STI Update for the Busy Clinician

Rachel Safran, MD FACP AAHIVS

Disclosures

- I have no actual or potential conflict of interest in relation to this program/presentation.
- I will mention off-label medication use.
- I do serve as a principal/sub investigator for current investigational studies
  - Merck
  - Gilead
  - AstraZeneca

Goals & Objectives

- Review current STI epidemiology and trends
- Describe the clinical presentation of common STIs
- Review key changes and updated recommendations from the CDC's 2021 STI Treatment Guidelines
- Discuss new and evolving therapy options for STI prevention

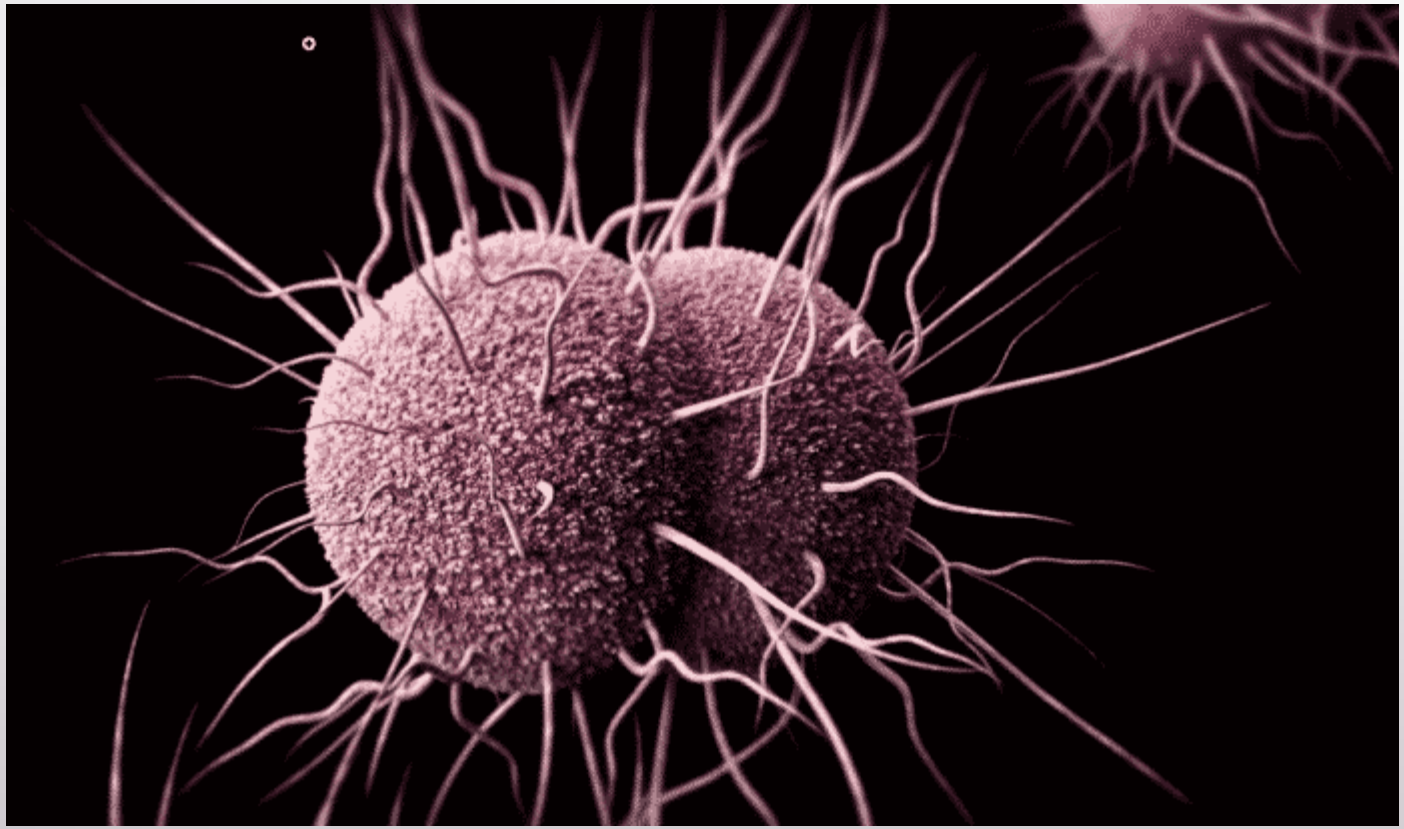
Current epidemiology of STIs

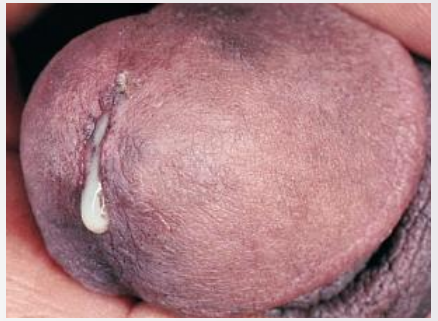
Highest risk populations

- Youth nearly 50% of all STIs are in 15-24 year olds
- Racial/ethnic minorities
  - In 2018 African Americans
    - Syphilis 4.7x the rate among whites
    - Chlamydia 5.6x the rates among whites
    - Gonorrhea 7.7x the rate among whites
- MSM account for more than half the new syphilis cases

CDC 2018 STD Surveillance Report

Onto something new!





Gonorrhea presentation

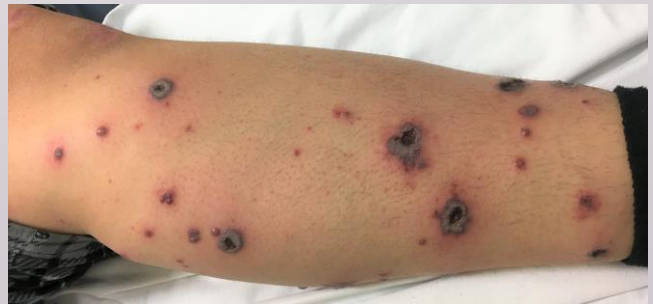
- Urethritis
- Cervicitis
- Pelvic inflammatory disease (PID)
- Epididymitis
- Prostatitis

} Typically painful with purulent drainage

- Proctitis
- Pharyngitis

} May be asymptomatic

- Disseminated – petechial/pustular skin rash, septic arthritis, tenosynovitis, rarely perihepatitis



STI Treatment Guidelines

2021 RECOMMENDATIONS NOW AVAILABLE

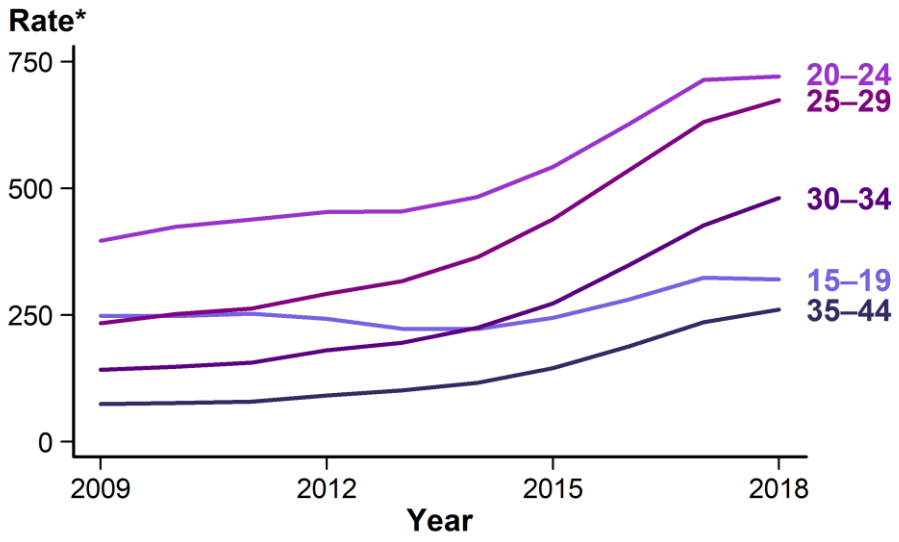
Morbidity and Mortality Weekly Report

Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020

Sancta St. Cyr, MD[1]; Lindley Barbee, MD[1,2]; Kimberly A. Workowski, MD[1,3]; Laura H. Bachmann, MD[1]; Cau Pham, PhD[1]; Karen Schlanger, PhD[1]; Elizabeth Torrone, PhD[1]; Hillard Weinstock, MD[1]; Ellen N. Kersh, PhD[1]; Phoebe Thorpe, MD[1]

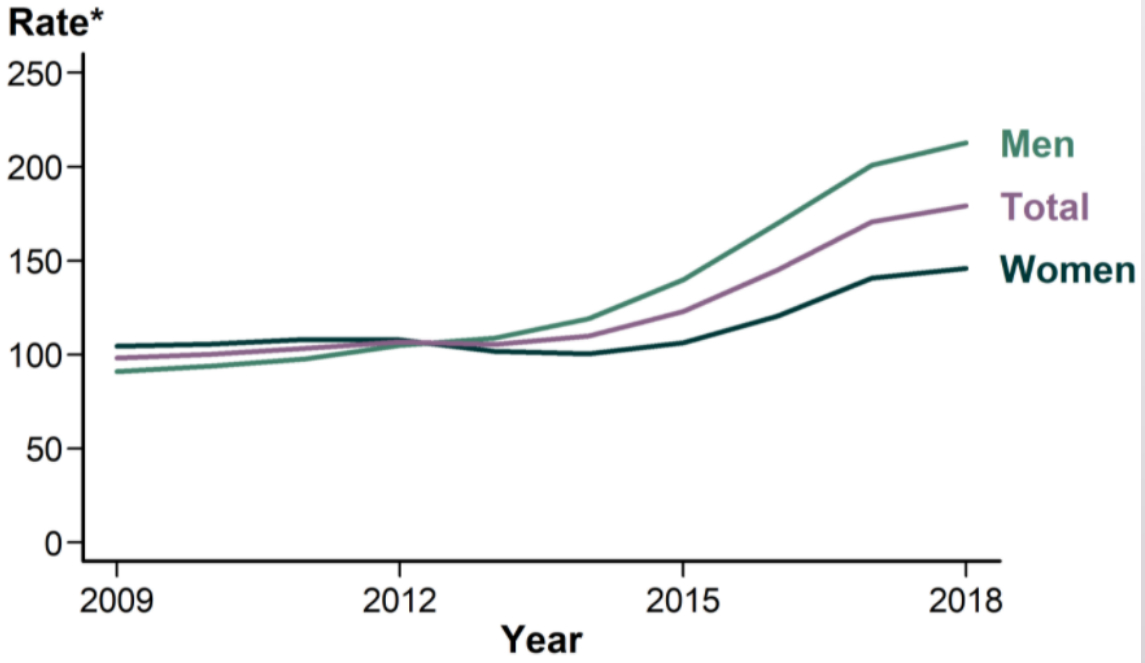
Cyr S, Barbee L, et al. Update to CDC's Treatment Guidelines for Gonococcal infection, 2020. MMWR. 2020;69:191106.

Figure 21. Gonorrhea — Rates of Reported Cases Among Males Aged 15–44 Years by Age Group, United States, 2009–2018



* Per 100,000.

Figure 18. Gonorrhea — Rates of Reported Cases by Sex, United States, 2009–2018



What we used to do…

Ceftriaxone 250mg IM + 1g azithromycin PO

Cephalosporin allergy →

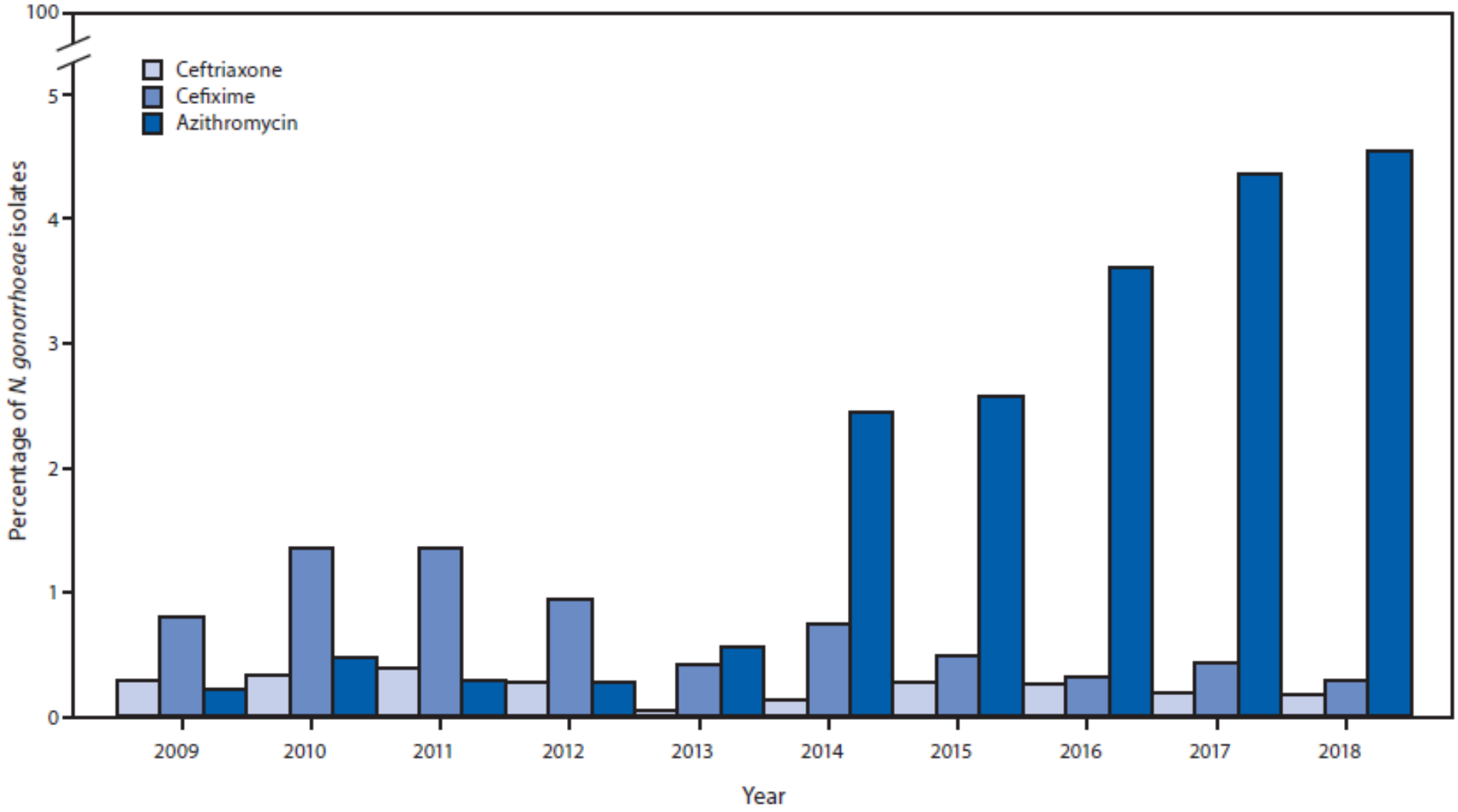
2010 = 2g azithromycin PO

2015 = gentamicin or gemifloxacin

Test of cure recommended only if an alternative regimen used

STD Treatment Guidelines 2010 and 2015 for uncomplicated gonococcal infection

FIGURE. Percentage of *Neisseria gonorrhoeae* isolates with elevated minimum inhibitory concentrations (MICs)* to ceftriaxone, cefixime, and azithromycin — Gonococcal Isolate Surveillance Project, United States, 2009–2018



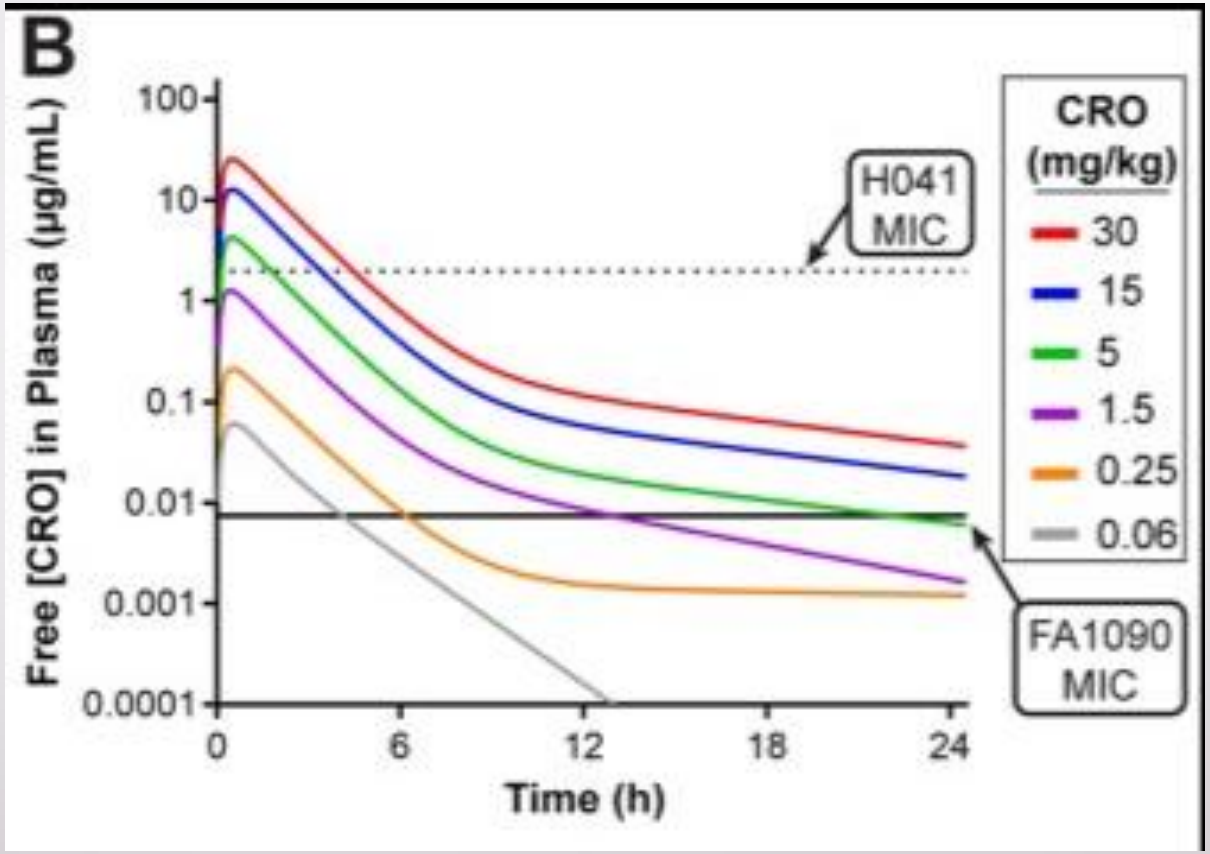
Source: CDC. Sexually Transmitted Disease Surveillance 2018. https://www.cdc.gov/std/stats18/default.htm.
* Elevated MIC = ceftriaxone ≥0.125 μg/mL; cefixime ≥0.25 μg/mL; azithromycin ≥2.0 μg/mL.

What we do now…

- Ceftriaxone 500mg IM for most patients*
  - Weight based dosing 1g IM if >150kg or 300lbs
- If chlamydia has not been excluded → doxycycline 100mg BID x 7days
- Test of cure recommended for all *pharyngeal* infections, regardless of regimen used
  - NO recommended alternative for pharyngeal infections in cephalosporin allergies

But why?

Ceftriaxone activity is best predicted by the time serum free drug is higher than MIC.



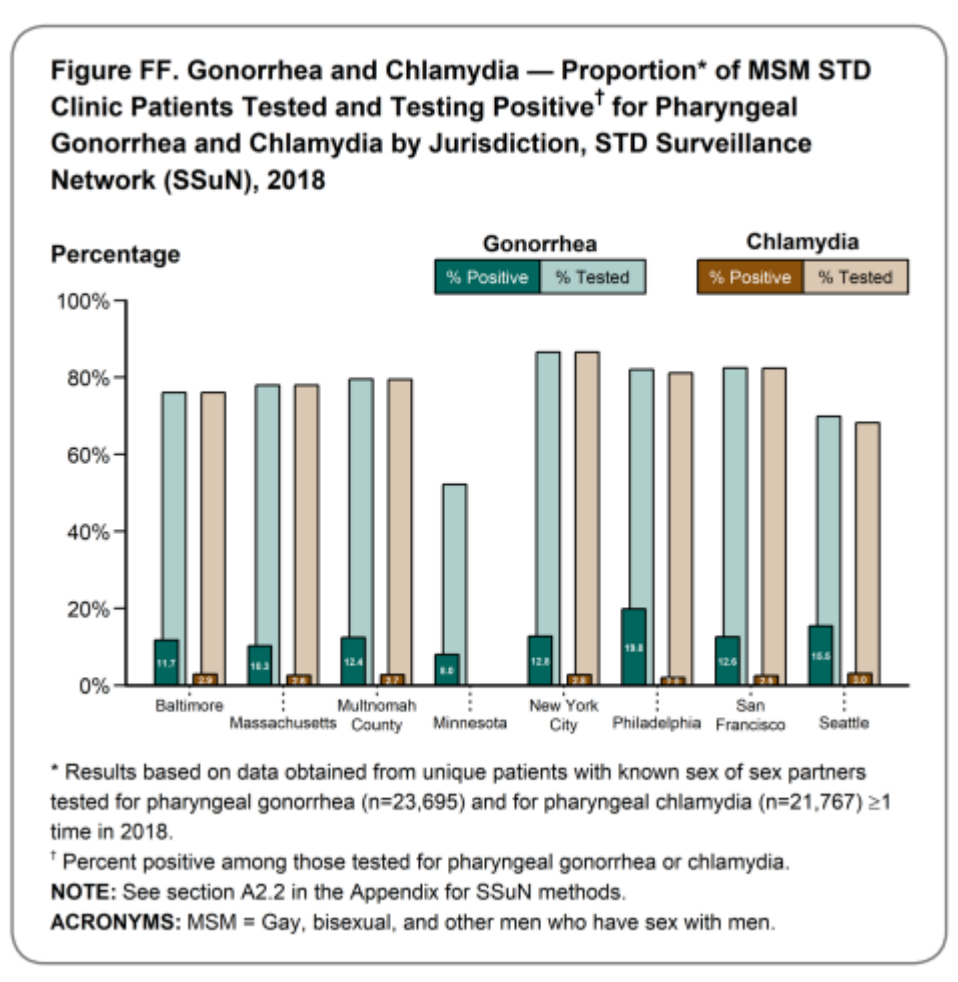
Connolly KL, et al. Antimicrob Agents Chemother 2019;63:e01644–18.

But not all sites are equal

Oropharynx is…

- the least tested site in most clinics
- most common site of treatment failure
- known to have lower drug concentrations

- HENCE we do recommend a test of cure!



Alternatives

- True cephalosporin allergy?
  - Gentamicin 240mg IM
- No ceftriaxone available?
  - Gentamicin 240mg IM
  - Cefixime 800mg PO

**cervix, urethra, rectum*

Key changes for uncomplicated gonorrhea

- Higher dose of ceftriaxone → 500mg IM
  - Weight based dosing – increase to 1g IM if patient is over 150kg (~300lbs)
- Do not treat empirically for chlamydia co-infection if testing was completed and negative at all at-risk sites.
  - If you DO need to treat – used doxycycline 100mg BID X 7days
- Test of cure for pharyngeal infection

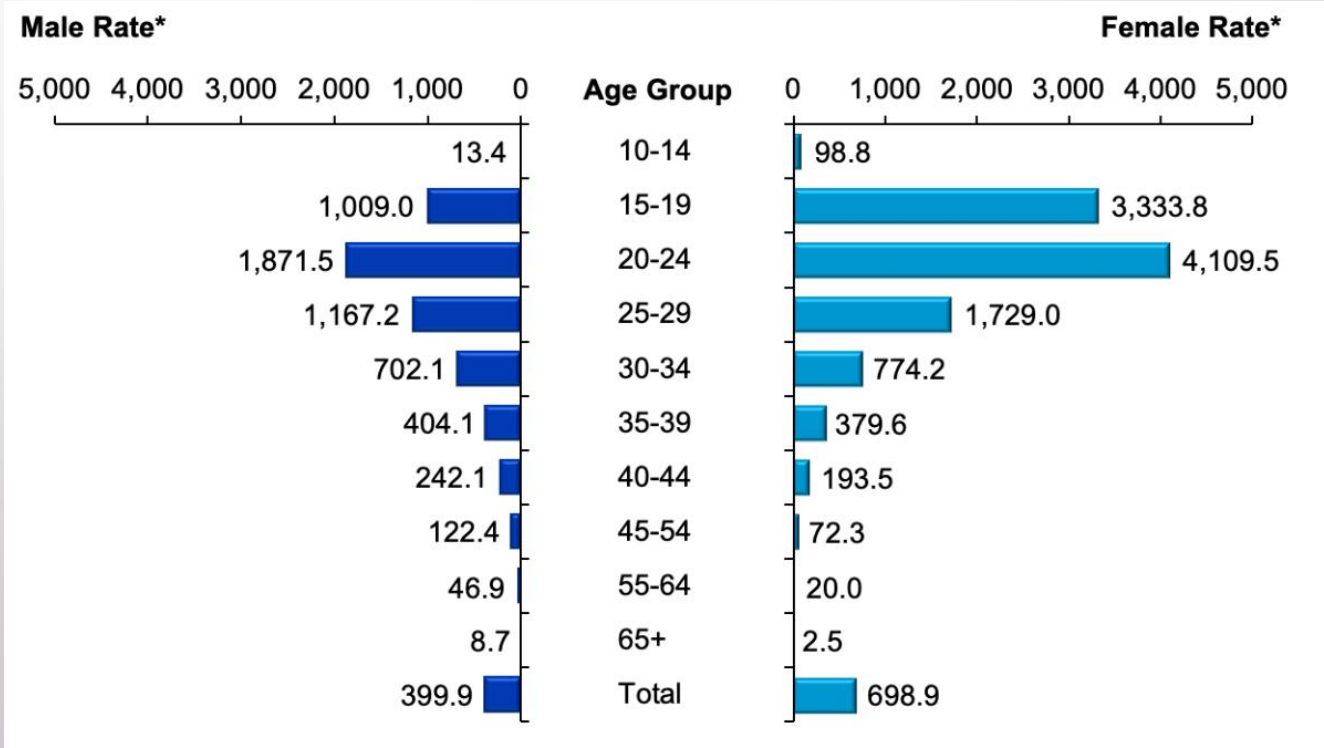
  *But should be re-screening everyone within 3-12months

Unless the patient is pregnant

Chlamydia trachomatis

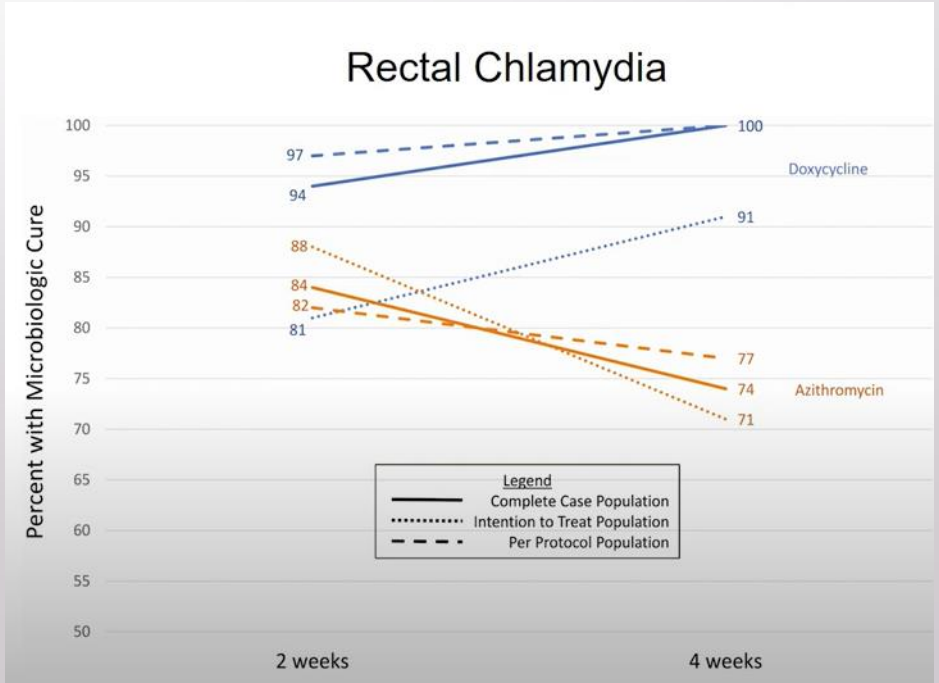
Presentation – ASYMPTOMATIC infection is common in men and women!

- Cervicitis
- Urethritis
- Epididymitis
- Proctitis
- Prostatitis
- Pelvic inflammatory disease (PID)



Chlamydia treatment updates

- Doxycycline preferred treatment for chlamydia at all sites
  - 100mg orally BID x 7days
  - Alternatives: azithromycin 1g or levofloxacin 500mg orally daily x 7days
  - When azithro should still be considered:
    - Pregnancy
    - Concerns about adherence with 7 day regimen
    - Allergy/intolerance



Dombrowski 2021, CID
https://doi/org/10/1093/cid/ciab153

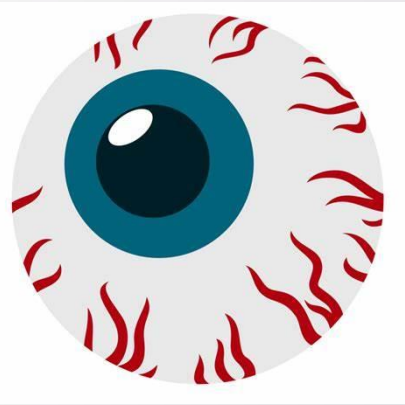
Lymphogranuloma venereum (LGV)

- Presentation:
  - Classic = unilateral tender inguinal/femoral lymphadenopathy followed by transient ulcer
  - NEW = proctocolitis including anal ulcers, mucus/bloody discharge, tenesmus
- Consider this in symptomatic proctitis in high-risk patients
- Treatment: 21 days doxycycline 100mg BID
  - Alternative: azithromycin 1g weekly x 3 weeks

Mycoplasma genitalium

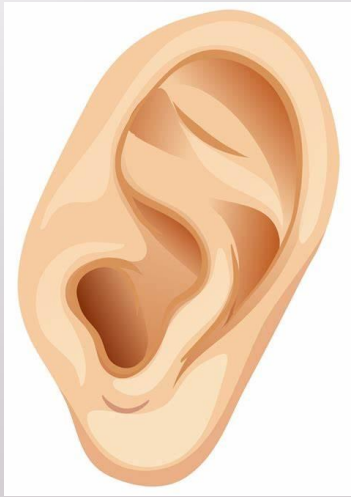
- Most common cause of non-gonococcal urethritis (1 in 4 men)
- Population based screening is NOT recommended, but diagnostic testing with NAAT should be considered for persistent NGU urethritis/cervicitis.
- Treatment:
  - Doxycycline 100mg BID x 7days THEN moxifloxacin 400mg daily x 7days

Syphilis



Ocular syphilis

- Usually early but can occur at any stage with panuveitis, retinal vasculitis, cranial nerve II-VI dysfunction
- May or may *not* involve the CSF but is treated the same
  - Isolated ocular symptoms confirmed on exam + reactive serology → TREAT
  - CSF may be helpful if exam is normal



Otosyphilis

- Isolated auditory abnormalities + reactive serology → TREAT
  - CSF is almost always normal

TREATMENT = aqueous penicillin G 18-24million units per day for 10-14 days

CDC 2021 STI Treatment Guidelines

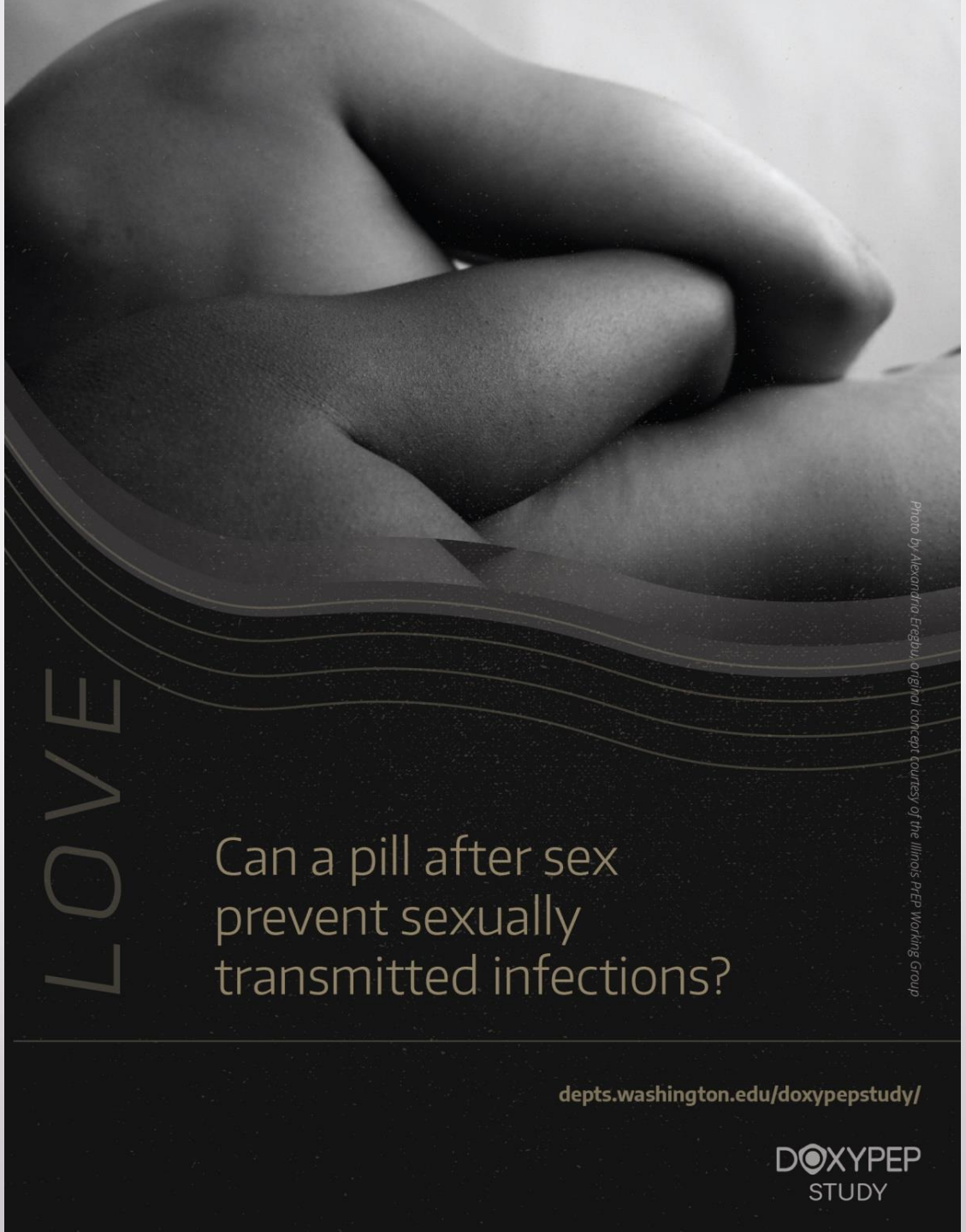
- What else is new?
  - Inclusivity:
    - Language around diagnosis = STD → STI
    - 5Ps: ***p***artners, ***p***ractices, ***p***rotection, ***p***ast history, ***p***regnancy (intention and prevention)
    - Updated testing recommendations based on current anatomy and gender of sex partners

CDC 2021 STI Treatment Guidelines

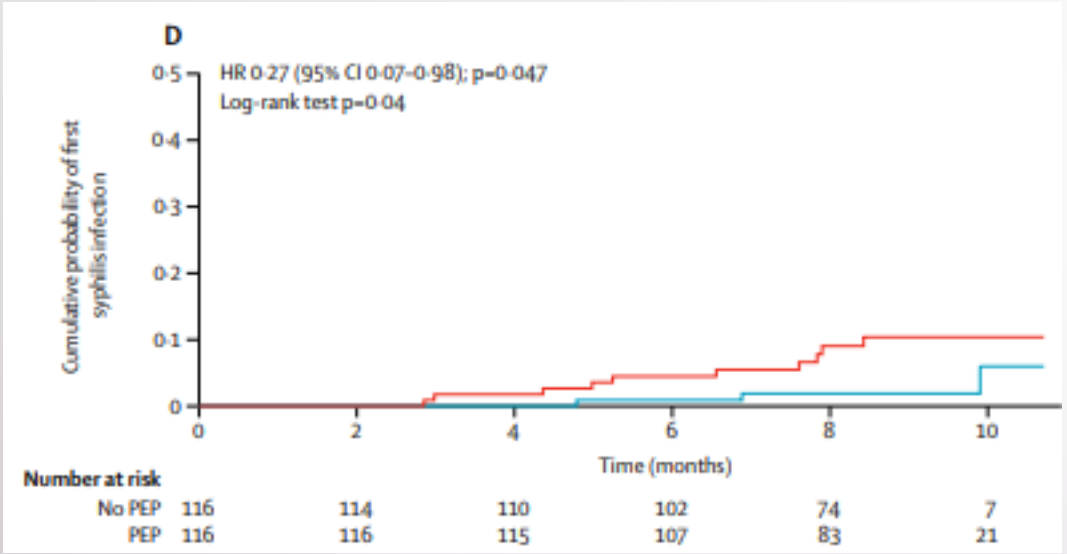
- What else is new?
  - Expedited partner therapy (EPT)
    - Chlamydia – doxycycline only (100mg orally BID x 7days)
    - Gonorrhea – cefixime 800mg PO x 1 (add doxy if chlamydia cannot be excluded)
    - More permissive for MSM
      - *"In light of limited data and the potential for inadequate treatment of bacterial STI in MSM partners, shared clinical decision-making regarding EPT is recommended".*
  - Metronidazole recommended in all cases of PID
  - More frequent syphilis screening during pregnancy

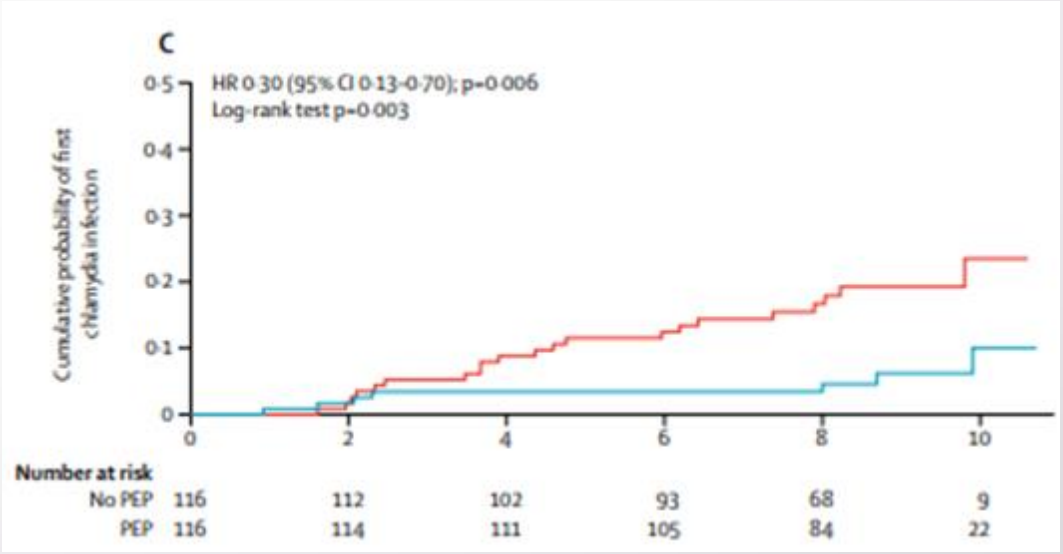
CDC 2021 Treatment Guidelines Webinar

- Video https://www.youtube.com/watch?v=azXn_Bv_R7Y
- Q&A www.cdc.gov/std/treatment-guidelines/qa.htm


LOVE
Can a pill after sex prevent sexually transmitted infections?
Photo by Alexandria Eregbu, original concept courtesy of the Illinois PrEP Working Group
depts.washington.edu/doxypepstudy/
DOXYPEP
STUDY

STI Prevention with doxycycline





Molina et al Lancet 2018;18(3): 308-317

OFF LABEL

Intervention: Open label doxycycline 200mg taken as PEP within 72 hours after condomless sexual contact

Maximum of 200 mg every 24 hours

Inclusion Criteria:

- Male sex at birth
- With HIV or on PrEP
- ≥1 STI in last 12months
- Condomless sex with ≥1 male partner in last 12months

STI Testing: Quarterly 3 site GC/CT tests + RPR

* GC culture before treatment

Sites: San Francisco, Seattle

OFF LABEL

Primary Endpoints

- At least 1 incident STI (GC/CT/syphilis) during a follow-up quarter
  - All STI endpoints were adjudicated by a blinded committee
- Power: 80% power to detect a decrease in quarterly STI prevalence from 10% → 5%
  - Powered separately for PrEP and PLWH cohorts

OFF LABEL

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5/13/22 scheduled interim analysis → recommended STOPPING enrollment due to significant effectiveness in both cohorts

OFF LABEL

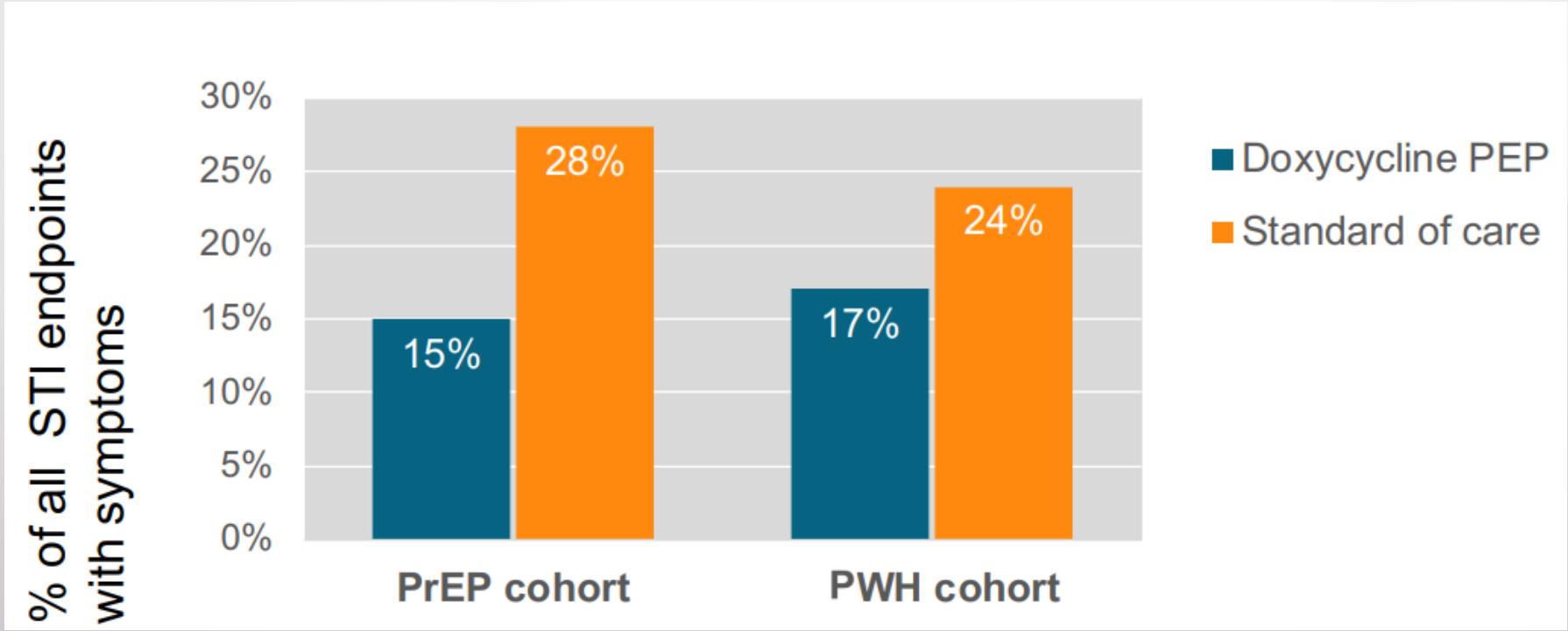
Primary Endpoint: STI Incidence per quarter

	HIV uninfected MSM/TGW on PrEP		MSM/TGW living with HIV		Total	
	Doxy arm N=240	Control arm N=120	Doxy arm N=134	Control arm N=60	Doxy Arm N=374	Control arm N=180
Follow up quarters	491	220	266	108	757	328
Participants with an incident STI (GC, CT or syphilis)	41	42	24	18	65	60
Primary STI endpoints	47 (9.6%)	65 (29.5%)	31 (11.7%)	30 (27.8%)	78 (10.3%)	95 (29.0%)
Gonorrhea	40 (8.1%)	45 (20.5%)	21 (7.9%)	20 (18.5%)	61 (8.1%)	65 (19.8%)
Chlamydia	7 (1.4%)	23 (10.5%)	12 (4.5%)	16 (14.8%)	19 (2.5%)	39 (11.9%)
Syphillis	1 (0.2%)	5 (2.3%)	3 (1.1%)	2 (1.9%)	4 (0.5%)	7 (2.1%)

https://programme.aids2022.org/abstract/abstract/?abstractid=13231

OFF LABEL

STI endpoints with symptoms reported at diagnosis



Graphic courtesy of Dr. Connie Celum, MD MPH

MWAETC

OFF LABEL

What now?

Data was presented at the 2022 International AIDS Conference with the following CDC response:

> "The first look at the data presented at the 2022 International AIDS Conference showed doxy-PEP *demonstrated significant effectiveness and tolerability* against these common STIs in gay and bisexual men and transgender women with HIV or taking HIV pre-exposure prophylaxis (PrEP) over the course of this study. The findings indicate *this approach has the potential to be an additional option* to prevent these bacterial STIs among some individuals at substantial risk for repeated STI acquisition. We look forward to seeing additional data from the study to evaluate the potential individual and public health risks of doxy-PEP.
>
> … We must move quickly to implement powerful STI prevention strategies. And it is our public health imperative to develop responsible guidance, based on a careful consideration of all available data and public health risks and benefits – we cannot take short cuts when it comes to people's health.
>
> *In the coming months, CDC in collaboration with trial investigators and other partners, will be reviewing the data, both to develop interim clinical guidance, as well as to outline key additional research questions moving forward*."

OFF LABEL

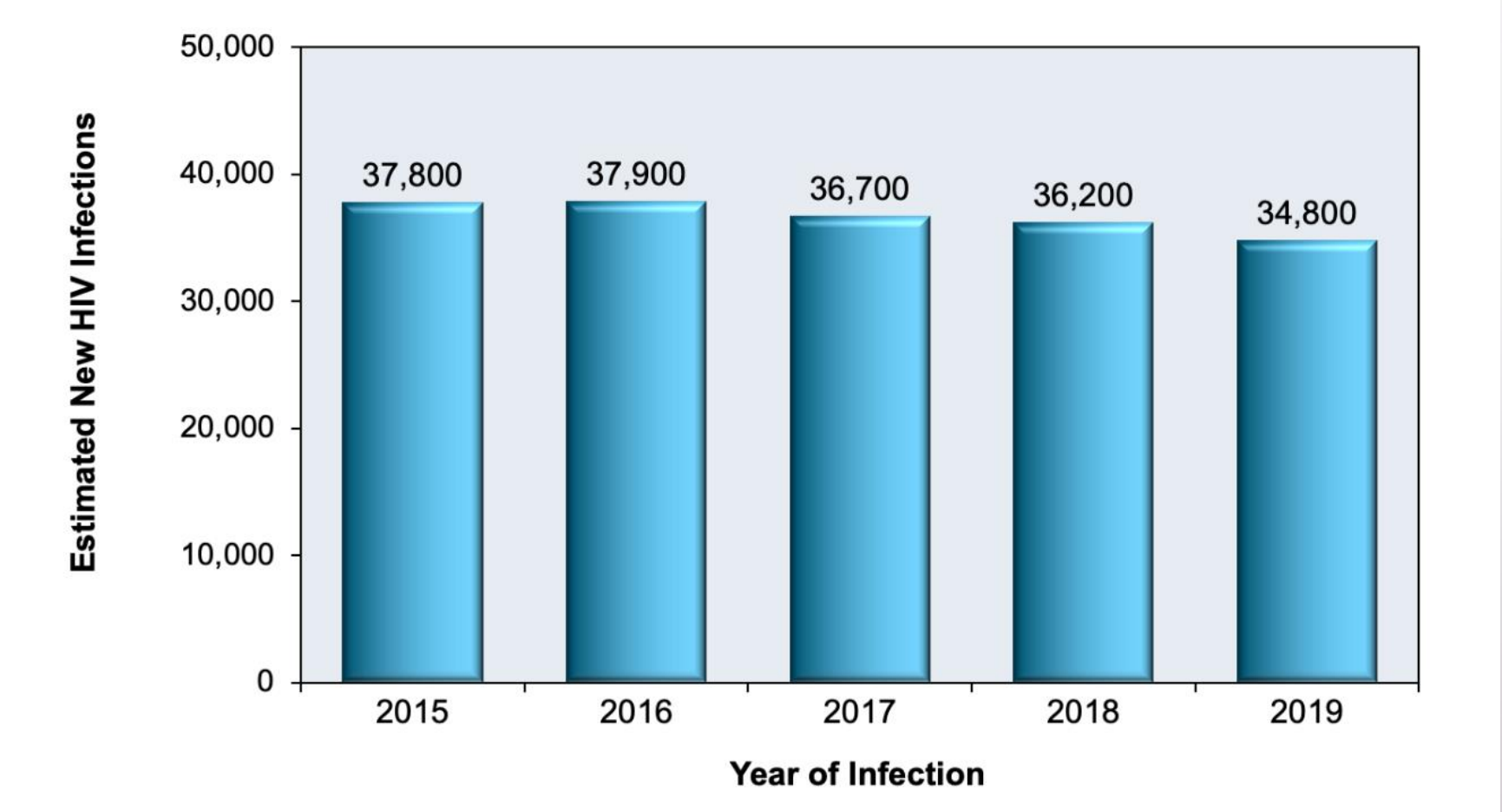
Doxy-PEP as an STI Prevention Strategy: Considerations for Individuals and Healthcare Providers of Gay or Bisexual Men or Transgender Women

As CDC and others work quickly to evaluate data to inform clinical guidance on the safe and effective use of doxycycline post-exposure prophylaxis (doxy-PEP) to prevent gonorrhea, chlamydia, and syphilis, we acknowledge there are individuals and clinicians who are already engaged in the off-label use of doxycycline as bacterial STI post-exposure prophylaxis or considering it. As such, we are providing the following considerations to inform those decisions:

- Current efficacy data only applies to gay and bisexual men and transgender women. Studies among heterosexual cis-gender women are ongoing.
- Doxycycline 200 mg administered within 24-72 hours of condomless sex was the regimen evaluated in this study. Other antibiotics should not be considered for PEP.
- In addition to informing patients about the potential STI prevention benefits of doxy-PEP, providers should also counsel patients about potential adverse side effects of doxycycline including phototoxicity, gastrointestinal symptoms, and more rarely esophageal ulceration.
- Providers should continue to screen, test, and treat for bacterial STIs in accordance with CDC's STI Treatment Guidelines and CDC's PrEP for the Prevention of HIV guidelines , even among people who may be using doxycycline as PEP or PrEP.


STOP AIDS
WORLD AIDS DAY
1 DECEMBER

Estimated HIV Incidence in the US 2015-2019



CDC HIV Surveillance Supplemental Report 2021;26(No. 1):1-81. Published May 2021.

Major PrEP Studies

- MSM and transgender women who have sex with men
  - **PROUD**: 544 patients → 86% relative risk reduction
  - **IPERGAY**: 400 patients →86% relative risk reduction
  - **iPrEX**: 2499 patients → 47% reduction
  - **DISCOVER**: Confirmed efficacy for TAF vs TDF
  - **HPTN-083**: cabotegravir found to be non-inferior to TDF-3TC
    - Oral = 39 new infections (1.22 per 100 person years)
    - Long acting IM = 13 new infections (0.41 per 100 person years)
- Cisgender heterosexual men and women
  - **Partners PrEP**: 4758 serodiscordant couples → 75% reduction in HIV acquisition
  - **TDF2**: 1219 patients → 62% reduction in HIV acquisition
- People who inject drugs (PWID)
  - **Bangkok TDF**: 2712 persons over 4.6years → 49% relative risk reduction, but 70% RRR in subgroup with detectable drug levels.

HIV PrEP (Pre-Exposure Prophylaxis)

A GRADE

- Risk assessment:
  - Men who have sex with men and 1 other risk factor
  - Heterosexually active men/women and 1 other risk factor
  - Persons who inject drugs and either
    - Shared use of drug injection equipment
    - Risk of sexual acquisition of HIV
  - Persons who engage in transactional sex, persons who are trafficked for sex work

HIV PrEP Options

FDA Approved:

- Daily oral medication
  - TDF-emtricitabine (Truvada)
  - TAF-emtricitabine (Descovy)
- Long acting injectable cabotegravir (Apretude; approved Dec 2021)

OFF LABEL

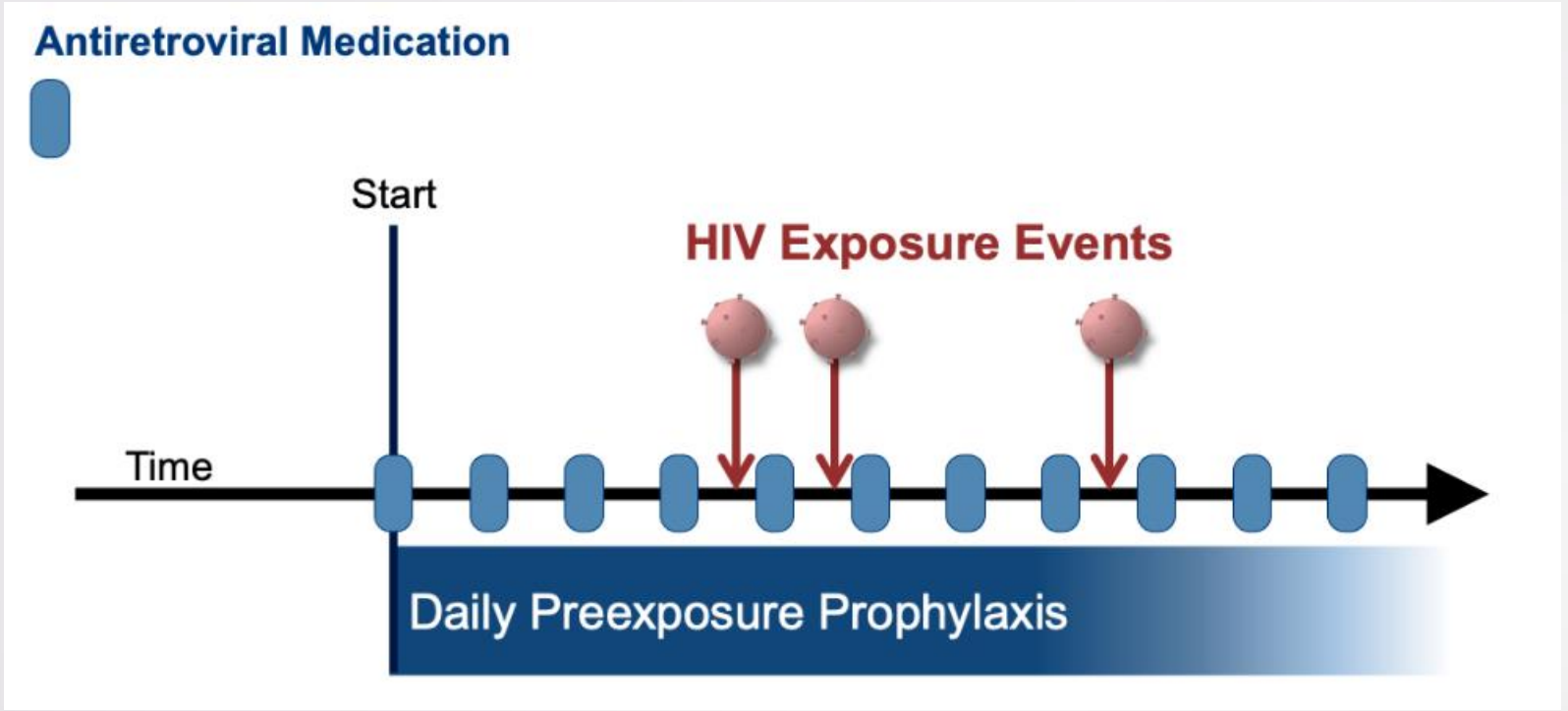
Off-label:

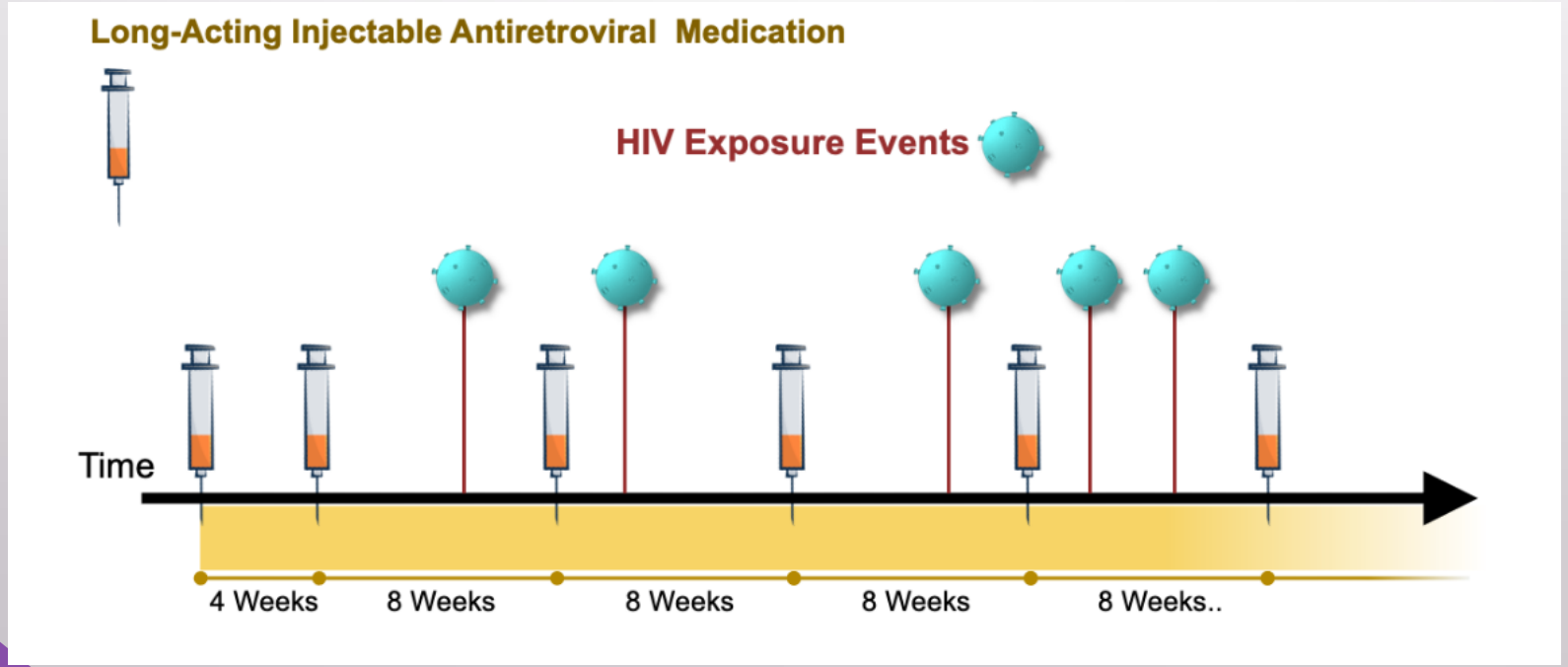
- 2-1-1 on demand dosing

Other long-acting options may be coming…

Long acting - lenacapavir, islatravir

Vaginal - dapivirine ring





Illustrations courtesy of Dr. David Spach

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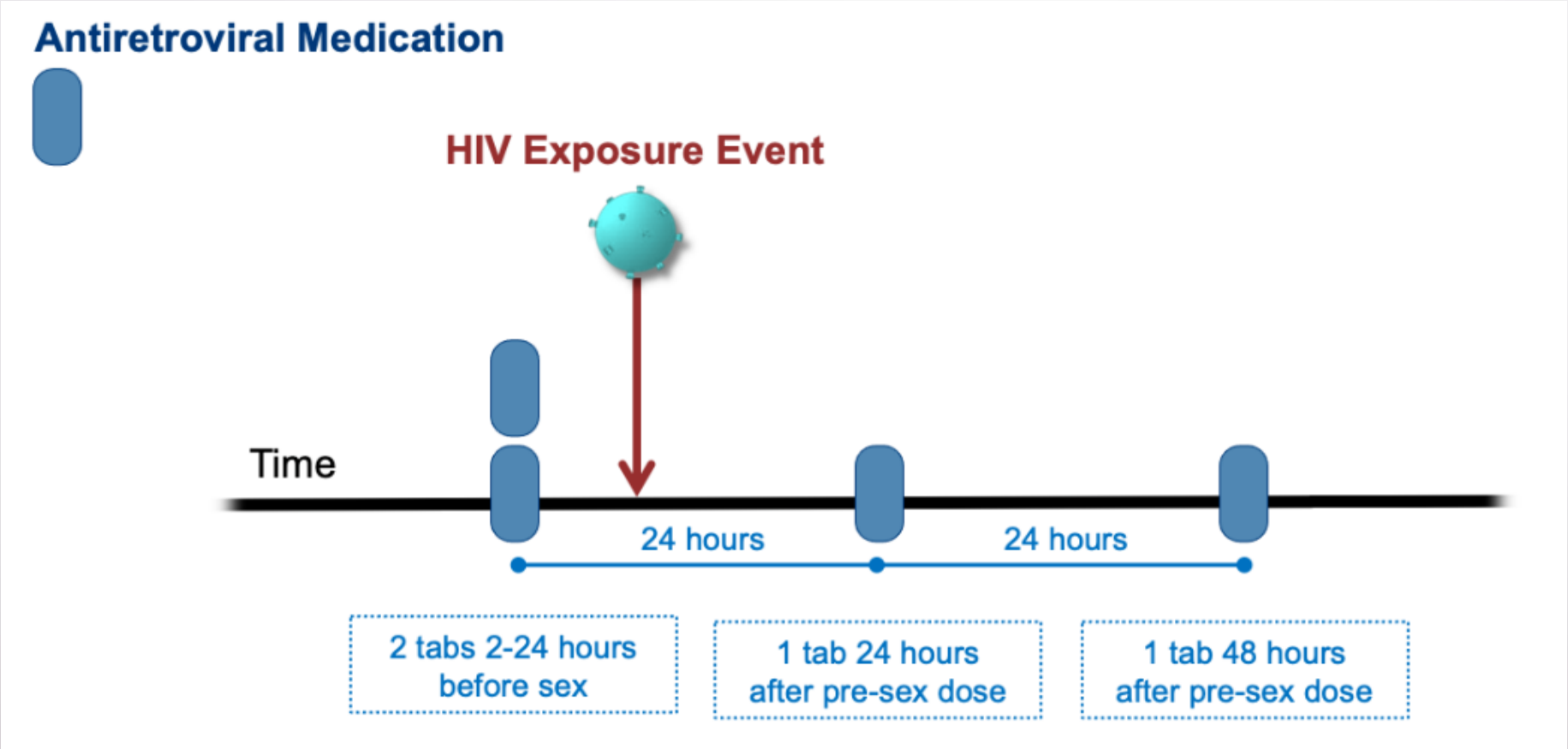


Illustrations courtesy of Dr. David Spach

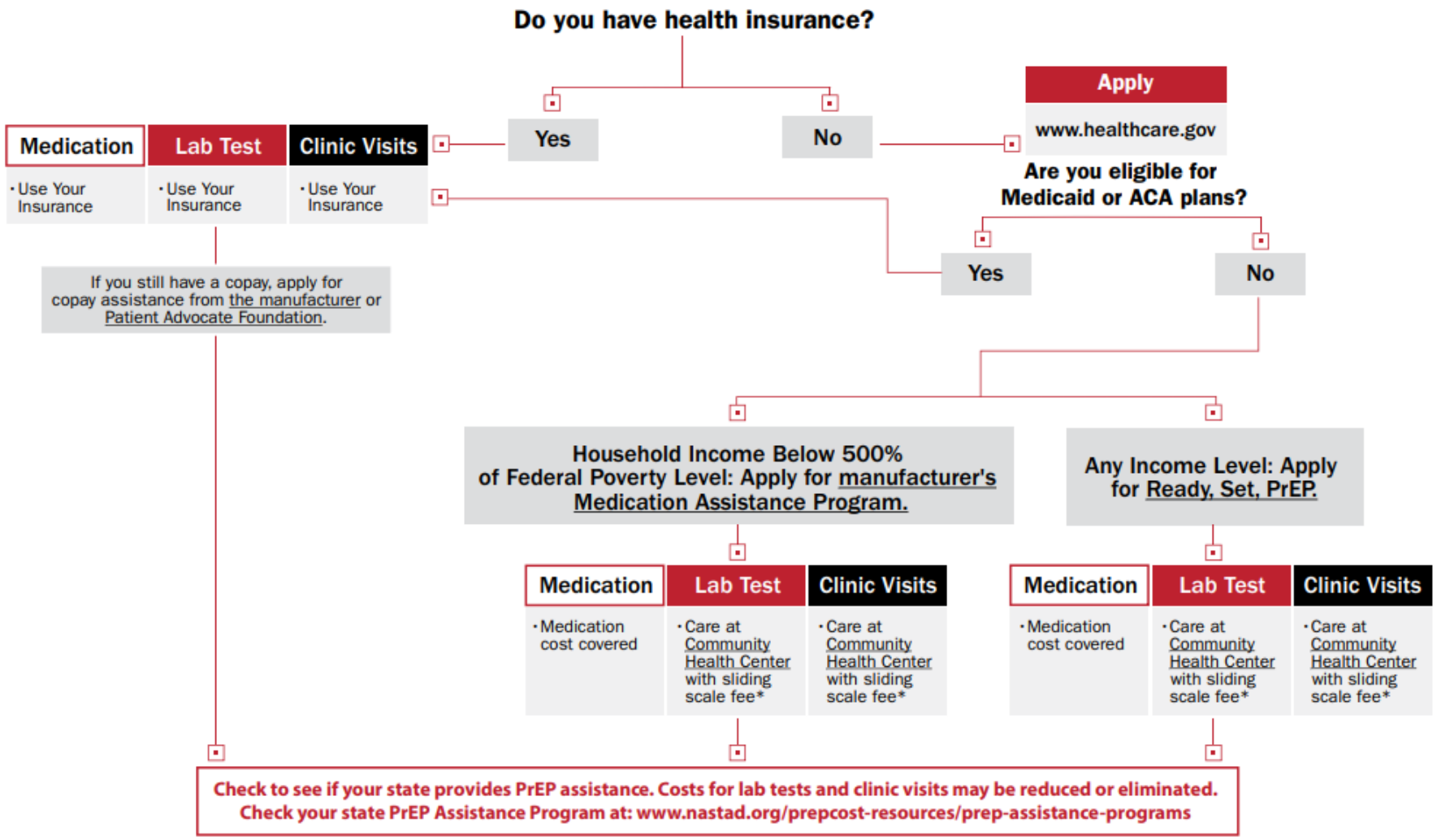
Access and coverage

Highly available and affordable on almost all insurance plans, but as of 2018 in Washington state only ~25% of people with an indication were prescribed PrEP.

- Under the ACA – PrEP must be free under almost all insurance plans
- PrEP DAP (Drug Assistance Program)
- WA-SB 5693 should provide open access starting Jan 1, 2023

  for all FDA approved HIV medications
  - All Washington Managed Medicaid and Fee for Service Plans

How do I Pay for Pre-Exposure Prophylaxis (PrEP)?



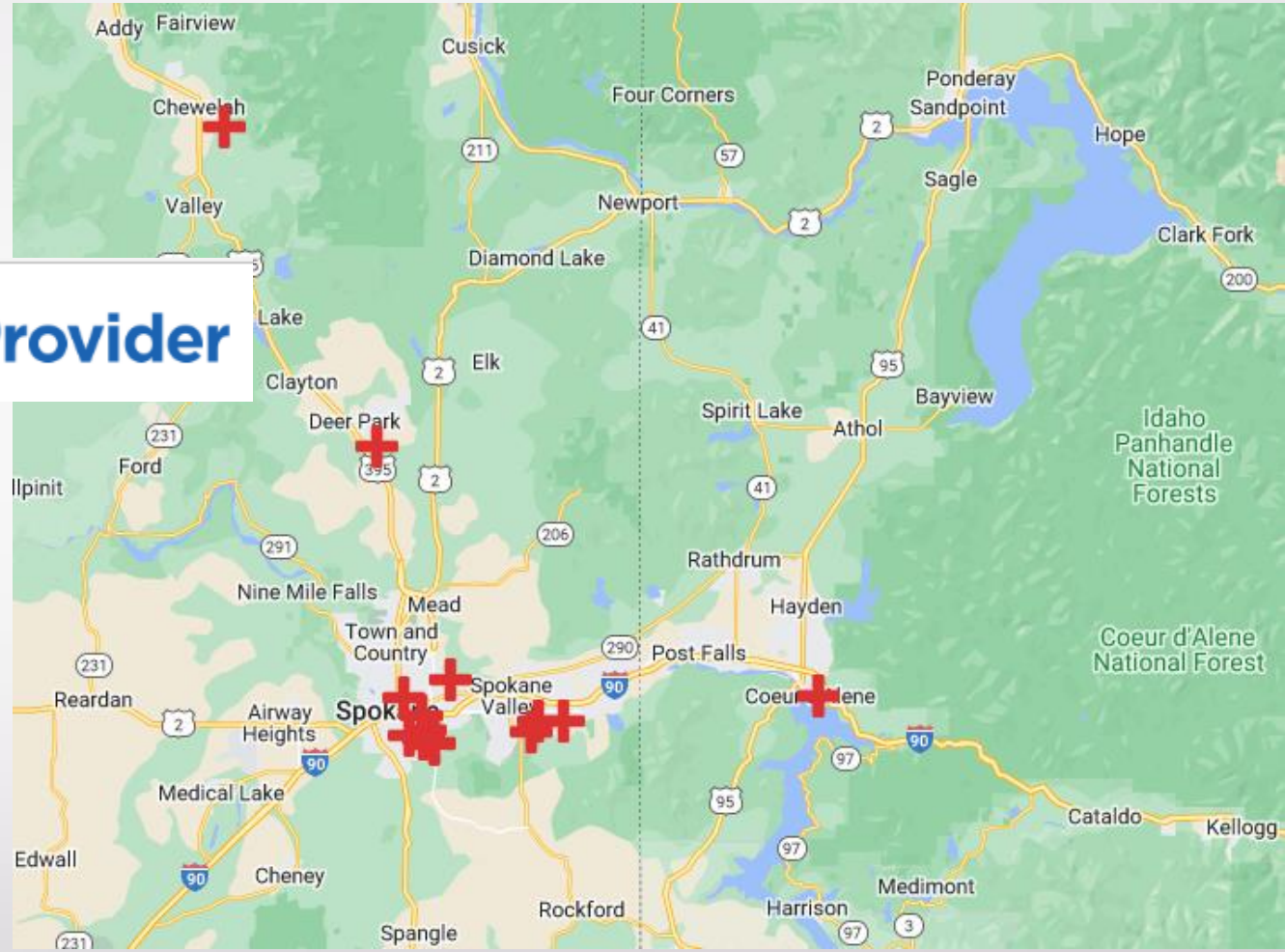
* To find a Community Health Center: findahealthcenter.hrsa.gov

CDC

LET'S STOP HIV TOGETHER

Ending the HIV Epidemic

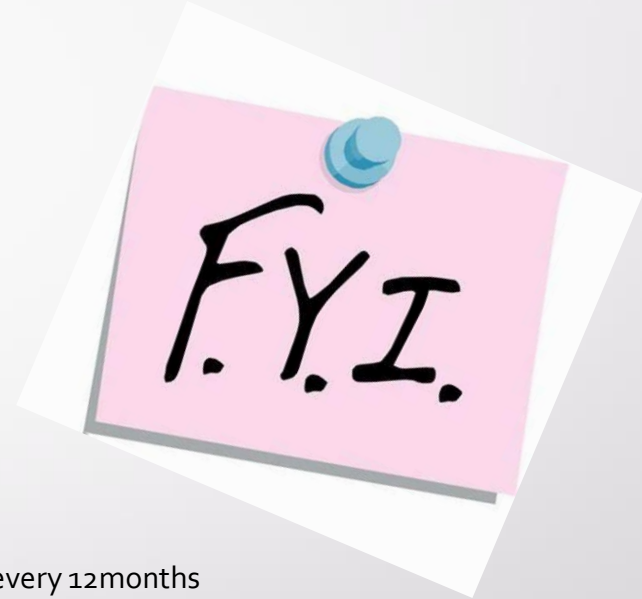
PrEP Locator **Find Your Provider**



Keith Harris – SRHD PrEP Coordinator
509-324-1438 kharris@srhd.org

Monitoring patients on PrEP

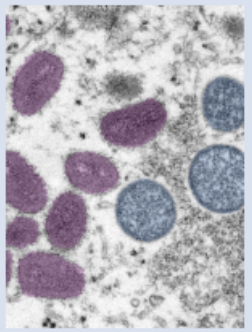
- HIV testing
  - Ab/Ag at baseline within 1 week and then every 2-3months
    - If starting cabotegravir – also need basline viral load
  - NEW recommendation for HIV viral load testing at each subsequent visit + Ab/Ag
- Renal function – at baseline for patients on oral medications then
  - If age <50 and baseline CrCl >90mL/min → every 12months
  - If age>50 or baseline CrCl <90mL/min → every 6months
- STI screenings - Baseline and
  - MSM/transgender women → quarterly screening for gonorrhea/chlamydia/syphilis
  - Heterosexual cisgender women and men → syphilis/gonorrhea every 6months and chlamydia every 12months
- Lipid panel – baseline for patients that will be on TAF-emtricitabine
- Pregnancy testing at least every 3months for anyone on PreP who could become pregnant
- Hepatitis B –
  - Screen all persons if unknown status – if nonimmune offer vaccination
  - Persons with active HepB can still received PreP but need close follow-up and evaluation upon discontinuation.
- Hepatitis C – baseline screening for all MSM, transgender women, PWID



mpox

- Spokane Regional Health District and the DOH are the experts in the most up to date trends and treatment/prevention.
- Email: **monkeypox@srhd.org**

Monkeypox is a rare disease caused by infection with the Monkeypox virus. Monkeypox was first identified in 1958 when two outbreaks of pox-like disease occurred in colonies of research monkeys. The source of monkeypox is unknown.



MONKEYPOX FAQ

NATIONAL INFORMATION

STATE INFORMATION

FOR HEALTHCARE PROVIDERS

VACCINATION CLINICS

Thank you!

Rachel Safran, MD FACP AAHIVS

rachel.safran@multicare.org