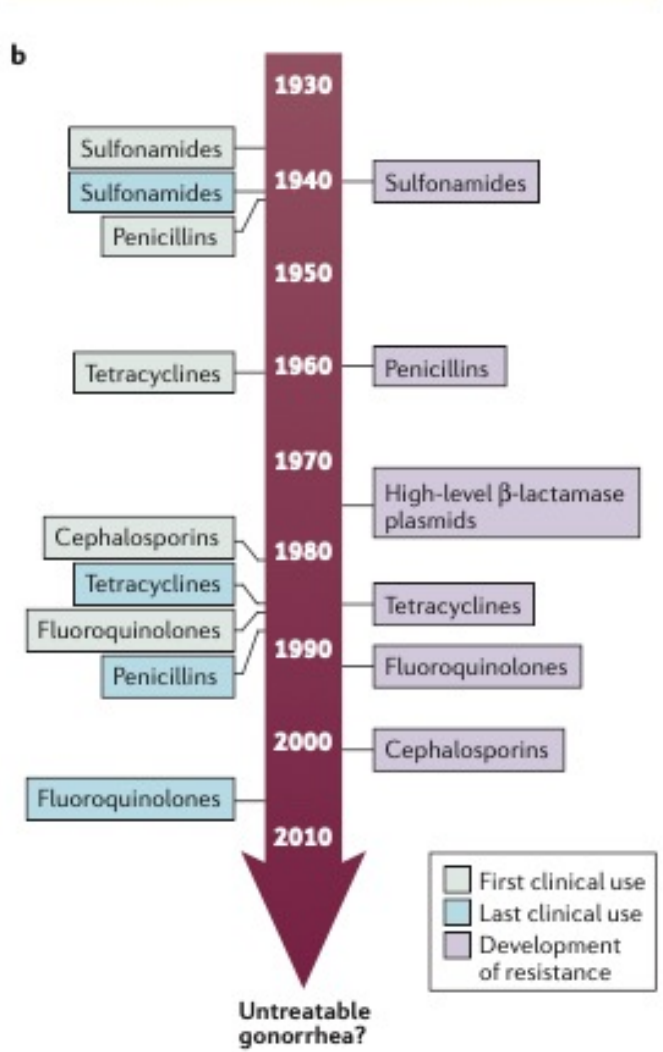
More importantly…why do I care?!?

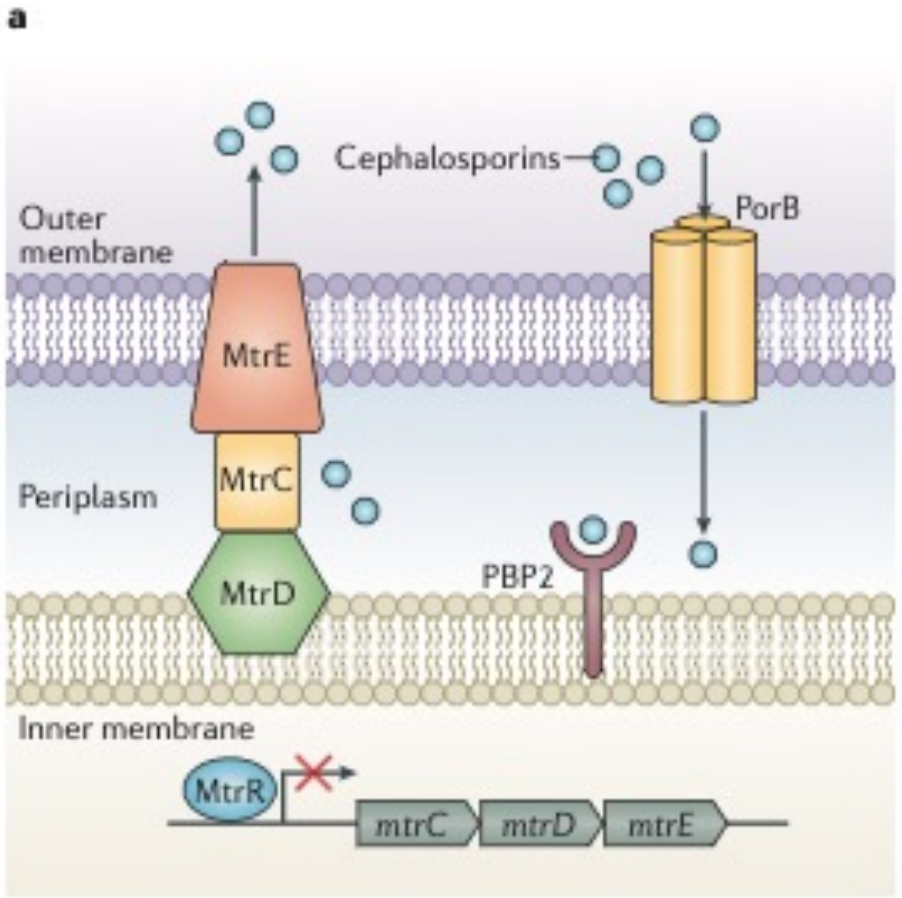
Multi-drug resistant *Neisseria gonorrhoea*

- Antimicrobial resistance in gonorrhoea has increased rapidly in recent years and has reduced the options for treatment.
- Eighty-two million new cases of gonorrhoea occurred in 2020.
- Most gonorrhea cases in 2020 were in the WHO African Region and the Western Pacific Region.
- Most people affected are aged 15–49 years.

https://www.who.int/news-room/fact-sheets/detail/multi-drug-resistant-gonorrhoea

Antibiotic resistance in *Neisseria gonorrhoeae*





Quillin, S., Seifert, H. *Neisseria gonorrhoeae* host adaptation and pathogenesis. *Nat Rev Microbiol* 16, 226–240 (2018). https://doi.org/10.1038/nrmicro.2017.169

OPEN ACCESS

SHORT REPORT

Low gonorrhoea antimicrobial resistance and culture positivity rates in general practice: a pilot study

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► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/sextrans-2019-054006).

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ABSTRACT

Objective In the Netherlands, the Gonococcal Resistance to Antimicrobials Surveillance (GRAS) programme is carried out at Centres for Sexual Health (CSH), which provide care for sexual high-risk populations. However, half of gonorrhoea infections are diagnosed in general practice (GP). We performed a pilot study to explore expanding GRAS to GPs using laboratory-based surveillance. Additionally, antimicrobial resistance patterns of GP and CSH patients were compared.

Methods Three laboratories from different regions were included, which all perform gonorrhoea diagnostics for GPs and used 5[illegible] for surveillance. Additional

and ceftriaxone using Etest.

Results During the study period, 484 samples were put in culture. 16.5% of cultures were positive (n=80).

in CSH GRAS data (first half of 2018) were 19.2% for azithromycin, 31.5% for ciprofloxacin, 1.9% for cefotaxime and 0.0% for ceftriaxone.

Conclusions Culture positivity rates for GP patients were low, probably due to long transportation times and awaiting PCR test results before attempting culture. Positivity rates might be improved by making changes in sampling and/or transportation methods, but that would require involvement of GPs and patients instead of keeping the surveillance lab based. Resistance levels appeared to be lower at GPs than at the CSH, indicating that resistance might emerge first in more high-risk populations. It is important to consider all potentially relevant patient populations when establishing a gonococcal antimicrobial resistance surveillance programme. However, based on the findings from this study the current GRAS programme will not be extended to GPs.

Netherlands,[2] but has been seen in other countries, including the UK.[3]

To monitor gonorrhoea antimicrobial resistance in the Netherlands, the Gonococcal Resistance to Antimicrobials Surveillance (GRAS) programme was established in 2006. GRAS is a sentinel surveillance system including 18 out of 24 Centres for Sexual Health (CSH). However, more than half of gonorrhoea diagnoses in the Netherlands are carried out in general practice (GP) (in 2016: 6092 CSH diagnoses vs approximately 9000 GP diagnoses).[2] Thus, many patients are not included in GRAS. Currently, it is unknown to what extent but it is known that, for example, extragenital testing is less often performed by GPs.[4] Culture is also not routinely performed, but is necessary to determine antimicrobial susceptibility. Because it requires more effort from GPs and their patients to collect additional samples for culturing, we first wanted to explore implementation of a laboratory-based surveillance that requires no additional sample collection. Therefore, the primary goal of this pilot study was to explore the feasibility of a laboratory-based GP surveillance of gonococcal antimicrobial resistance. Additionally, we aim to describe antimicrobial resistance patterns of patients with gonorrhoea in GP, and compare these to patterns of CSH patients.

METHODS

Published in final edited form as:
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Molecular characterization of markers associated with antimicrobial resistance in *Neisseria gonorrhoeae* identified from residual clinical samples

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Abstract

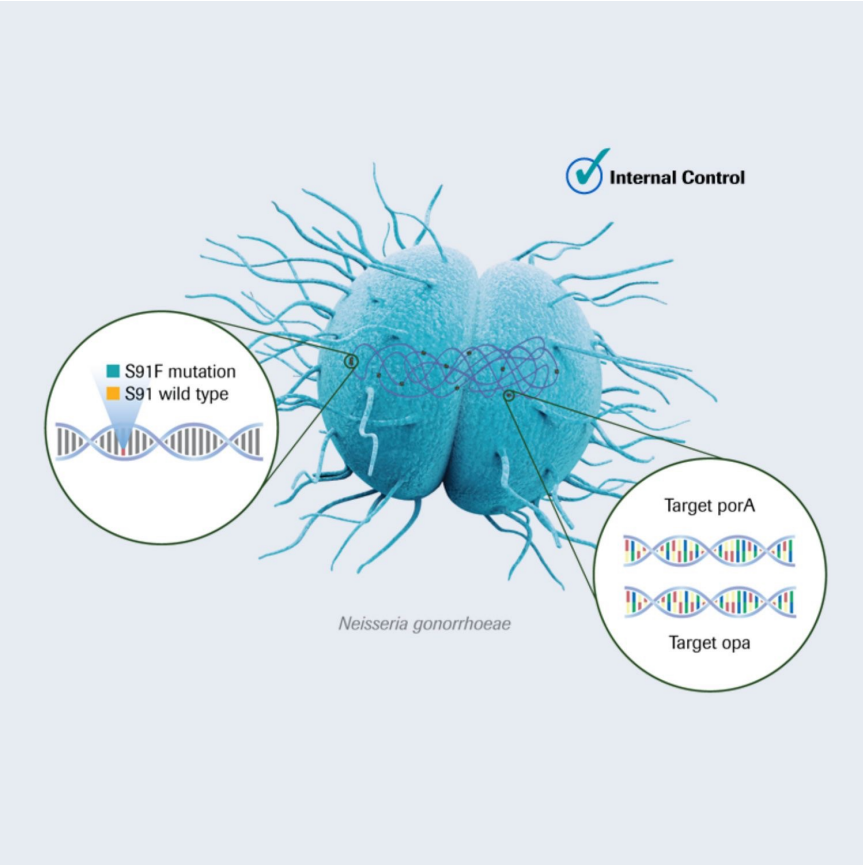
Background—The emergence and spread of antimicrobial-resistant (AMR) *Neisseria gonorrhoeae* (NG) is a major public health concern. In the era of nucleic acid amplifications tests (NAATs), rapid and accurate molecular approaches are needed to help increase surveillance, guide antimicrobial stewardship, and prevent outbreaks.

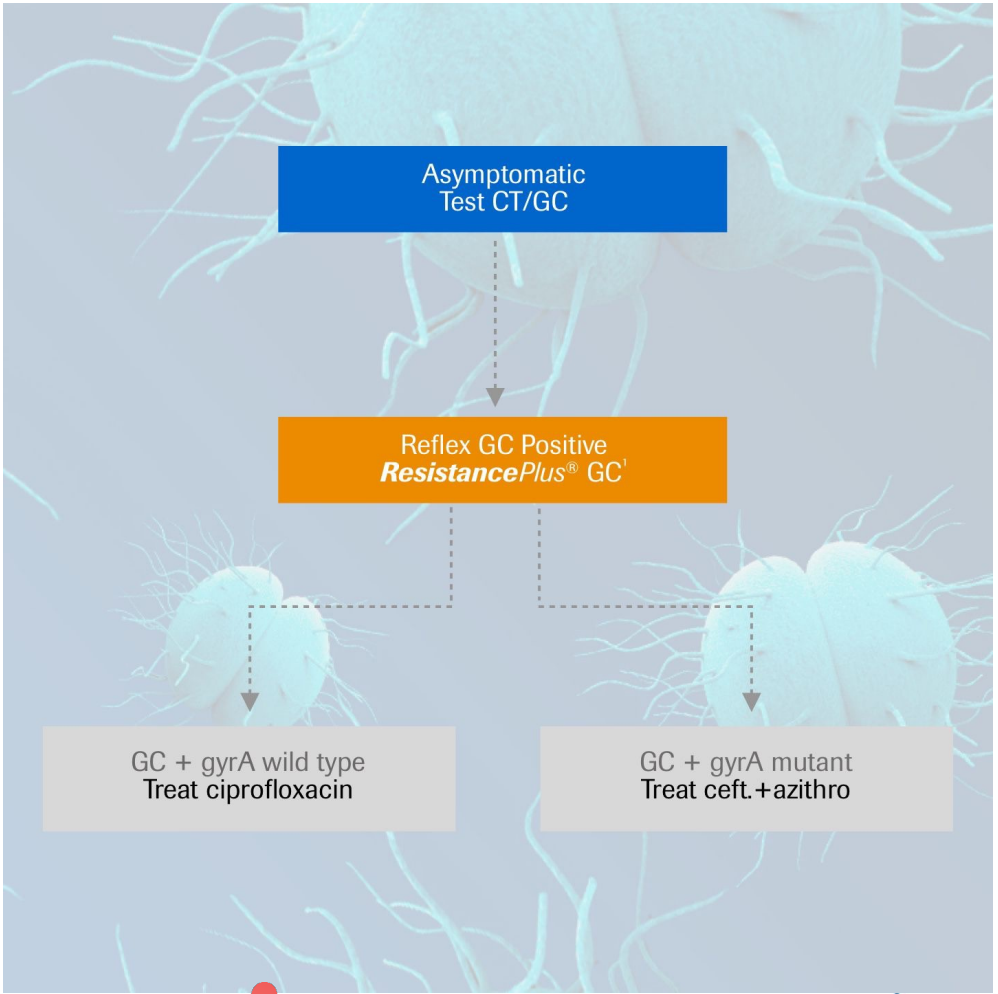
Methods—Residual urethral swabs, collected prospectively in the Baltimore City Health Department during a six-month period, were analyzed by real-time PCR assays for NG DNA and AMR determinants to fluoroquinolones, penicillin, and extended-spectrum cephalosporins (ESCs).

Results—NG DNA was detected in 34.8% (73/210) of samples, including 67.3% (68/101) of the swabs which had been previously identified as NG-positive by culture. Markers associated with decreased susceptibility to fluoroquinolones were detected in 22.4% of the PCR NG-positive samples. The rate of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) was very low (1.6%) and no markers associated with decreased susceptibility to ESCs were detected in this cohort of men using the AMR assays herein described.

Conclusions—Detection of molecular markers associated with AMR in NG can be performed directly from residual clinical samples, even though the recovery rate of adequate DNA for molecular testing from these samples can be sub-optimal. A high number of samples with mutations associated with decreased susceptibility to fluoroquinolones were identified.

N. gonorrhoeae resistance testing





Registration status: CE-IVD, not yet available in the U.S.

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https://diagnostics.roche.com/global/en/products/params/resistanceplus-gc.html

Antibiotic Resistant *Mycoplasma genitalium*

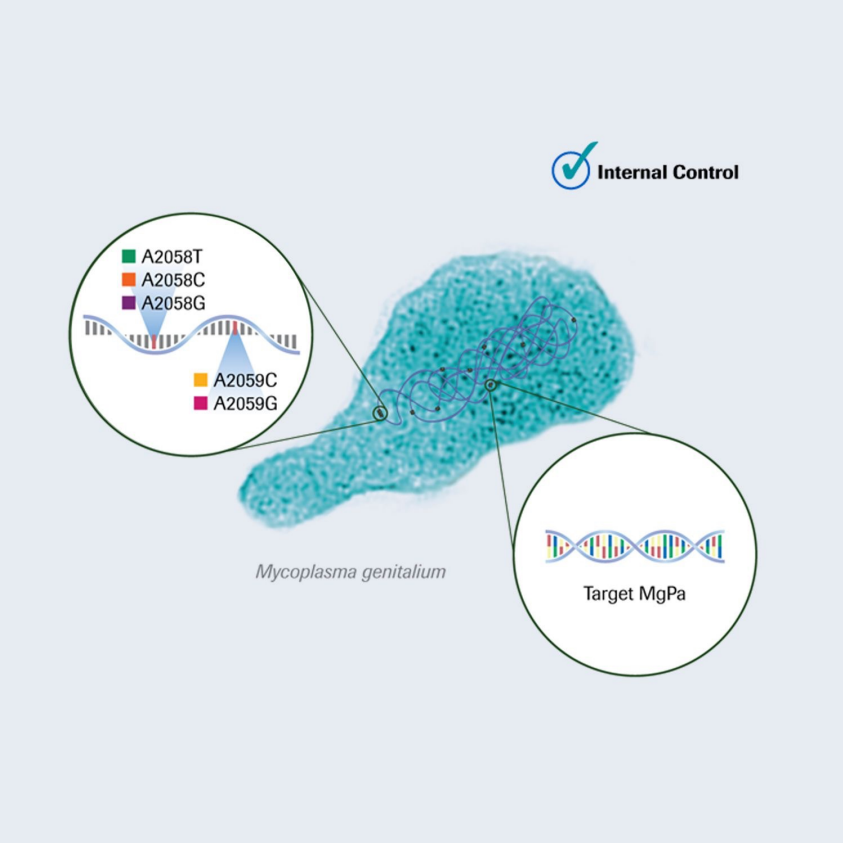
- *M. genitalium* cases are on the rise in both men and women

- Resistance to azithromycin rapidly increasing

- Molecular markers for macrolide resistance strongly correlate with treatment failure
  - Studies have shown prevalence ranging from 44% to 90% in the United States, Canada, Western Europe, and Australia

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

Mycoplasma genitalium resistance testing



- detection of 5 mutations in the 23S rRNA gene (A2058G, A2059G, A2058T, A2058C, and A2059C) associated with resistance to azithromycin

Registration status: CE-IVD, not yet available in the U.S.

https://diagnostics.roche.com/global/en/products/params/resistanceplus-mg.html

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Mycoplasma genitalium resistance testing

- Detection of 4 mutations in the 23S rRNA gene (A2058G, A2059G, A2058T, A2058C) associated with resistance to azithromycin

ResistancePlus*® MG FleXible is validated on a wide range of sample types including rectal, male and female urine, and common collection swab kits including Xpert® CT/NGVaginal/Endocervical Specimen Collection kit and Xpert® CT/NG Urine Specimen Collection Kit.*

CE-IVD *in Vitro* Diagnostic Medical Device. Not available in the U.S.

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https://www.cepheid.com/en/tests/Sexual-Health/SpeeDx-RPMG-FleX

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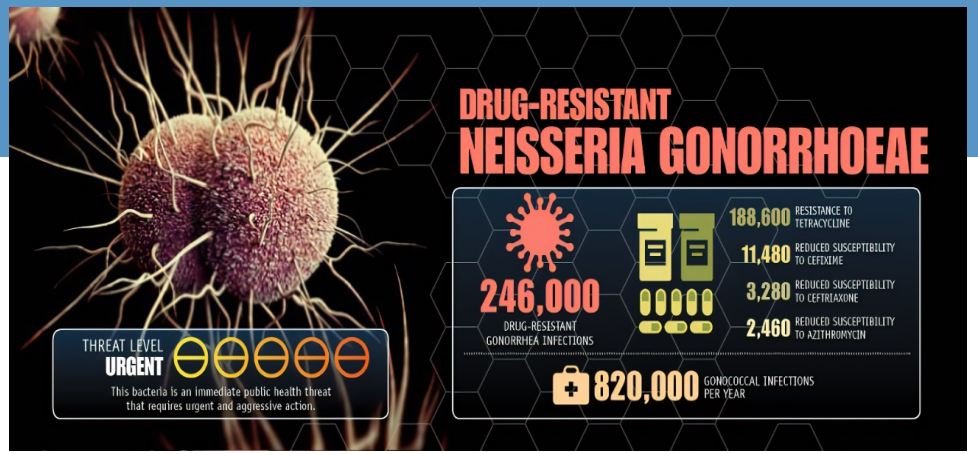
What is in the pipeline?

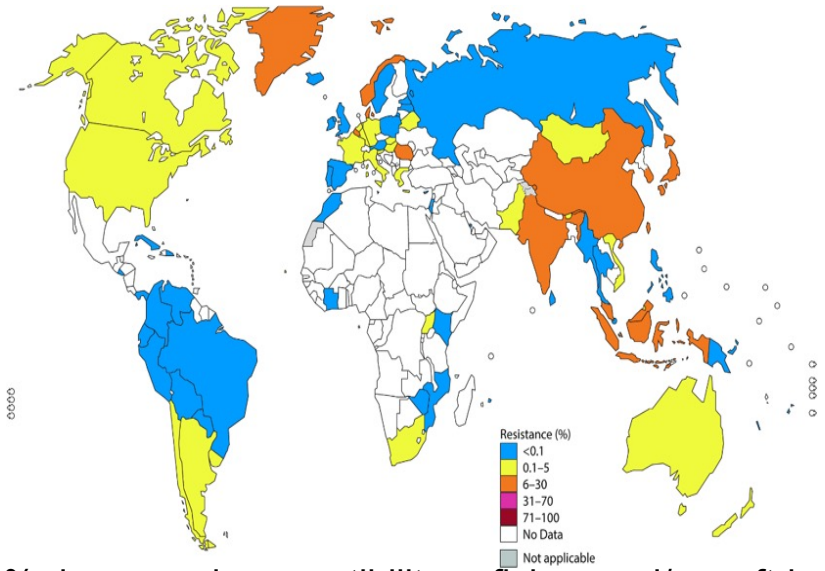
Diagnostic Summary- STI testing

- Molecular techniques have largely replacing traditional culture-based ID
  - Dramatically increased sensitivity, turnaround time
- Trend toward near patient testing will continue
- There is a critical need for continued development and implementation of molecular-based antimicrobial resistance testing to combat antibiotic resistance.

Conclusion



https://thenativeantigencompany.com/gonorrhea-whats-currently-in-the-clinical-pipeline/ Feb 26, 2020



% decreased susceptibility cefixime and/or ceftriaxone WHO Gonococcal Antimicrobial Surveillance Programme

Resistance
Orange 6-30%
Red 71-100%

- Neisseria gonorrhea continues to be a significant STI
- Resistance in GC isolates is a problem
- Guidelines are created and updated based on susceptibility testing at GISP sites
- Pipeline for new therapeutics is limited but there are some new drugs
- Control of GC includes:
  - Screening and testing
  - Successful treatment- resistance based treatment
  - Implementation of new diagnostics
  - Possible new principals for prevention increased testing and DoxyPEP

NYC STD PREVENTION TRAINING CENTER (PTC)

The CDC-funded NYC STD Prevention Training Center at Columbia University provides a continuum of education, resources, consultation and technical assistance to health care providers, and clinical sites. www.nycptc.org

Didactic Presentations

Webinars, conferences, trainings and grand rounds presentations to enhance and build knowledge

Technical Assistance

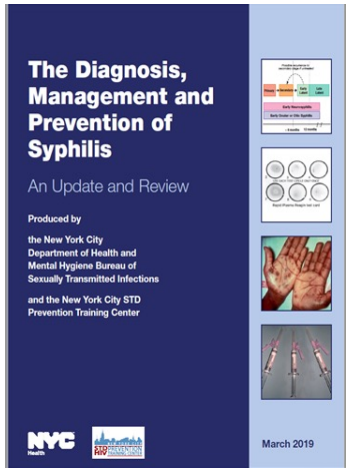
Virtual and on-site technical assistance regarding quality improvement, clinic implementation and best practices around sexual health provision

Clinical Consultation Warmline

Clinical guidance regarding STD cases; no identifying patient data is submitted
www.stdccn.org

Resources

Clinical guidance tools regarding the STD treatment guidelines, screening algorithms and knowledge books, such as the **Syphilis Monograph**. To download a copy please visit:
http://bit.ly/SyphilisMonograph2019PTC



STI Treatment Guide Mobile App

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www.cdc.gov/std