# The Importance of Integrating Doxy PEP into HIV Prevention and Treatment Services

## *THURSDAY, MAY 8, 2025*

*12:00 PM - 1:00 PM ET*

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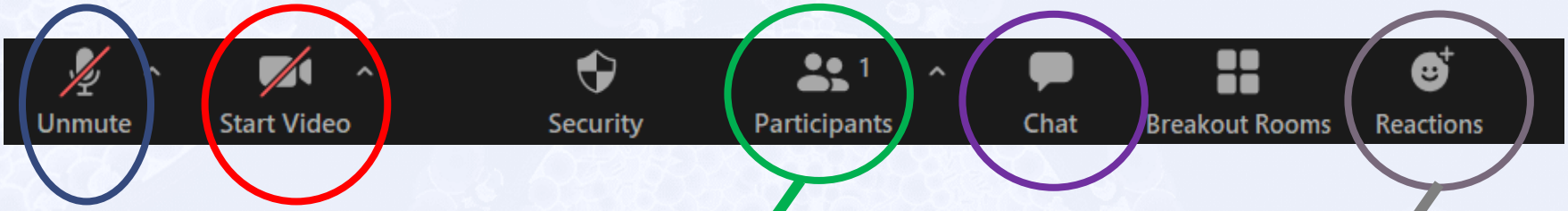


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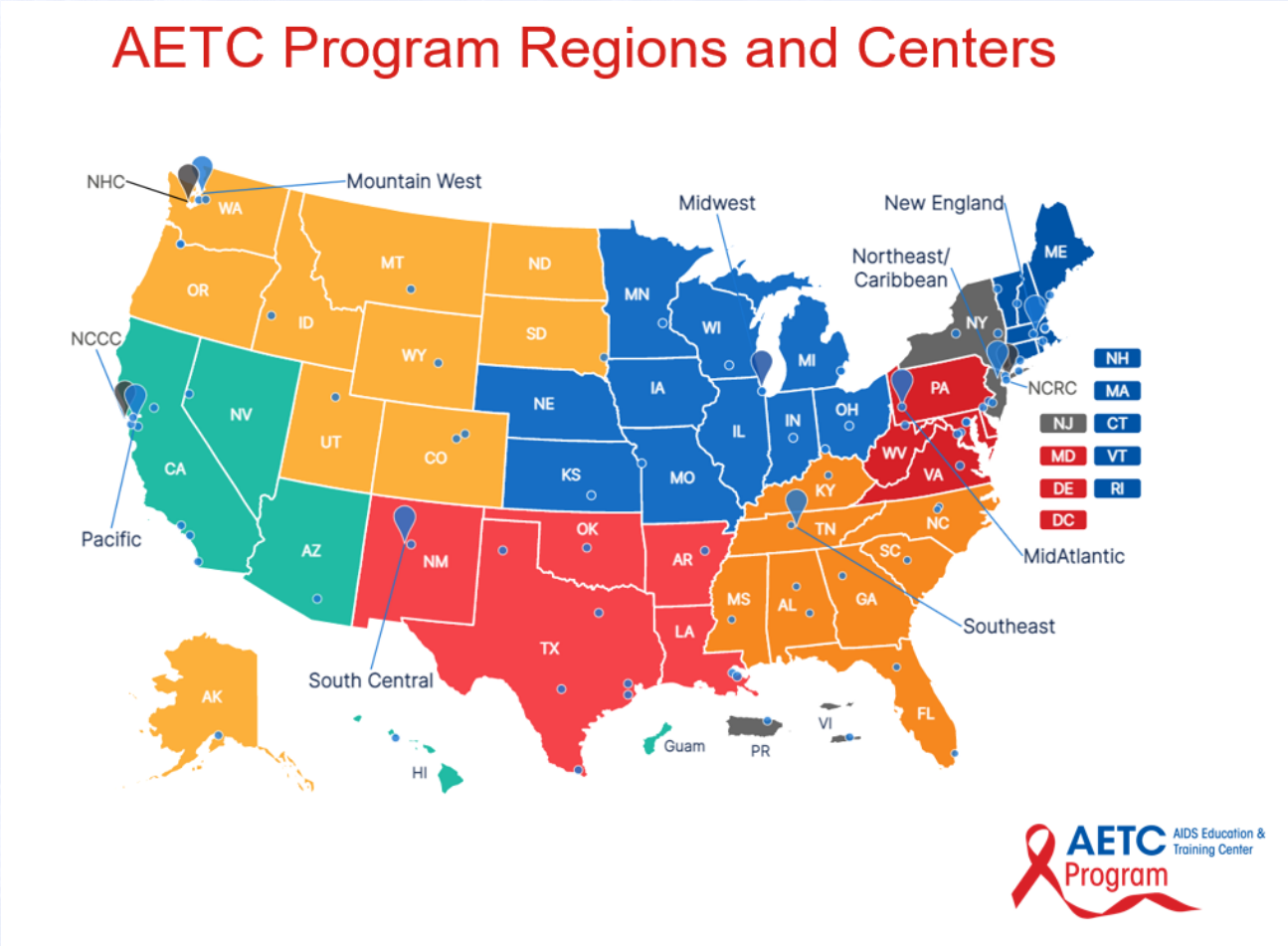
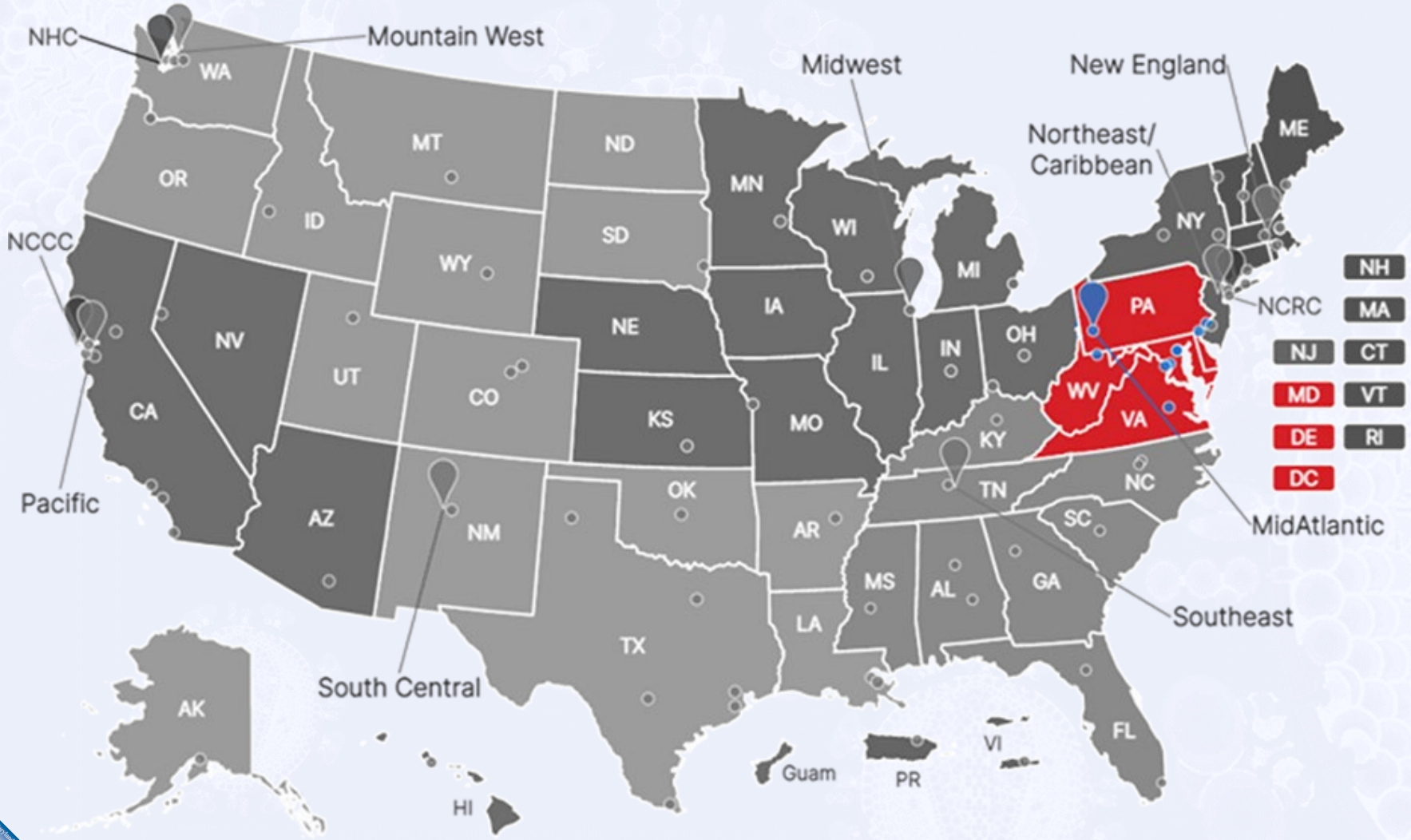
# Nationwide AETC Network



# MidAtlantic AIDS Education and Training Center



# AETC Program – National Centers and National HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web-based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
  - New HIV Clinical Tools app for Android and iPhone:
    - https://targethiv.org/news/hiv-care-tools-app-providers
- **National Clinician Consultation Center** – provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc.ucsf.edu
- **National HIV Curriculum** – provides ongoing, up-to-date HIV training and information for health professionals through a free, web-based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

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The staff and faculty involved with the planning of today's event **do not** have any conflicts of interest to disclose.

# Speaker Disclosure

Speaker has no conflicts of interest to disclose

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# The Importance of Integrating Doxy PEP into HIV Prevention and Treatment Services

May 8, 2025

**Travis Hunt, MD**

# Disclosures

- No conflicts of interest.

# Objectives

1. Describe the Doxy PEP protocols and best practices for patient education.
2. Review clinical trial findings supporting doxycycline as post-exposure STI prophylaxis.
3. Incorporate quality improvement measures to increase integration of STI and HIV prevention in their healthcare setting

# Outline

Background

1. Importance: Why Doxy PEP?

Data

2. Clinical Trial Efficacy Summary: HIV + HIV PrEP
3. Adjunctive Early Study Findings
4. Real-World Data After Local Implementation
5. Ongoing Research and Open Questions

Implementation

6. CDC 2024 National Guideline and Clinical Implementation Toolkit
7. Summary: Key Points to Remember

*Bonus (if time): Select CROI 2025 Abstracts of Interest*

Language and content of these slides reflect the primary evidence base that supports the current 2024 CDC doxy PEP guideline.

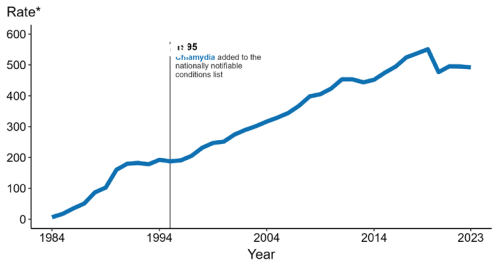
We will not dig into all of the data density, but the goal is to summarize so educators, clinical workers, and public health practitioners can understand the evolving trajectory of doxy PEP to the extent required to have initial risk-benefit discussions with stakeholders and program-builders.

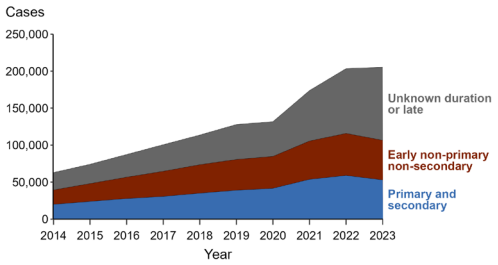
*Slides prepared April 25, 2025*

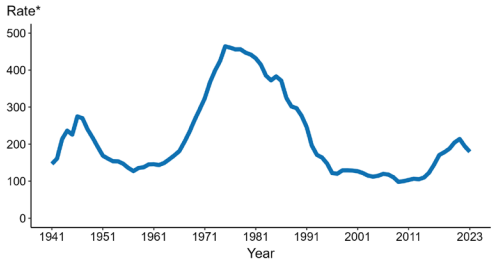
# Section 1
# Importance: Why Doxy PEP?

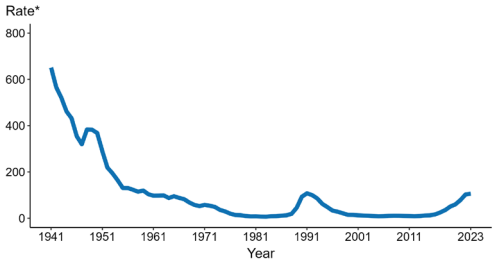
# State of the US STI Epidemic

Source: CDC STI Surveillance, 2023. Division of STD Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Centers for Disease Control and Prevention (CDC).



# History of VD prophylaxis

- By 1950s, PCN-PEP use decreased in US Navy due to emergent GC resistance
- Minocycline-PEP: 54% lower GC incidence; limited effectiveness due to induced TCN resistance

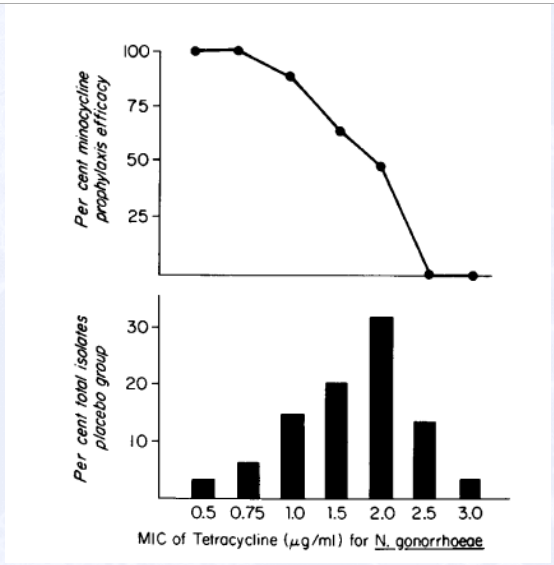
Although we are offering PEP to a new population, could the same issue happen again?

Harrison W ,et al. *NEJM* 1979

Table 1. Prophylactic Effect of 200 mg of Oral Minocycline.*

| Hours between Exposure & Prophylaxis | Placebo | Minocycline |
|---|---|---|
| < 6 | 9/135 (6.7) | 3/133 (2.3) |
| ≥ 6 to <12 | 20/277 (7.2) | 11/244 (4.5) |
| ≥12 to <18 | 13/86 (15.1) | 4/62 (6.5) |
| ≥18 | 15/67 (22.4) | 6/76 (7.9) |
| Total | 57/565 (10.1) | 24/515 (4.7) |

*No. infected/no. exposed, with percentages in parentheses.



# Repurposed intervention for STI prevention

- **Doxycycline post-exposure prophylaxis (doxy-PEP):** strategy of taking 200mg of doxycycline PO within 24-72 hrs after condomless sex to prevent bacterial STI
- Sex-positive, user-controlled tool for persons at increased risk for bacterial STI
- Safe, cheap, well tolerated, highly acceptable in RCT participants and real-world users


NCSD Doxy-PEP Social Media & Marketing Toolkit
Spinelli M, et al. *Sex Transm Dis* 2019

# Why doxycycline?

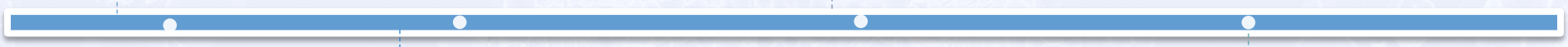
- 2nd generation tetracycline FDA approved in 1967; broadly active against bacteria and parasites
- Inexpensive, rapid absorption, crosses placenta/BBB, acceptable safety profile
- Wide clinical experience treating and preventing acne, chronic periodontitis, cholera, malaria, Lyme, leptospirosis, *Staph* infections, etc.
- STI world: syphilis, chlamydia, LGV, *Mycoplasma genitalium*, donovanosis (Klebsiella granulomatis)

# Section 2
# Clinical Trial Efficacy Summary: PLWHIV and Persons Taking PrEP

# Core 4 Efficacy Trials: HIV and HIV PrEP

**ARNS IPERGAY (France)**
47% RRR for CT & syphilis

**ARNS DOXYVAC (France)**
83% reduction in first episode CT & syphilis; 33% for first GC




**DoxyPEP (US)**
~66% RRR for all 3 bacterial STI in PWH & PrEP users

**dPEP Kenya (Kenya)**
RR for GC/CT reduction was not significant in cis women

***Timeline of major efficacy evidence supporting CDC guideline***

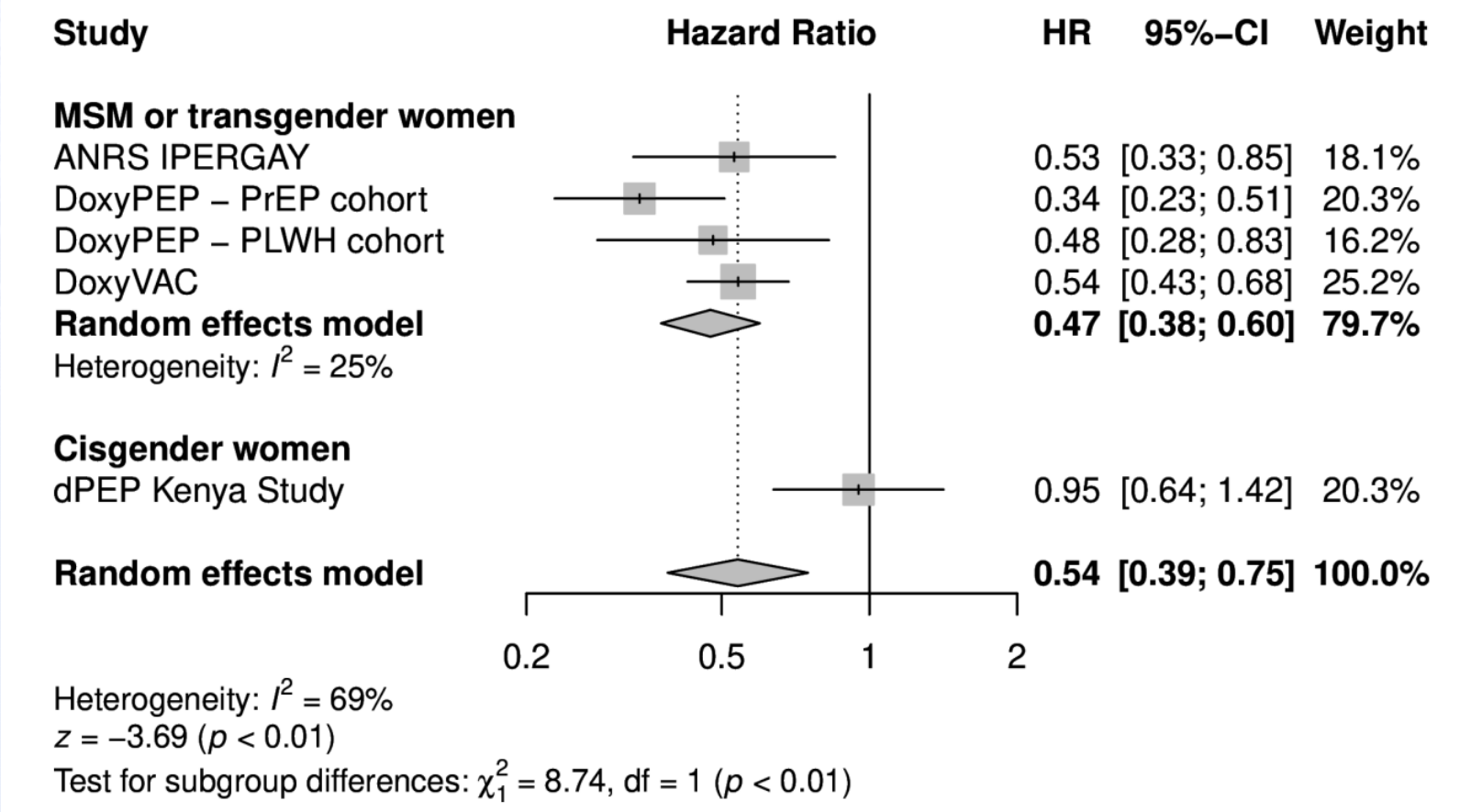
# Core 4 Efficacy Trials: HIV and HIV PrEP

| Study | Participating population | | STI rate or outcome | | Relative risk reduction | Absolute risk reduction |
|---|---|---|---|---|---|---|
| | | | Doxy-PEP | No doxy-PEP | | |
| **IPERGAY*** (France, 2015-2016) | 232 MSM on HIV PrEP | | 37.7 per 100 person-years | 69.7 per 100 person-years | 47%* (15-67%) | 32 per 100 person-years |
| **DoxyPEP** (Seattle & SF, 2020-2022) | 501 MSM & TGW with recent bact. STI | **PWH (n=174)** | 11.8% per quarter | 30.5% per quarter | 62% (40-76%) | 18.7% per quarter |
| | | **PrEP (n=327)** | 10.7% per quarter | 31.9% per quarter | 66% (54-76%) | 21.2% per quarter |
| **DOXYVAC*** (France, 2021-2022) | 545 MSM on HIV PrEP with recent bact. STI | | 8.8 per 100 person-years | 53.2 per 100 person-years | 83%* (74-88%) | 44 per 100 person-years |
| ***dPEP*** *(Kenya, 2020-2022)* | *449 cis women on HIV PrEP* | | *50 CT/GC infections total* | *59 CT/GC infections total* | *12% (P=0.51)* | *9 total infections at 12 months* |

*Point estimates are for CT & syphilis only

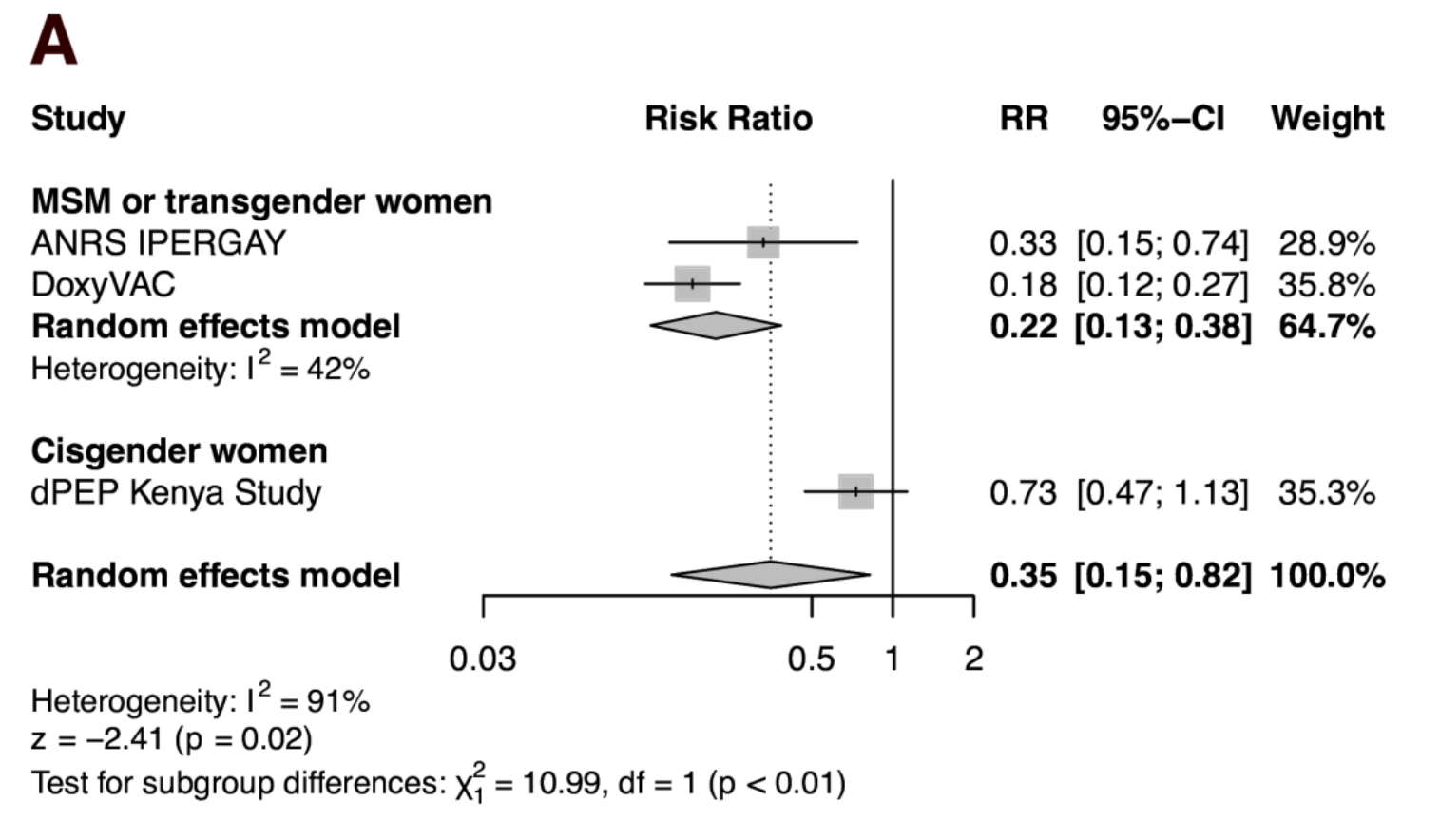
Molina JM et al, *Lancet Infect Dis* 2018; Luetkemeyer A et al, *NEJM* 2023; Molina JM, CROI 2023, Stewart J, CROI 2023; Molina JM et al, *Lancet Infect Dis* 2024
Updated from Cannon, presented at IAS 2023

# Meta-Analysis: Doxy PEP reduces overall STI risk by 46%



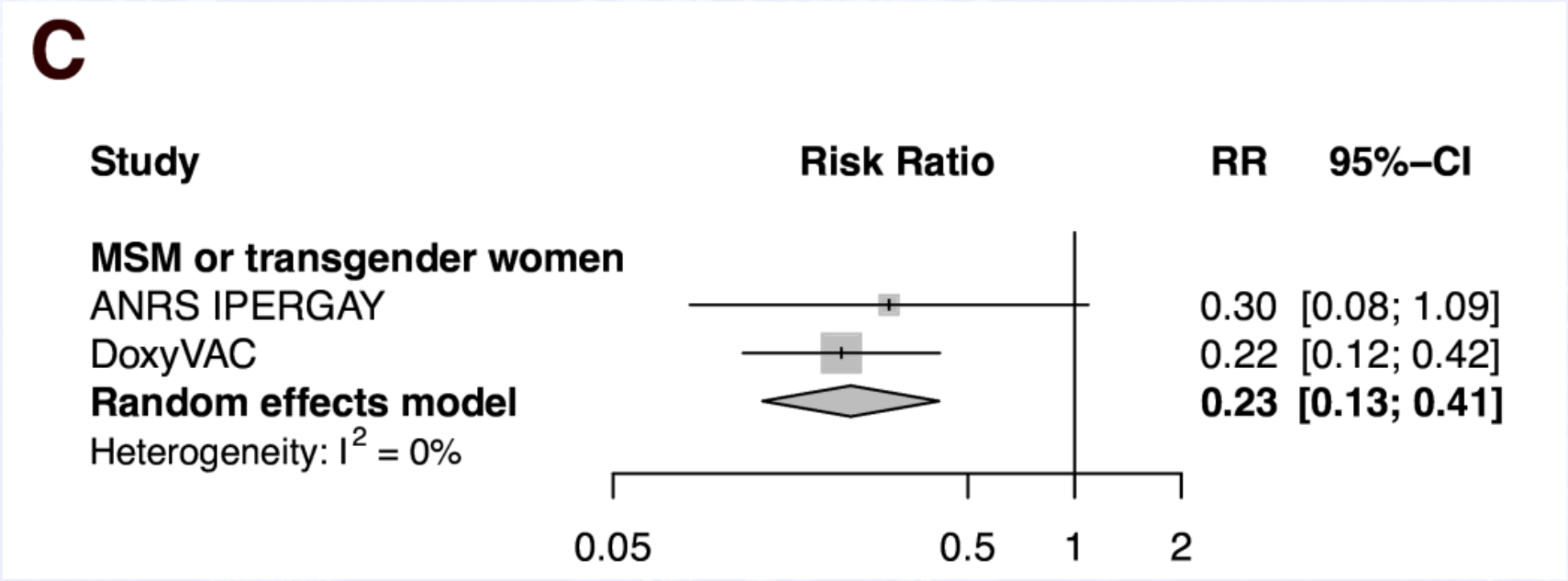

Sokoll PR et al, *Sex Transm Infect* 2024

# Meta-Analysis: Doxy PEP reduces chlamydia by 65%



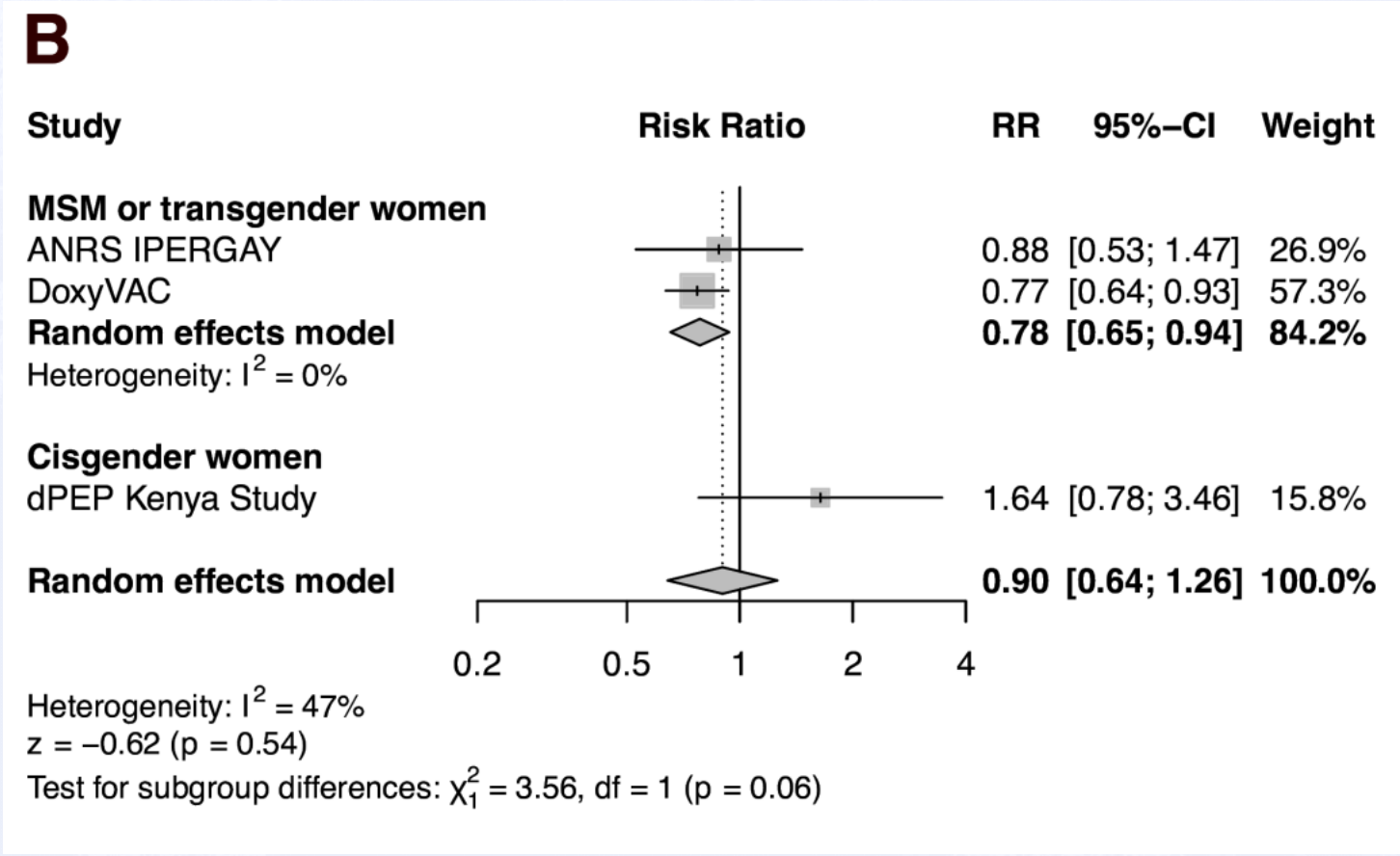

Sokoll PR et al, *Sex Transm Infect* 2024

# Meta-Analysis: Doxy PEP reduces syphilis by 77%




Sokoll PR et al, *Sex Transm Infect* 2024

# Meta-Analysis: Doxy PEP *may* reduce gonorrhea




Sokoll PR et al, *Sex Transm Infect* 2024

# Qualitative benefits of doxy PEP

*Emotionally…that confidence [due to doxy-PEP] counts for a lot in terms of my mood, and my positivity, and my…sex positivity…before, there would be this kind of cloud of shame come over [a sex act]. (Age 44, HIV-, Seattle)*

**Sex-positive and person-first intervention**

- Improved peace of mind & sexual pleasure
- Decreased stigma around STI diagnosis and disclosure
- Increased self-awareness about sexual behavior
- Facilitates communication with partners

Fredericksen, et al. *AIDS Patient Care STDs* 2024
Image: Pexels

# Adherence likely explains low efficacy in Kenyan women

**High Self-reported adherence**

**Quarterly surveys**

- 77% (579/755) coverage of last sexual exposure

**Timeline follow-back calendar**

- In 72.8% of the quarterly surveys, >80% of sexual acts were covered

**Weekly SMS**

- 64% (134/211) participants reported full coverage in at least 80% of weeks
- 78% of weekly SMS reported full coverage

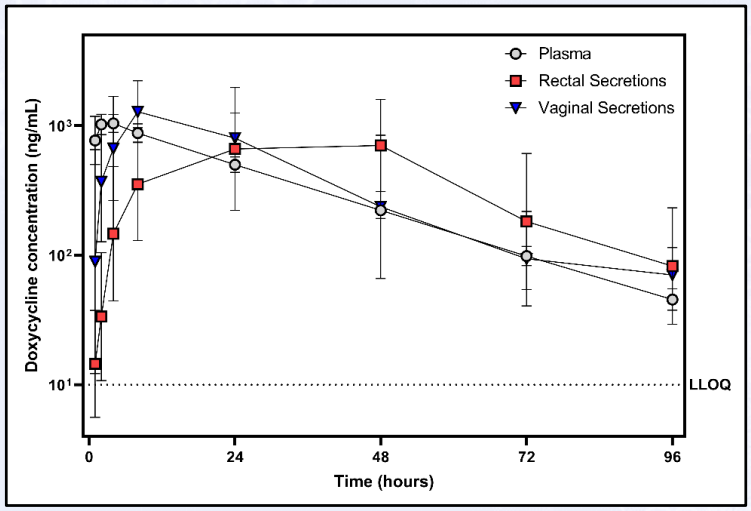
**Doxy Hair testing: 44% without doxy detected**

**Results:** Hair drug testing

- In a randomly selected subset of 50 participants assigned to doxycycline PEP
  - 56.0% (28/50) of participants had doxycycline detected at least once
  - 29.0% (58/200) of all quarterly visits had doxycycline detected,
    - 32.6% (58/178) when medication holds excluded
- 6.7% (3/45) of enrollment visits had doxycycline detected
- 5.1% (2/39) of follow up visits among SOC group had doxycycline detected

Stewart J, ISSTDR 2023

# Mucosal Doxycycline Concentrations




| | *C trachomatis* | | *T pallidum* | | *N gonorrhoeae* | |
|---|---|---|---|---|---|---|
| | $C_{max}$* | Time >4x MIC | $C_{max}$* | Time >4x MIC | $C_{max}$* | Time >4x MIC |
| Plasma | 16x | 44h | 10x | 32h | 4x | 3h |
| Rectal Secretions | 11x | 62h | 7x | 51h | 3x | NA |
| Vaginal Secretions | 20x | 45h | 12x | 38h | 5x | 11h |

*Fold above MIC

Minimum Inhibitory Concentrations (MIC):

*N gonorrhoeae* (NG) MIC = 250 ng/mL CDC Antimicrob Resist Susc Test

*T pallidum* (TP) $MIC_{90}$ = 100 ng/mL Edmondson *Antimicrob Agents Chemother* 2020

*C trachomatis* (CT) $MIC_{90}$ = 64 ng/mL Zheng *Sex Transm Dis* 2015

Haaland CROI 2023, abstract 118

# Section 3
# Adjunctive Early Study Findings

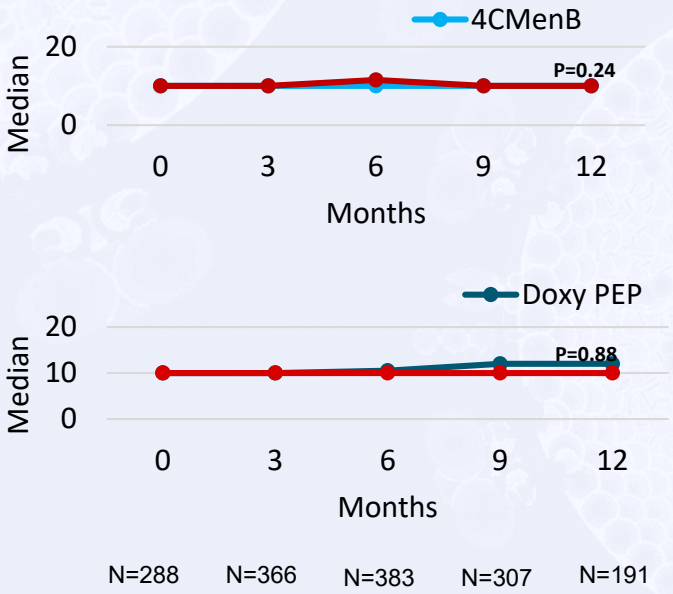
# Sexual behavior, adherence & antibiotic use

- Sexual behavior at enrollment:
  - Median of 9 sexual partners (IQR 4, 17) with 5 sexual acts per month (IQR 1.7, 10.7) and 90.1% of sex as condomless.
- No significant change in sexual behavior during follow-up in doxy PEP arm
- Adherence to doxy PEP:
  - 86% reported doxy PEP always/often after anal/vaginal sex
  - Median doxy PEP doses: 4.0 per month (IQR 1.0- 10.0)
  - 25% with ≥10 doses/month, based on quarterly interview
- Ceftriaxone use: 50% less in doxy PEP arm
  - Doxy PEP: 48.4 person-years vs SOC: 103.6 person years

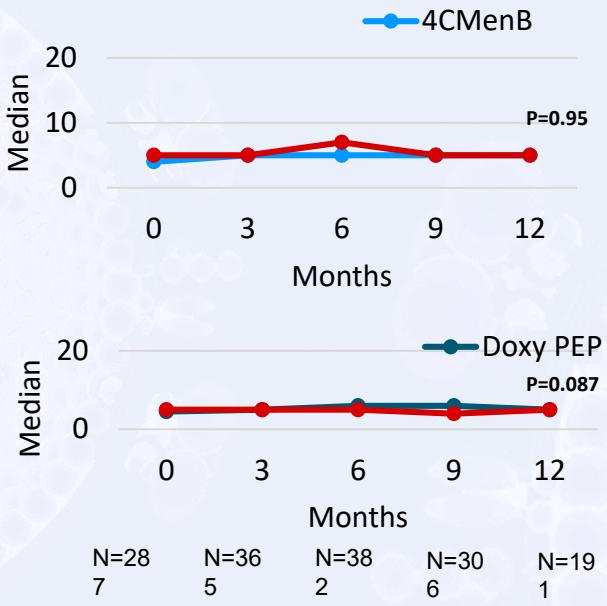
Luetkemeyer,AIDS 2022

# Sexual Behavior and Attitudes

**No. of sexual partners in prior 3 months**




**No. of condomless sex acts in prior 4 weeks**




Graphs: Molina et al DOXYVAC CROI 2023

Fredericksen et. al:

- Acceptable
- Participants felt more “control” in preventing STIs
- Most reported no change or brief initial change in sexual behavior

(AIDS PATIENT CARE AND STDS, 2024)

# Long term doxycycline use is safe

Systematic review from 1987-2022
10,106 people using doxycycline doses from 20-200 mg/day ranging from 8 weeks to >3 yrs

- Moderate AE (0-88%) and severe AE (0-14%) not always attributed to doxycycline
- GI effects common (n/v, abd. pain): 0-50%
- Derm. effects (rash): 0-38%
- Metabolic effects: no comprehensive studies, results vary. Weight gain paper retracted for ethical misconduct
- Microbiome effect: small, descriptive studies with limited data

**TABLE 2.** Relative Risk of Adverse Events Between Doxycycline and Placebo Arms of Randomized Controlled Trials

| Outcome | $\kappa$ | Relative Risk (95% CI) | $I^2$% | $P$ |
|---|---|---|---|---|
| Included RCT studies | | | | |
| Any AE | 9 | 1.03 (0.89–1.21) | 59.6 | 0.66 |
| Severe AE | 12 | 0.83 (0.59–1.16) | 2.20 | 0.28 |
| Neurological AE | 11 | 0.88 (0.73–1.05) | 0.90 | 0.15 |
| Gastrointestinal AE | 12 | 1.68 (1.19–2.38) | 72.2 | <0.01 |
| Dermatological AE | 9 | 3.55 (1.39–9.01) | 45.9 | 0.01 |
| Dropped due to AE | 18 | 1.62 (1.12–2.34) | 7.50 | 0.01 |
| 100- to 200-mg dosages | | | | |
| Any AE | 3 | 1.35 (0.69–2.64) | 74.7 | 0.38 |
| Severe AE | 6 | 0.94 (0.65–1.34) | 0.00 | 0.73 |
| Neurological AE | 5 | 0.99 (0.97–1.02) | 0.17 | 0.68 |
| Gastrointestinal AE | 6 | 1.78 (1.16–2.74) | 81.9 | 0.01 |
| Dermatological AE | 4 | 5.52 (1.75–17.42) | 68.3 | <0.01 |
| Dropped due to AE | 10 | 1.82 (1.06–3.11) | 20.9 | 0.03 |

$I^2$ variation across studies because of heterogeneity rather than chance.
AE indicates adverse event; $\kappa$, number of studies; RCT, randomized controlled trial.

Chan, et al. Sex Transm Dis 2023

# Low rate of adverse events in doxy PEP trials

| Randomized clinical trial | Laboratory abnormalities | Adverse events | Discontinuations | Other outcomes |
|---|---|---|---|---|
| **IPERGAY** | Grade 4 transaminitis due to acute hepatitis C infection (n = 3) | Drug-related gastrointestinal adverse events (n = 29); more common in PEP group ($P$ = .03) | 29 (26%) for all reasons; 8 (7%) due to drug-related adverse events | No difference between groups in serious adverse events |
| **DoxyPEP** | Grade 2 transaminitis (n = 1) | Grade 3 diarrhea or headache (n = 5) | 2% | No weight gain compared to standard of care |
| **DOXYVAC** | None as of July 2023 | Gastrointestinal adverse events (n = 2) | 3 (0.9%) due to gastro-intestinal adverse events or fear of adverse events | Further data pending final review |
| **dPEP (Kenya)** | Not collected | 7% (gastrointestinal side effects) | 5% | Social harms related to PEP use among 3 participants |

No serious AEs related to doxycycline in DoxyPEP, DOXYVAC, or dPEP trials

Cannon & Celum, Top Antivir Med 2023. Hazra, et al. Clin Infect Dis 2024.

# Section 4
# Real-World Data After Local Implementation

# Real-World Data from San Francisco: Two Studies

Study 1

Background:

- SF has a sexual health clinic targeting gender and sexual minorities in the Castro named “Magnet,” based at Strut. It is run by the SF AIDS foundation. Patient base is >8,000 and there are >3,000 patients on PrEP. It is one of the largest doxy PEP prescribers in SF.

Hypothesis:

- Observational data will show doxy PEP efficacy outside of ITT RCT setting.
- Methods/Design:
- Two-cohort retrospective cohort study of all active PrEP clients with observations in both pre- and post-doxy PEP rollout (6/2022 through 11/2022 and 12/2022 through 9/2023.

*H Scott, CROI 2024*

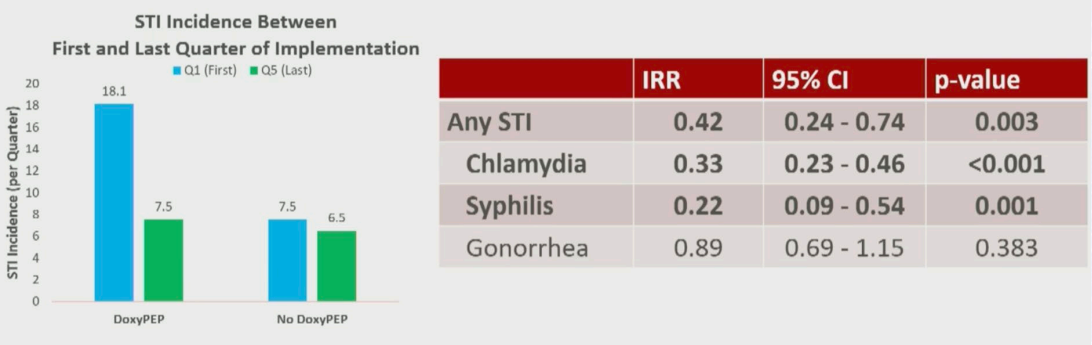
# Race/Ethnicity Data—Compare to RCTs

| Race /Ethnicity | Total PrEP Clients N=3,081 n | DoxyPEP Uptake n=1,209 % |
|---|---|---|
| American Indian or Alaska Native | 9 | 56% |
| Asian | 509 | 37% |
| Black or African American | 126 | 37% |
| Hispanic or Latinx | 723 | 43% |
| Multi-Racial | 408 | 41% |
| Native Hawaiian or Pacific Islander | 16 | 25% |
| White | 1,095 | 37% |
| Declined/Other/Unknown | 195 | 45% |

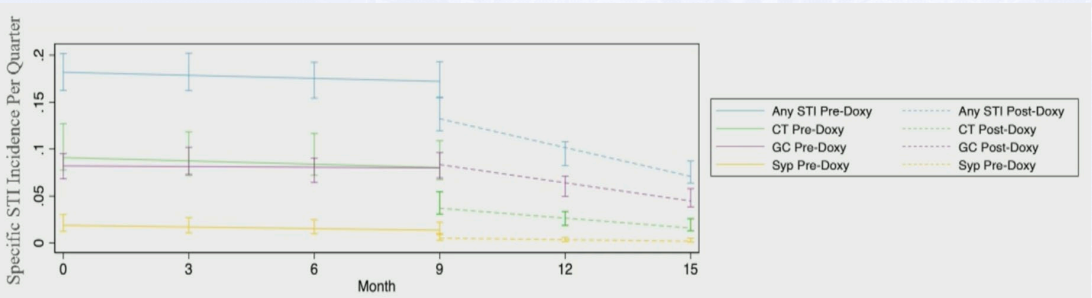
→More diverse population than original trials

*H Scott, CROI 2024*

# STI Incidence Per Quarter (Incidence Rate Ratios and Interrupted Time Series)




| | IRR | 95% CI | p-value |
|---|---|---|---|
| Any STI | 0.42 | 0.24 - 0.74 | 0.003 |
| Chlamydia | 0.33 | 0.23 - 0.46 | <0.001 |
| Syphilis | 0.22 | 0.09 - 0.54 | 0.001 |
| Gonorrhea | 0.89 | 0.69 - 1.15 | 0.383 |




ITS: Any STI: p=0.032; Chlamydia: p=0.021; Gonorrhea: p=0.003; Syphilis: p=0.360

GC impact only in ITS analysis!!

GC impact minimal and/or inconsistent across studies

*H Scott, CROI 2024*

# Study 2: Ecologic study from Public Health Surveillance Data

Background:

SF DPH release guidelines on doxy PEP suggest recommendation to MSM and TGW with bacterial STI or *condomless* anal/oral sex within last year. The SF DPH guideline offers the intervention to men and TGW without requirement of bacterial STI in last year who (a broader guidelines than most jurisdictions).

Hypothesis:

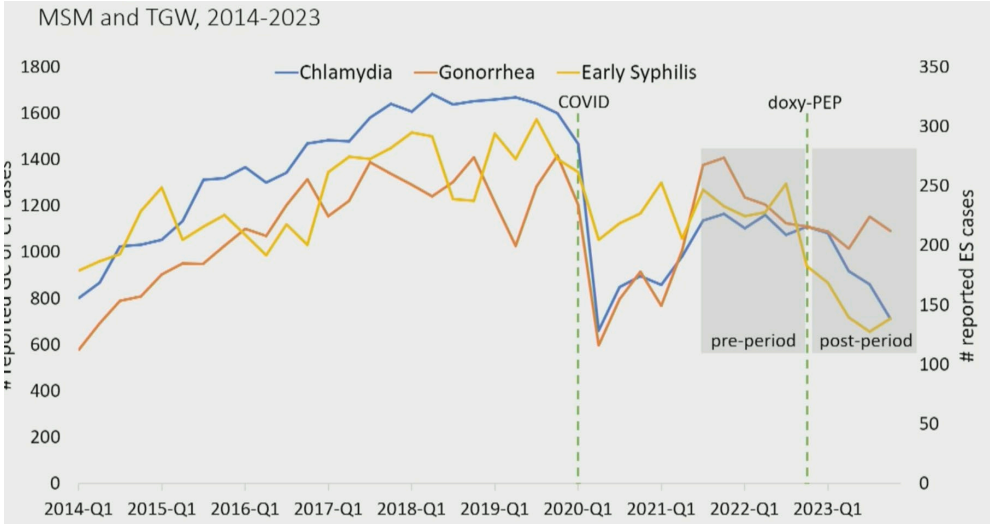
Doxy PEP has led to a decrease incidence of STIs in San Francisco.

Methods/Design:

Ecologic study of STI incidence from public health surveillance data in various demographics in SF using interrupted time series analysis (ITS) to compare pre- and post-doxy PEP rollout STI incidence (7/2021 to 10/2022 and 11/2022 to 11/2023, respectively). Autoregressive integrated moving average (ARIMA) to model post-period incidence in hypothetical absence of doxy PEP.

*Sankaran CROI 2024*

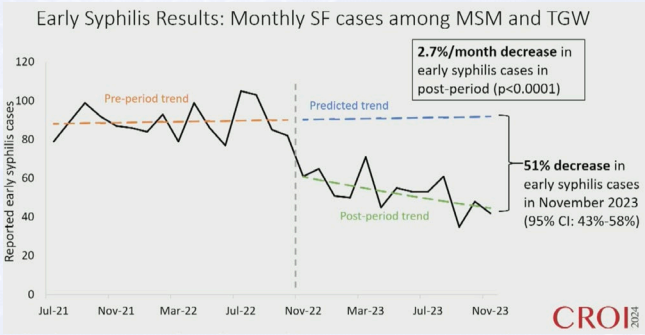
# STI Trends in San Francisco

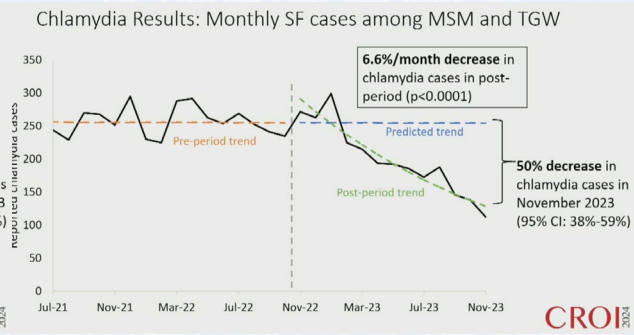


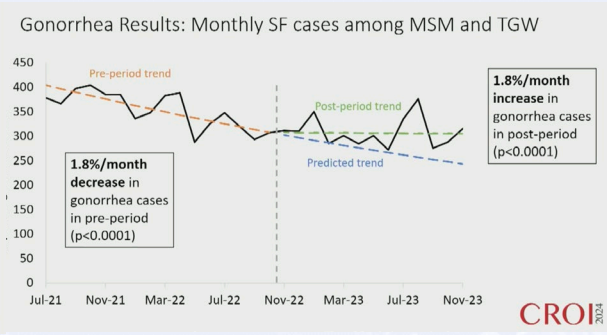

These are the city-wide surveillance data without statistical analysis

*Sankaran CROI 2024*

# Statistical Analysis of Ecological Data




Much of the syphilis decrease due to drop at time of period transition

Strong decrease

Not consistent with GC impact

*Sankaran CROI 2024*

# Observational Data Reflection

- Takeaways
  - Observational data support the implementation of doxy PEP
  - Intervention now supported by data more inclusive of racial/ethnic minorities
  - Will need to pay attention to GC efficacy
- Criticisms
  - Study 1
    - Discordance of incidence rate ratios and interrupted times series analysis is concerning
    - ITS suggests trend toward impact
    - Two modes of analysis invited opportunity for inflation of error (however, GC efficacy has failed in some trials, so difficult to assess likelihood of Type 2 Error)
  - Study 2
    - These are early data, so it will be interesting to see effect variation over time
    - Ecological studies cannot easily adjust for confounding
    - Public health surveillance data can lack granularity by design

# Section 5
# Evolving Research and Open Questions

# AMR questions (and some data)

- What level of tetracycline resistance in *Neisseria gonorrhoeae* will render doxy-PEP ineffective when used for prevention vs treatment?
- What will be the impact on bystander bacteria like *Staphylococcus aureus*, commensal Neisseria spp, gut microbiome?
- Could resistance develop in *T. pallidum* and *C. trachomatis*?

*Clinical Infectious Diseases*

MAJOR ARTICLE

Infectious Diseases Society of America

HIV Medicine Association

OXFORD

# Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in *Neisseria gonorrhoeae* and Colonization With Tetracycline-Resistant *Staphylococcus aureus* and Group A *Streptococcus*

Olusegun O. Soge,[1,2,3,4] Christina S. Thibault,[5] Chase A. Cannon,[2,4,5] Stephanie E. McLaughlin,[2,4] Tim W. Menza,[2,4,5] Julia C. Dombrowski,[2,4,5,6] Ferric C. Fang,[1,2,3] and Matthew R. Golden[2,4,5,6]

From the authors:

- 2312 MSM with NG, tetR was stable 2017 to quarter 1 (Q1) 2023 (mean = 27%) and thereafter rose to 70% in Q2 2024 ($P < .0001$). (King County released doxy PEP guidelines in Q2 2023.)
- NG with high-level (HL) tetR increased Q1 2021 to Q2 2024 (2% to 65%) ($P < .0001$).
- Taking >3 doses of doxy PEP/month was associated with both tetR and HL tetR ($P \leq .01$ for both),
- However, "*any*" use of doxy PEP was not associated with tetR or HL tetR.
- *S. aureus* colonization was less common among doxy PEP users than non-users (27% vs 36%, $P = .02$),
  - But, colonization with both tetracycline-resistant *S. aureus* and GAS were more common among doxy PEP users than non-users (18% vs 8%, $P < .0001$% and 9% vs 4%, $P = .008$, respectively).

# What are the implications if doxy PEP use increases *N. gonorrhoeae* TCN resistance?

TREATMENT: Will not impact gonorrhea therapy: doxycycline/tetracycline not used for treatment

OVERALL RESISTANCE: Could potentially drive resistance to other classes- data are mixed

OVERALL EFFICACY: may drop, with only contribution from chlamydia and syphilis?

Impact of high-level vs lower-level TCN resistance in GC could vary?

# Microbiome Data—Stay Tuned!

Version 1. Res Sq. Preprint. 2024 Apr 17.
doi: 10.21203/rs.3.rs-4243341/v1
PMCID: PMC11065088
PMID: 38699315

This is a preprint.

**It has not yet been peer reviewed by a journal.**

The National Library of Medicine is running a pilot to include preprints that result from research funded by NIH in PMC and PubMed.

## Doxycycline post-exposure prophylaxis for sexually transmitted infections impacts the gut antimicrobial resistome

Charles Langelier, Victoria Chu, Abigail Glascock, Deborah Donnell, Cole Grabow, Clare Brown, Ryan Ward, Christina Love, Katrina Kalantar, Stephanie Cohen, Chase Cannon, Michael Woodworth, Colleen Kelley, Connie Celum, and Anne Luetkemeyer

- RCT based on rectal swab at 0 and 6 months
- Posited resistance changes but not taxonomic changes
- Posited no change in bacterial stool burden
- Needs peer review still

# Potential doxy PEP impact on other STIs

## Chlamydia

- Doxy is now 1st line treatment for CT
- No clinical resistance to TCN class reported
- TCN resistance has been seen in *C. suis* (pig chlamydia) – could this be transferred to humans or acquired de novo?

## Syphilis

- Doxy is an alternative tx, used more when there's Bicillin shortage
- No clinical resistance to TCN class reported
- TCN resistance is with single point mutation
- Potential impact on syphilis serologies- delayed diagnosis or false negative?

## M. genitalium

- Doxy not very effective - poor cure rate as monotherapy, but part of two-step therapy for *M. genitalium*
- Substantial resistance to macrolides & fluoroquinolones
- Clinical *M. genitalium* resistance not yet described – clinical impact?

Slide courtesy of Stephanie Cohen

Dugan 2004 AAC, Stamm AAC 2010

# Who *should be using* doxy PEP for syphilis?

- How do we effectively reach Black, Latino, Native and other GBMSM & TGW of color?
- Can we better understand why people decline to use doxy PEP?
- Messaging strategies to increase uptake in young people (age <30)
- Focus on potential for reducing CS rates
  - Men who have sex with women
  - Partners of people who can become pregnant
  - Women with a history of bacterial STI, especially syphilis
  - Female sex workers?

Source: Cannon, IDWeek 2024

# Ongoing doxy PEP research and implementation

Worth noting new efforts from other countries:



- **Syphilaxis:** Ongoing study in Australia testing efficacy of doxy-P(r)EP and reasons for choosing/not choosing to use either strategy

- **DISCO** (**D**oxycycline as an **I**ntervention for bacterial **S**TI **C**hem**O**prophylaxis): Prospective, multicenter, open-label trial to examine acceptability, tolerability, safety of doxy-P(r)EP

*Clinical Infectious Diseases*

VIEWPOINTS

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

# Evidence-Informed Provision of Doxycycline Postexposure Prophylaxis for Prevention of Bacterial Sexually Transmitted Infections

**Julia C. Dombrowski,[1,2,3] Deborah Donnell,[4] Cole Grabow,[5] Stephanie E. Cohen,[6,7] Chase A. Cannon,[1,3] Clare E. Brown,[5] Susan P. Buchbinder,[6,7] Connie Celum,[1,2,5] and Anne F. Luetkemeyer[6,8]**

Question: Can STI screening frequency be reduced for persons on doxy PEP?

Answer: Screening at 6-month → delayed diagnosis of 22.6 asymptomatic STIs per 100 person-years on doxy PEP (nearly half)

Although syphilis incidence was low in the Doxy-PEP study, the potential health consequences of diagnosis are severe

Decreasing the frequency of syphilis screening could exacerbate the challenge of diagnosing syphilis among patients taking intermittent doxycycline, which likely affects rapid plasma reagin titers.

# Other Remaining/Evolving Unknowns

- How well does one need to take doxy PEP to be protected?
- How will intermittent doxycycline use impact our ability to diagnose syphilis?
- Efficacy & risk/benefit of using doxy PEP in MSW?
- Would another study of doxy PEP in women be useful?
- Could resistance develop in *T. pallidum* and *C. trachomatis*? Some evidence of resistance in pigs with *C. suis* (human transfer)?

# Section 6
# CDC 2024 Guideline and Clinical Implementation Toolkit

# CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024

*Recommendations and Reports* / June 6, 2024 / 73(2);1–8

**BOX 1. CDC recommendations for use of doxycycline as postexposure prophylaxis for bacterial sexually transmitted infections prevention**

Return

| Recommendation* | Strength of recommendation and quality of evidence† |
|---|---|
| • Providers should counsel all gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) with a history of at least one bacterial sexually transmitted infection (STI) (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months about the benefits and harms of using doxycycline (any formulation) 200 mg once within 72 hours (not to exceed 200 mg per 24 hours) of oral, vaginal, or anal sex and should offer doxycycline postexposure prophylaxis (doxy PEP) through shared decision-making. Ongoing need for doxy PEP should be assessed every 3–6 months. | AI<br>High-quality evidence supports this strong recommendation to counsel MSM and TGW and offer doxy PEP. |
| • No recommendation can be given at this time on the use of doxy PEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons. | Evidence is insufficient to assess the balance of benefits and harms of the use of doxy PEP |

*Although not directly assessed in the trials included in these guidelines, doxy PEP could be discussed with MSM and TGW who have not had a bacterial STI diagnosed during the previous year but will be participating in sexual activities that are known to increase likelihood of exposure to STIs.

# Dosing and Prescribing Guidance

- 200 mg of doxy taken ideally within 24 hours but no later than 72 hours after condomless oral, anal or vaginal sex.
- Take up to daily, depending on frequency of sexual activity, but no more than 200 mg within a 24-hour period.
- Immediate release 100 mg is fine; hyclate or monohydrate*
- Take with fluids and remain upright for 30 minutes after the dose. Taking with food may increase tolerability.
- Suggested: #30 tabs with 1 refill; may vary depending on frequency of sex and mutual agreement about need for monitoring

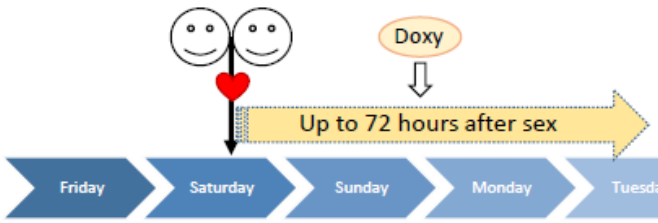
ICD-10 code: Z20 (Contact with and [suspected] exposure to infections with a predominantly sexual mode of transmission)

# *Doxy PEP – How to Take*

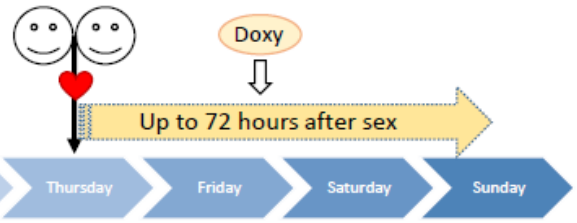
= sex without a condom, including oral sex

**Two 100mg pills of doxycycline ideally <u>within 24 hours</u> but no later than 72 hours after condomless sex**

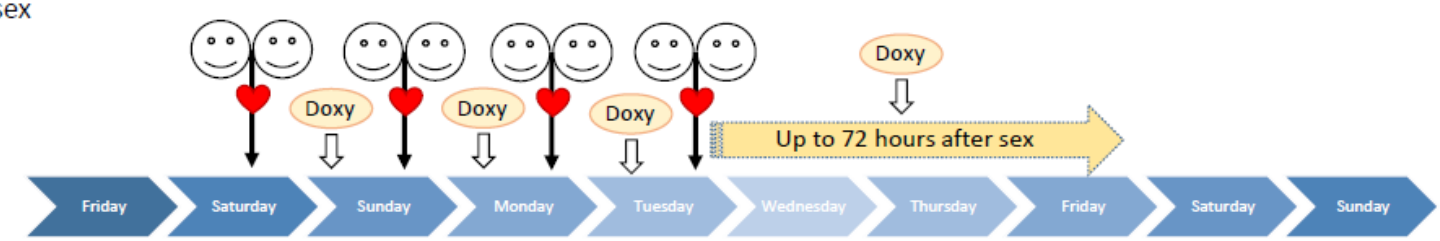
Example: Sex on Sat; take dose of doxy by Tues




Example: Sex on Thursday; take dose of doxy by Sunday




Example 2: Daily (or more) sex Sat-Tues; take daily dose of doxy and last dose within 24 hours *but not later than 72 hours* after last sex




***No more than* 200 mg every 24 hours**

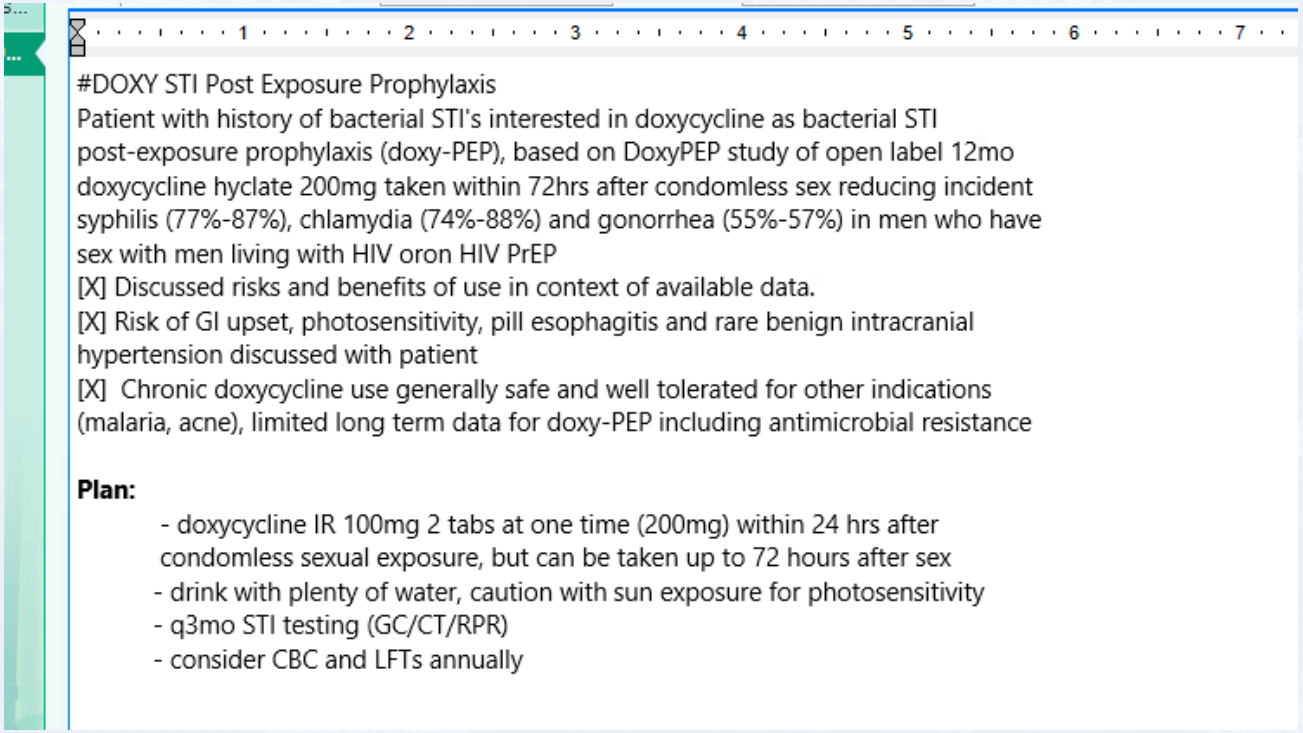
https://www.sfcityclinic.org/providers/guidelines/hiv-and-sti-prevention

# Initial and follow-up doxy PEP visit

| Initial Visit | Follow-Up Visits |
|---|---|
| **GC/CT (all sites), syphilis** | Same |
| **HIV** (per CDC HIV PrEP guidelines), or q 3-6 mos | Same |
| **Risk reduction counseling**: condoms, reducing partners, HIV PEP, PrEP or HIV treatment | Same |
| Counsel re: side effects: **Photosensitivity, esophagitis, GI intolerance**, potential for antibiotic resistance in other pathogen | **Assess side effects** |
| Counsel **no antacids or supplements** with Ca, Fe, Mg, or Na Bicarb within 2 hrs of dose | |
| Doxy may reduce efficacy of oral contraceptives, **use backup method** | |
| **Provide enough doses until next follow up visit** | **Reassess need for DPEP**, otherwise same as initial visit |

Slide courtesy of Ina Park
https://www.regulations.gov/document/CDC-2023-0080-0002

# .doxyPEP dot phase

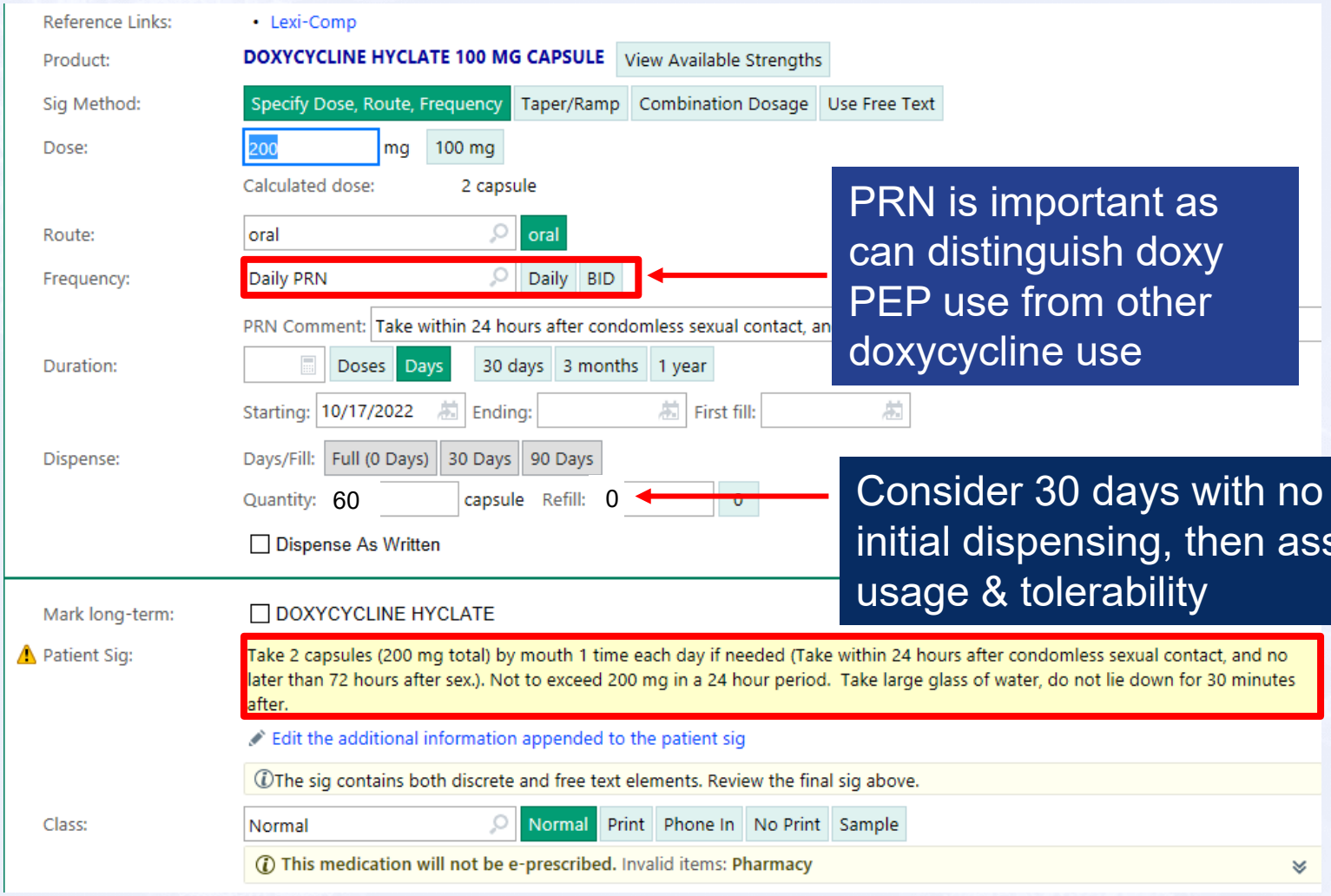


#DOXY STI Post Exposure Prophylaxis
Patient with history of bacterial STI's interested in doxycycline as bacterial STI post-exposure prophylaxis (doxy-PEP), based on DoxyPEP study of open label 12mo doxycycline hyclate 200mg taken within 72hrs after condomless sex reducing incident syphilis (77%-87%), chlamydia (74%-88%) and gonorrhea (55%-57%) in men who have sex with men living with HIV oron HIV PrEP
[X] Discussed risks and benefits of use in context of available data.
[X] Risk of GI upset, photosensitivity, pill esophagitis and rare benign intracranial hypertension discussed with patient
[X] Chronic doxycycline use generally safe and well tolerated for other indications (malaria, acne), limited long term data for doxy-PEP including antimicrobial resistance

**Plan:**

- doxycycline IR 100mg 2 tabs at one time (200mg) within 24 hrs after condomless sexual exposure, but can be taken up to 72 hours after sex
- drink with plenty of water, caution with sun exposure for photosensitivity
- q3mo STI testing (GC/CT/RPR)
- consider CBC and LFTs annually

- Sample doxy PEP phrase picture in EPIC
- Courtesy of Stephanie Cohen




PRN is important as can distinguish doxy PEP use from other doxycycline use

Consider 30 days with no refill for initial dispensing, then assess usage & tolerability

Doxy PEP specific instructions

Slide courtesy of Stephanie Cohen

# COST

- Doxycycline hyclate 100 mg tabs are very inexpensive
- Nonetheless: need to identify source of funds for uninsured patients

| Source | Cost/100 mg pill | Cost/month (taking 2 tabs daily) |
|---|---|---|
| 340b | 6¢ | $3.60 |
| GoodRx Coupon* | 8¢ | $5.00 |
| Discount online pharmacy | 23¢ | $13.80 |

*Requires redemption at specific pharmacy chain in your area

Slide courtesy of Stephanie Cohen

# Monitoring on doxy PEP

## Laboratory

- No serious lab abnormalities in DoxyPEP
- Package insert: LFTs, renal function & CBC checked “periodically” when taking doxycycline for a prolonged period
- Take home:
  - No baseline labs needed
  - Consider checking annually

Slide courtesy of Stephanie Cohen

## STIs

- Screen for STIs every 3-4 months
  - *Can we screen less frequently? May depend on patient factors*
- If diagnosed with an STI on doxy-PEP, treat according to the CDC STI treatment guidelines
- Consider no “epi-treatment” for GC & CT exposures

# Should asymptomatic STI contacts be empirically treated if taking doxy PEP?

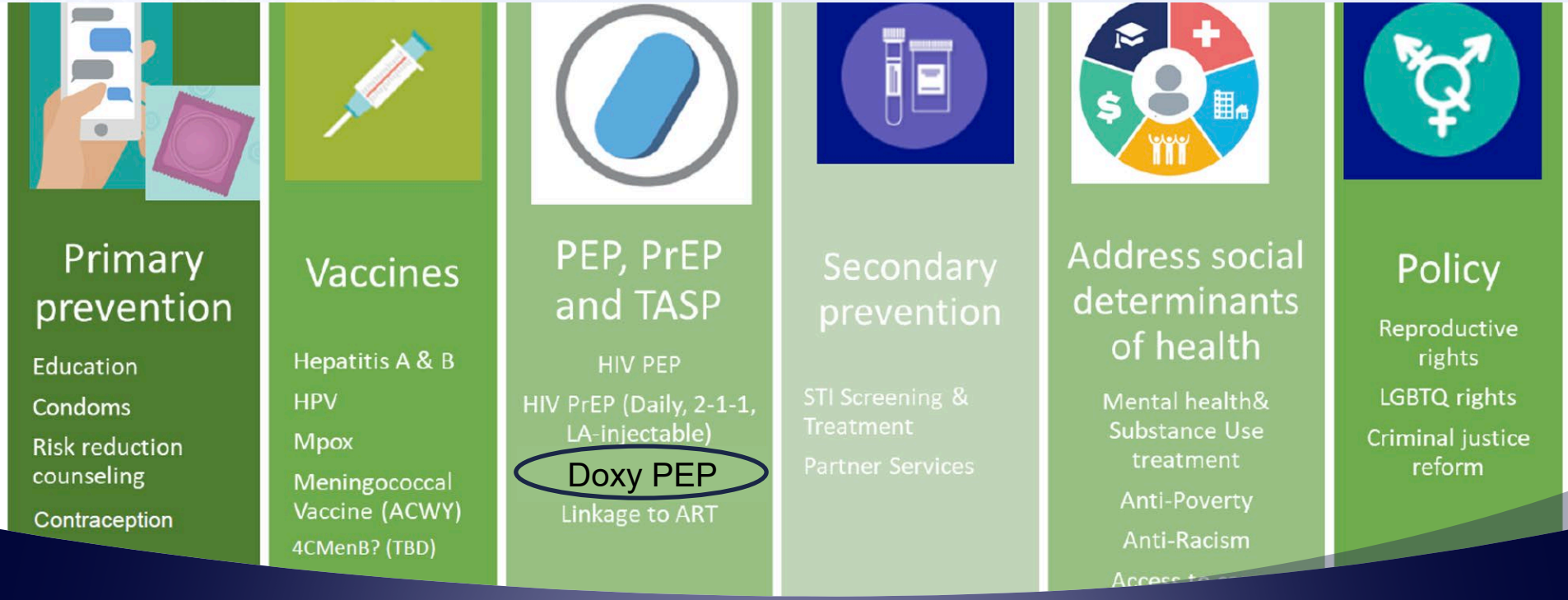
- Over 65% of MSM who are STI contacts test negative for GC/CT but receive empiric antibiotics unnecessarily
- Overtreatment of contacts represents an estimated 2-4% of the 47 million doses of overused antibiotics in the US

| STI | Pos. test rate among MSM contacts | RRR from doxy-PEP used in model | Estimated pos. test rate in contacts on doxy PEP |
|---|---|---|---|
| GC | 34% | 56% | 15% |
| CT | 34% | 81% | 6.5% |

Syphilis: test + empiric treatment due to transmission risk

Cannon, IAS 2023. Rowlinson E et al, STD 2020. US CDC. Antibiotic Use… 2018. Luetkemeyer A et al, NEJM 2023

# Section 7
# Summary: Key Points to Remember




Doxy PEP should be a part of comprehensive sexual health services

SLIDE COURTESY OF STEPHANIE COHEN

# Foci to keep in mind: the collective goal of doxy PEP

## Objectives for use

- To decrease population-level incidence of bacterial STI? Overall or among very high incidence populations?
- Prevent or decrease adverse sequelae (e.g., neurosyphilis, infertility, congenital syphilis, HIV transmission)?
- Targeted intervention for outbreak control – MSW, women?

## Strategies considered for balanced use

- Restrict eligibility criteria to select populations
  - Very high incidence of syphilis, other STI?
  - Only use for syphilis prevention?
- Minimize overuse of doxycycline while scaling up doxy PEP
- Limit overall antibiotic exposure

# Keeping our eyes on the prize

Decrease population-level incidence of STI

- Could reducing asymptomatic STI in some key populations lead to lower STI rates in others (e.g women and congenital syphilis)?
- Future research considerations
  - More data needed for efficacy in women
  - Revisiting dogma about teratogenicity of doxycycline
- What will it take?
  - More/less restrictive criteria? At what cost?
  - High interest among Black and Latino MSM(W), but uptake?
  - Community-informed delivery strategies that address syndemics, structural and economic barriers
  - Enhanced AMR surveillance and monitoring systems

Spinelli, et al. Sex Transm Dis 2019. Hazra, et al. Clin Infect Dis 2024.

# Conclusions

1. Doxycycline is effective for STI prophylaxis - multiple RCTs support benefit for STI reduction in MSM and TGW

2. Additional studies planned or ongoing for doxy PrEP, alternative doxy PEP dosing for people based on gender.

3. “Best use” will require balance of measured caution, shared decision making, and data-driven focus on key populations

4. We anticipate emerging data on AMR microbiome effects, but likely no comprehensive answer for many years

5. Implementation must be quality-focused, guided by clear goals, and include enhanced AMR monitoring and surveillance

# Questions?

Special Thanks to:
Chase Cannon, MD, MPH
Jehan Budak, MD
Debra D'Alessandro, MPH

Travis Hunt
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# Bonus: CROI 2025 Updates

# CROI 2025 Preliminary Updates

*1277: Characteristics of Breakthrough Chlamydia Cases among Cisgender Women Assigned to Doxycycline Postexposure Prophylaxis - Stewart et al*

- 85 incident cases of chlamydia including 35 among those assigned to doxy PEP
- Doxy PEP was inconsistently taken during the 30 days prior to visits with breakthrough *C.* trachomatis detection with 11/35 (31.4%) reports of one or more missed doses and 6/35 (17.1%) reports of not taking any doxycycline.
- Age less than 24 years and missed doses of doxy PEP were associated with incident *C. trachomatis* in women.

# CROI 2025 Preliminary Updates

1281: Increased knowledge and use of doxycycline postexposure prophylaxis (doxy PEP) in King County, Washington – Balkus et al

- Utilized data from PHSKC's annual Pride Survey to assess changes in knowledge and self-reported doxy PEP use among sexually active respondents from King County in the year after release of local guidelines.
- A total of 232 respondents in 2023 and 287 in 2024
- Doxy PEP knowledge and use increased, especially among GBMSM using PrEP; knowledge of doxy PEP was lower among trans women.
- Doxy PEP knowledge, use and interest was qualitatively similar by self-reported race and ethnicity.

# CROI 2025 Preliminary Updates

1283: Topical Doxycycline Inserts Show High Efficacy Against Vaginal Chlamydia Acquisition in Macaques – Garber et al

- Fast-dissolving doxycycline inserts w/ 10 or 50 mg 4h after vaginal challenge
- All CT-challenged macaques that received DOX inserts [50mg (N=4) or 10mg (N=4)] were protected against established CT infection, whereas 83% (5/6) controls became infected.
- Vaginal administration of a single 10mg DOX insert conferred DOX concentrations in vaginal swab eluates that exceeded the MIC90 of DOX against CT (0.064µg/ml) for ≥10 days, with undetectable systemic DOX exposure.

# CROI 2025 Preliminary Updates

1284 Antimicrobial Consumption Among Users of Doxycycline Post-Exposure Prophylaxis in Milan, Italy – Raccagni et al

- MSM in HIV care or PrEP Care receiving doxy PEP (inclusion criteria: 1+ STI in last year OR condomless sex with 1+ partner) w/ STI screen q3-6mo
- 754 prescribed and 222 reported use
- Regression for DOT per 1000-PD in the *absence of doxy PEP* was 4.85 [3.82-6.41] for CTX, 1.86 [1.17-2.87] for PCN, and 24.71 [17.18-37.36] for DOXY
- For *persons using doxy PEP*, DOT per 1000-PD was 1.26 for CTX, 0.37 for PCN and 3.21 for DOXY. Doxy PEP DOT per 1000-PD was 7.00. [No CI].
- Estimated reduction of DOXY use 24.1 → 13.21

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