

Integrating DoxyPEP into PrEP Prescribing: Experiences from San Francisco City Clinic

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Disclosures

Financial Disclosures: none

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Learning Objectives

By the end of this presentation, learners will be able to:

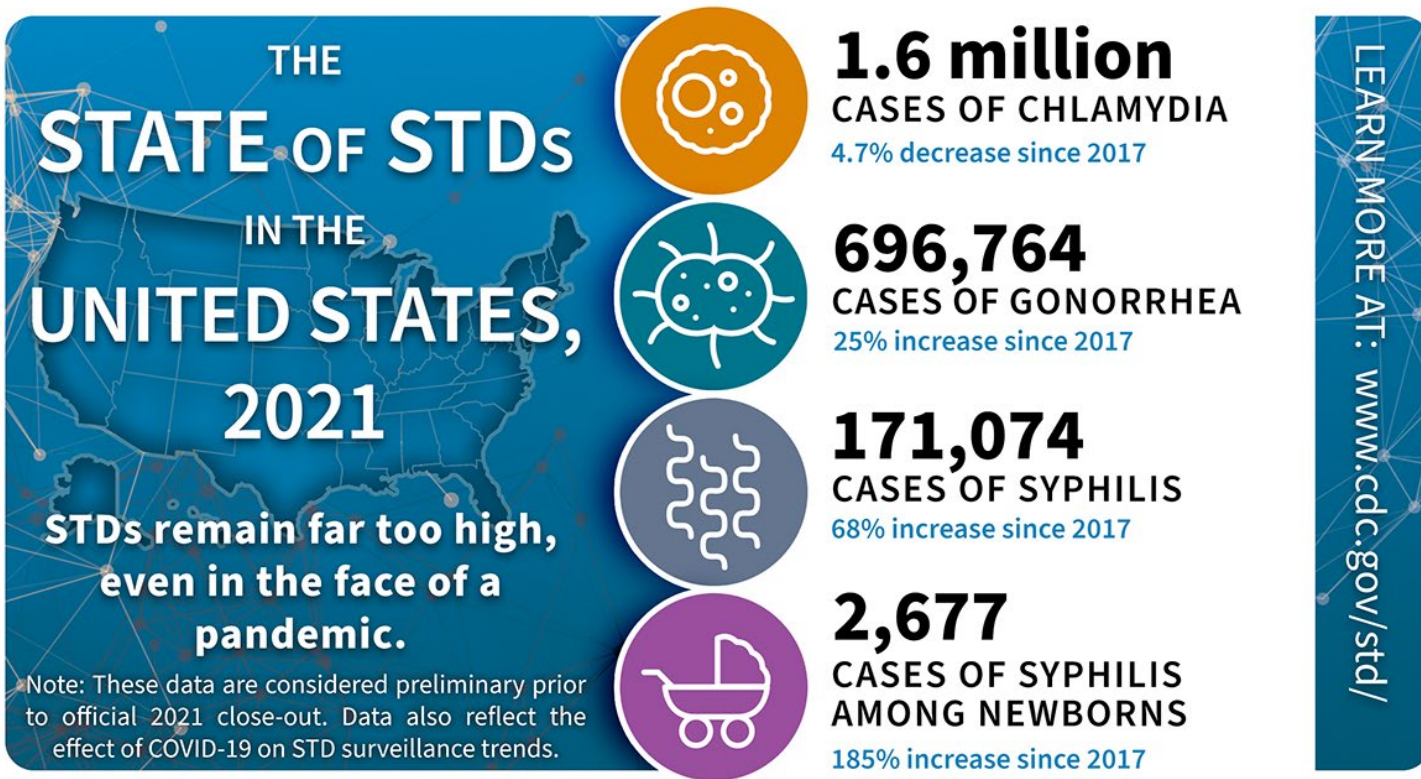
1. Describe the key findings of the DoxyPEP study and considerations for implementing DoxyPEP in clinical practice.
2. Demonstrate at least one way that local health departments can support integration of HIV and STI prevention.

Welcome to SF City Clinic

- High Volume: 17,000 visits annually
- Serve a diverse population
 - 39% B/AA or Latino, 15% Asian
 - 40% <30 years
 - 50% LGBTQ
- Integrated services:
 - STI, HIV, HCV screening, diagnosis and treatment
 - Women's health
 - Behavioral health
 - Pre- and Post-exposure prophylaxis (PrEP and PEP)
 - Doxy-PEP
 - On site laboratory
 - Immunizations (including COVID-19)
 - Overdose prevention (Narcan and fentanyl test strips)



The U.S. is experiencing steep, sustained increases in sexually transmitted infections



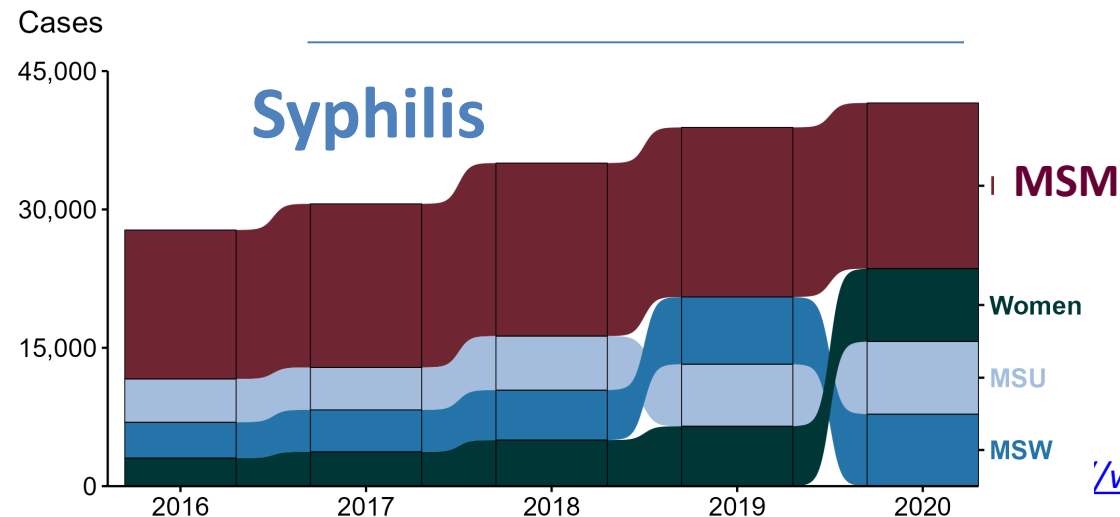
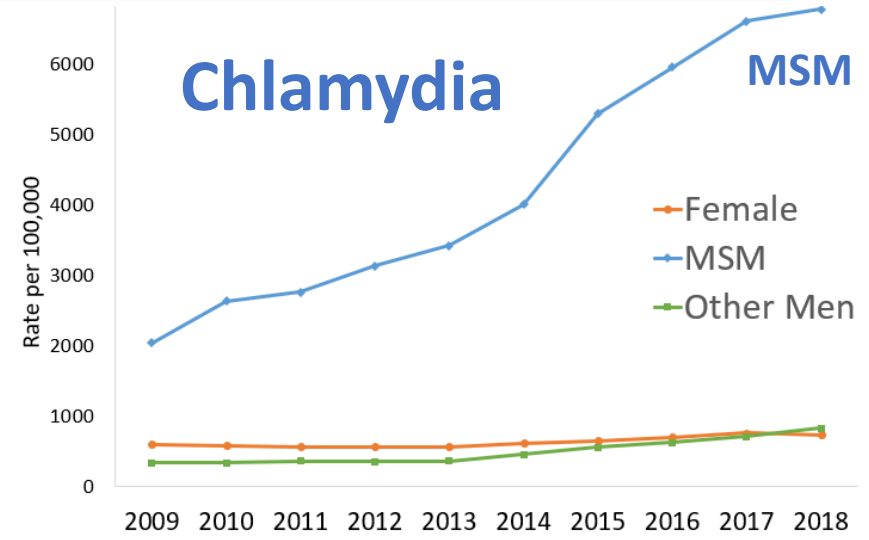
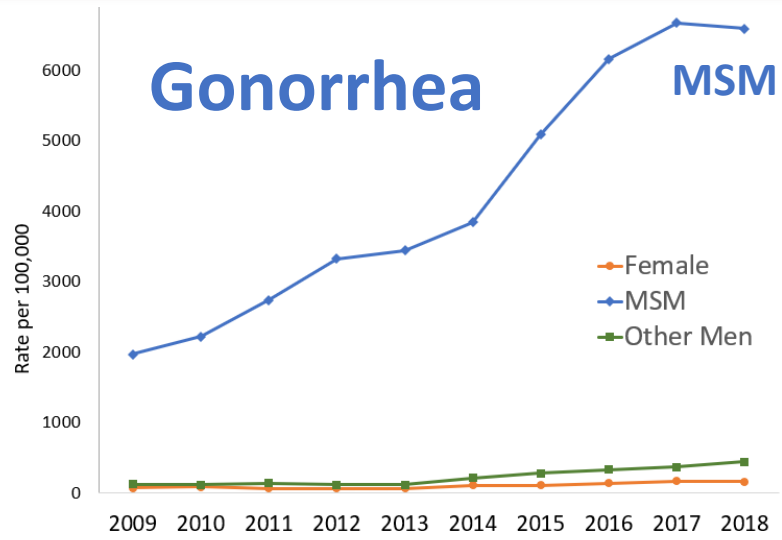
LEFT UNTREATED, STDS CAN CAUSE:

- INCREASED RISK OF GIVING OR GETTING HIV
- LONG-TERM PELVIC/ABDOMINAL PAIN
- INABILITY TO GET PREGNANT OR PREGNANCY COMPLICATIONS

PREVENT THE SPREAD OF STDs WITH THREE SIMPLE STEPS:

talk | test | treat

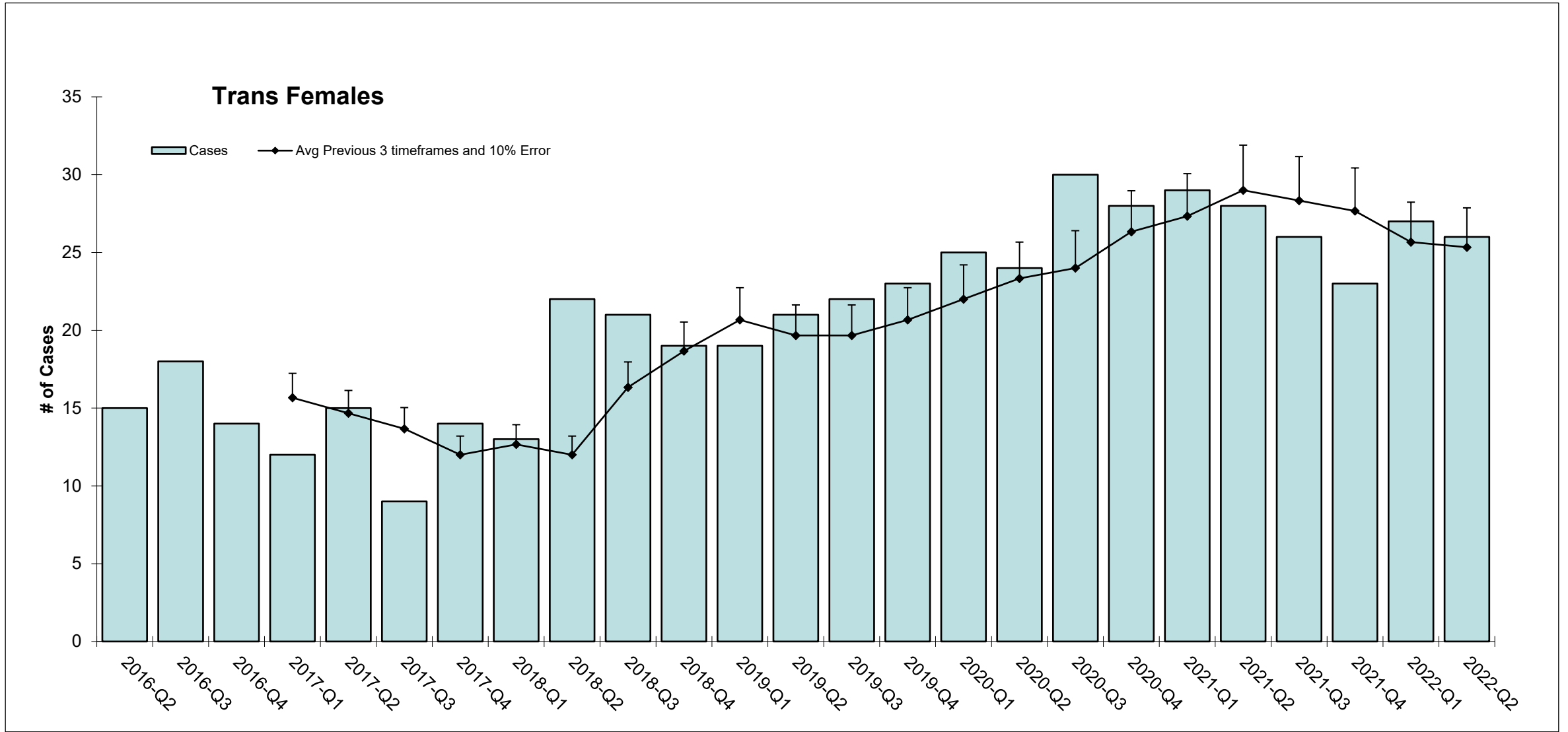
The global epidemic of STIs disproportionately impacts men who have sex with men (MSM)



San Francisco DPH
STI surveillance data 2018

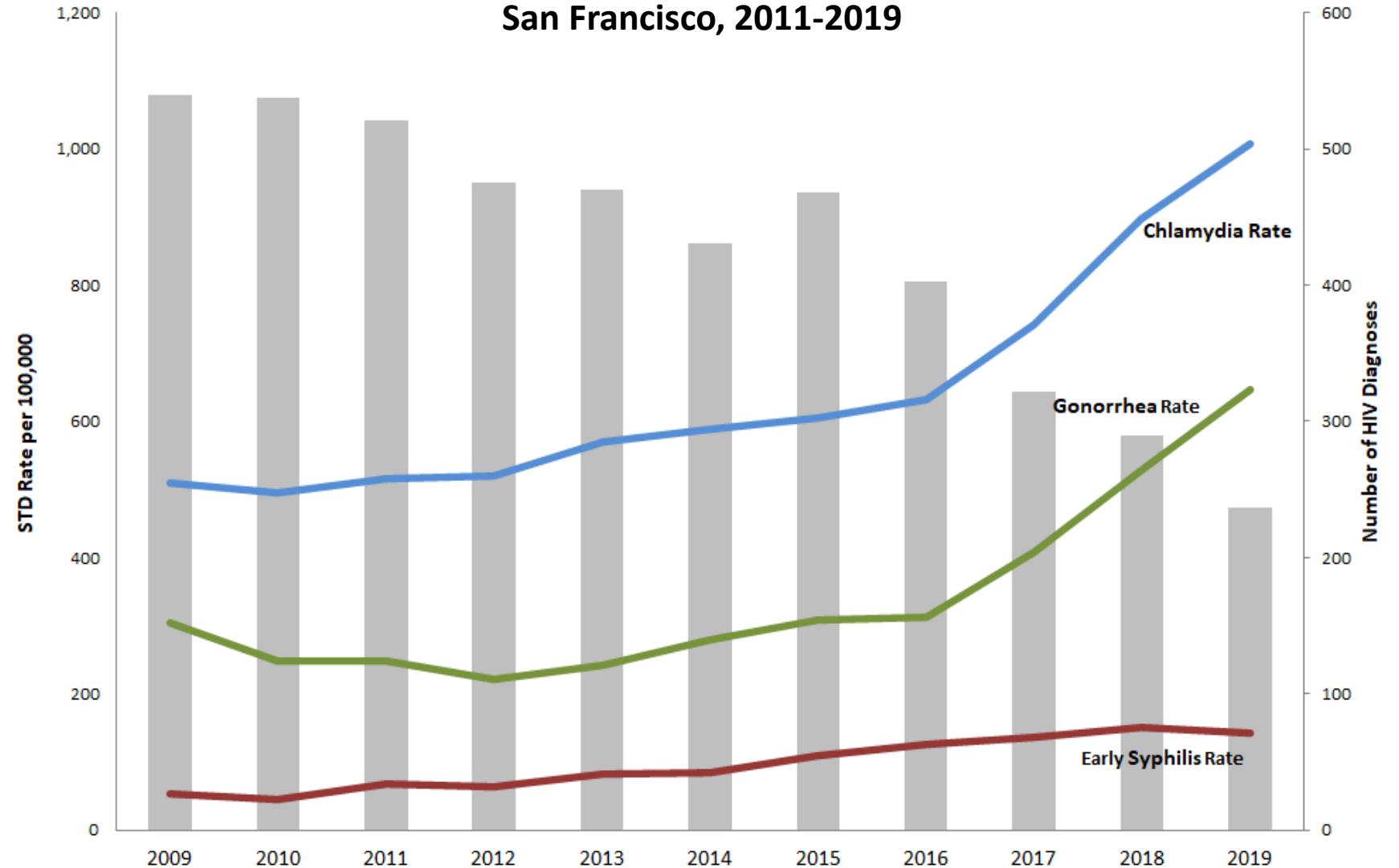
CDC 2020 STI surveillance
[/www.cdc.gov/std/statistics/2020/default.htm](https://www.cdc.gov/std/statistics/2020/default.htm)

Rising rates of gonorrhea in trans women in SF



**STIs rising
while HIV
diagnoses
decline in SF**

**Overall STI Rates and Number of HIV Diagnoses,
San Francisco, 2011-2019**



Currently available STI prevention tools



Primary prevention

Education
Condoms
Risk reduction counseling



Vaccines

Hepatitis A & B
HPV
Mpox
Meningococcal Vaccine (ACWY)



PEP, PrEP and TASP

HIV PEP
HIV PrEP (Daily, 2-1-1, LA-injectable)
Linkage to ART



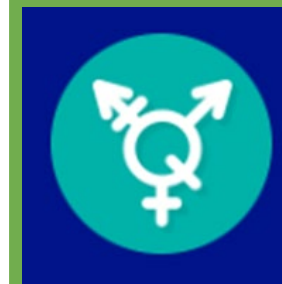
Secondary prevention

STI Screening & Treatment
Partner Services



Address social determinants of health

Mental health & Substance Use treatment
Anti-Poverty
Anti-Racism
Access to care



Policy

Reproductive rights
LGBTQ rights
Criminal justice reform

The newest tool: Doxycycline Post-Exposure Prophylaxis (doxy-PEP)

- Why Doxycycline?
 - Safe, well tolerated, and inexpensive
 - Active against chlamydia (CT) & syphilis
 - Some resistance in gonorrhea (GC), but not used as 1st line treatment for GC unknown how much activity needed for PEP
- Three recent RCTs:
 - Does taking doxy-PEP after sex decrease GC, CT and syphilis?
 - What is impact of intermittent doxy use on drug resistance (in STIs and other bacteria)

Intervention: Open label doxycycline 200mg taken as PEP within 72 hours after condomless oral, anal, or vaginal sexual contact
Maximum of 200 mg every 24 hours

Inclusion criteria:

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

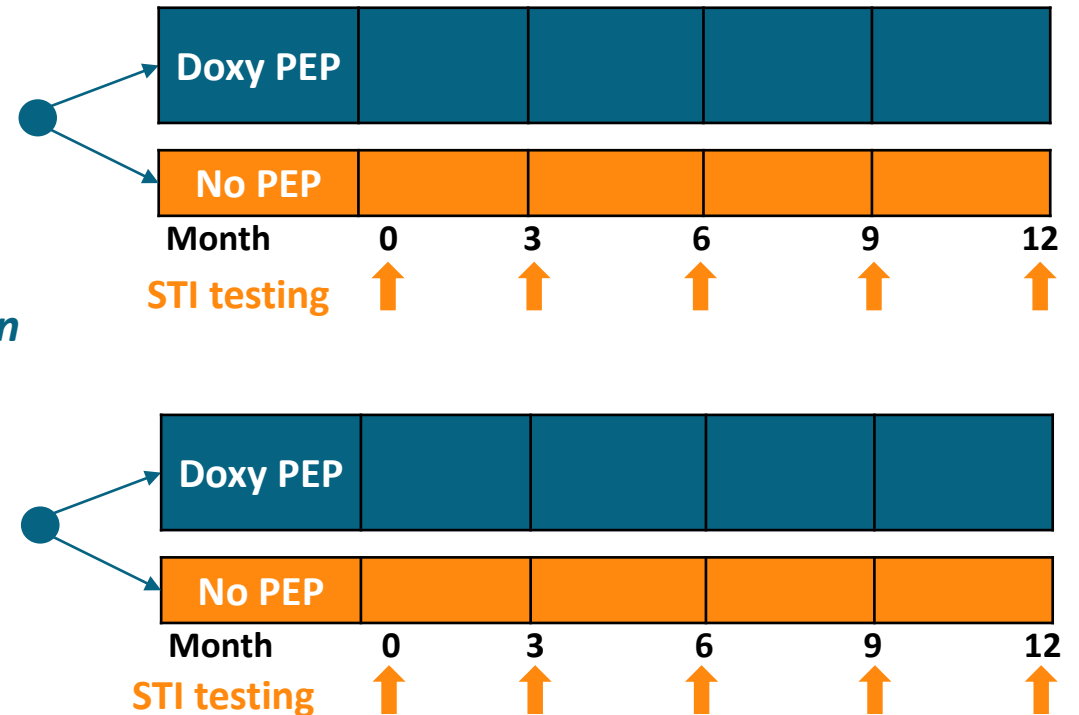
STI Testing: Quarterly 3 site GC/CT testing + RPR, GC culture before treatment

Sites: San Francisco & Seattle HIV & STI clinics

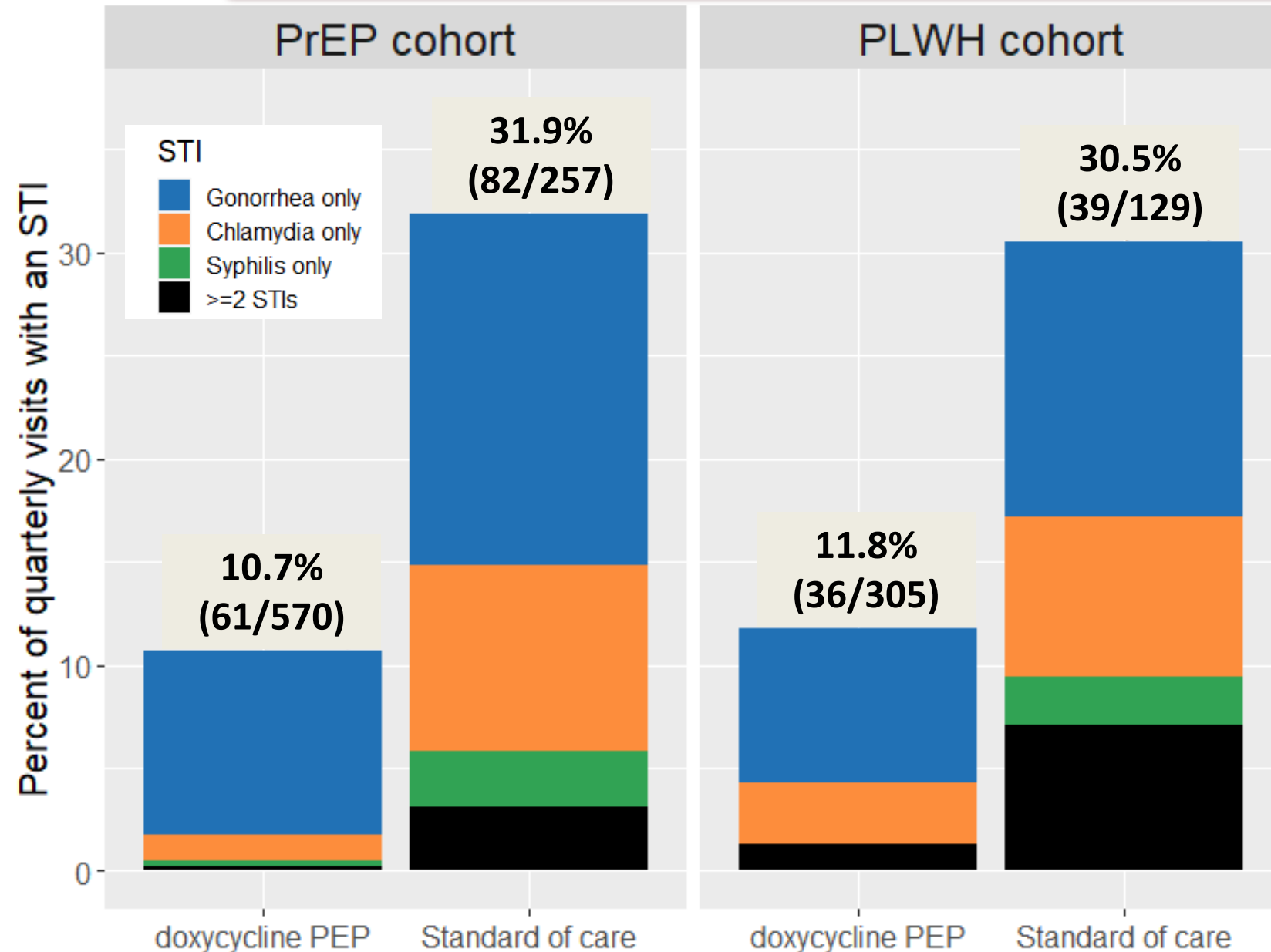
**MSM & TGW
living with HIV**
(planned n = 390)

2:1 randomization

**MSM & TGW
on HIV PrEP**
(planned n = 390)



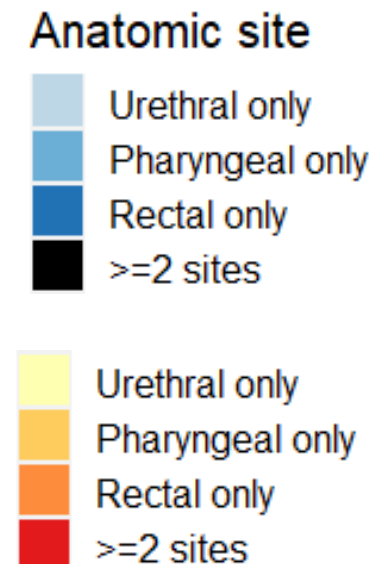
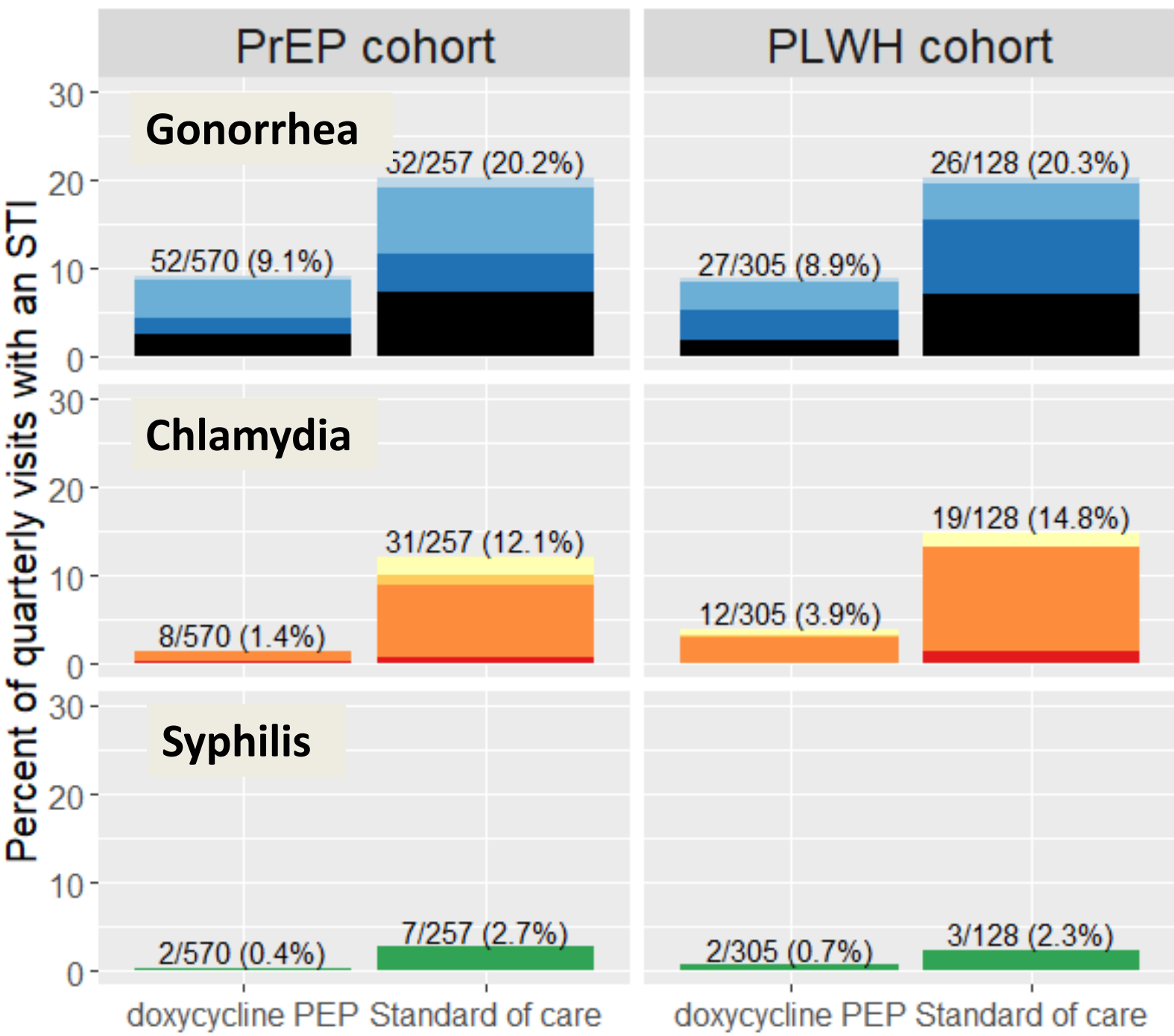
Primary Endpoint: STI incidence per quarter



Risk reduction in STI incidence/quarter (95% CI)	
PrEP	66% (54% - 76%)
People with HIV	62% (40% - 76%)
Total	65% (54% - 73%)

all p < 0.0001

Doxy-PEP reduced EACH individual STI in both arms



Risk reduction in each STI per quarter

	PrEP	PLWH
GC	55% (35%-68%) <i>p</i> <0.0001	57% (29%-74%) <i>p</i> =0.001
CT	88% (75%-95%) <i>p</i> <0.0001	74% (43%-88%) <i>p</i> =0.0007
Syphilis	87% (41%-97%) <i>p</i> =0.0084	77% (-71%, 96%) <i>p</i> =0.095

Sexual behavior, adherence & antibiotic use

- **Sexual behavior at enrollment:**
 - Median of 9 sexual partners (IQR 4,17) in prior 5 months
 - 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 in analyses to date**
- **Adherence to doxy-PEP:**
 - 86% reported doxy-PEP always/often after anal/vaginal sex
 - Median doxyPEP 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: 48.4/100 person-years vs SOC: 103.6/100 person years

Doxy-PEP does not prevent STIs in cisgender women

https://www.natap.org/2023/CROI/croi_10.htm

Doxycycline does not prevent STIs among cisgender women



**EMBARGOED FOR RELEASE UNTIL:
Monday, February 20, 2023
11 a.m. PT**

February 20, 2023 — Researchers from the University of Washington (UW), Kenya Medical Research Institute (KEMRI), and Hennepin Healthcare Research Institute (HHRI) announced results at CROI from a clinical trial demonstrating that doxycycline taken after sex does not prevent bacterial sexually transmitted infections (STIs) — chlamydia or gonorrhea — among cisgender women. The dPEP Kenya Trial was conducted in Kisumu, Kenya, to evaluate the effectiveness of doxycycline postexposure prophylaxis (PEP) to prevent bacterial STIs. The results of the study have been highly anticipated, as this is the first study of doxycycline PEP among cisgender women, following multiple studies that showed a high level of STI protection with doxycycline use among cisgender men and transgender women in France and the United States.

Differences in anatomy, antibiotic resistance, and adherence offer possible explanations for the lack of efficacy among cisgender women when it worked for cisgender men and transgender women, and the research team is working to understand the potential role of these differences. **"Doxycycline PEP didn't work for cisgender women in Kenya, but the need for STI prevention is increasing around the world,"** said Dr. Jenell Stewart, the dPEP Kenya Study Director, Infectious Disease Physician at Hennepin Healthcare and University of Minnesota.

Biological differences between the vagina/cervix and rectum may explain why doxycycline didn't prevent STIs in cisgender women; however, the approach to treatment of STIs doesn't differ by sex. Antibiotic resistance offers an explanation for why gonorrhea wasn't prevented, but it doesn't explain why chlamydia wasn't prevented. There are no known cases of antibiotic resistant chlamydia; however, the rate of doxycycline resistant gonorrhea was very high, including 100% of the infections acquired prior to starting the study. Self-reported adherence was high but imperfect and frequency and timing of doxycycline use among cisgender women in the trial is being evaluated further. All participants were also taking daily HIV PrEP pills (a medicine to prevent HIV), and none of the participants got HIV during the year they were in the study.

At a single site in Kisumu, Kenya, the study enrolled 449 cisgender women who were taking daily oral HIV pre-exposure prophylaxis (PrEP) and were randomized to receive doxycycline or standard of care. **18% of participants had an STI at the time they entered the study and over the course of the study the rate of STIs remained high — an annual incidence of 27%, which is comparable to rates among men who have sex with men in high income countries.** There were 109 new STIs diagnosed, 50 among those using doxycycline PEP compared to 59 among those randomized to no doxycycline and standard of care, during the course of the 12-month follow-up. **Most, 78%, of the new STIs diagnosed were chlamydia, 35 among people taking doxycycline PEP and 50 among standard of care, which was not statistically different.** Only one new case of syphilis was diagnosed in this study, consistent with other studies in the region, and therefore, the impact of doxycycline PEP on preventing syphilis among cisgender women could not be evaluated.

"The results from the study are deeply disappointing, and we are committed to understanding why doxycycline PEP did not work in this population and also determining the next steps for how to identify prevention tools that will work for and can be used by women," said Prof. Elizabeth Bukusi, a Principal Investigator of the dPEP Kenya Trial and Senior Principal Clinical Research Scientist at the Kenya Medical Research Institute.

Bacterial STIs in women can lead to lasting and severe consequences including pelvic inflammatory disease, chronic pain, infertility, pregnancy complications, and increased susceptibility to HIV. While the study team continues to investigate the potential role of biological and behavioral differences to explain why doxycycline PEP did not work, it is clear that cisgender women need primary STI prevention strategies.

The trial was funded by the National Institutes of Health (R01AI145971, P30AI027757, K23MH124466) and was conducted at the KEMRI Lumumba site in Kisumu, Kenya. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

DPEP Kenya Trial: Why?

- Anatomy: Endocervical tissue may differ from urethral, rectal, and pharyngeal tissue
- Exposures: Type and frequency of STI exposures may differ in high prevalence setting, and fewer average number of partners
- Resistance: To date, no known cases of resistant *C. trachomatis* globally; however, high rates of resistant *N. gonorrhoea*
- Adherence: Trial was designed to maximize adherence, and self-reported adherence was high but imperfect

Doxy-PEP Antimicrobial Resistance (AMR)

GC: Resistance testing through CDC SURRG & ARLN

Chlamydia: culture w/ phenotypic susceptibility

Syphilis- molecular testing (exploratory)

M. gen: Asymptomatic prevalence & symptomatic incidence, urine/rectal, & TCN-R

S. aureus & commensal *Neisseria*: tetracycline class resistance

Gut microbiome: change in flora, diversity & tetracycline resistance genes

What we know

- DoxyPEP works very well to prevent STIs in this study population: ↓ by more than **60%** each quarter
- ↓ in *each* bacterial STI per quarter, including gonorrhea
- Need to treat about 5 people to prevent a quarter with an STI, in a population with a high STI incidence (30% per quarter)
- Generally safe & well tolerated
- Doxy-PEP does not prevent STIs in cisgender women reporting receptive vaginal sex

What we don't know yet

- Efficacy for trans men and cis men who have sex with women
- Impact on bystander bacteria like *Staph aureus* and on gut
- Impact on doxy-susceptibility for chlamydia, gonorrhea, syphilis and *Mycoplasma genitalium*



Current State of Implementation

- Current CDC STI Treatment Guidelines do not include a recommendation for or against Doxy PEP
- Participants rolling-off of the doxy-PEP study requesting doxy-PEP from their PCPs
- Some clinicians prescribing, mostly on a case-by-case basis
- Community interest high

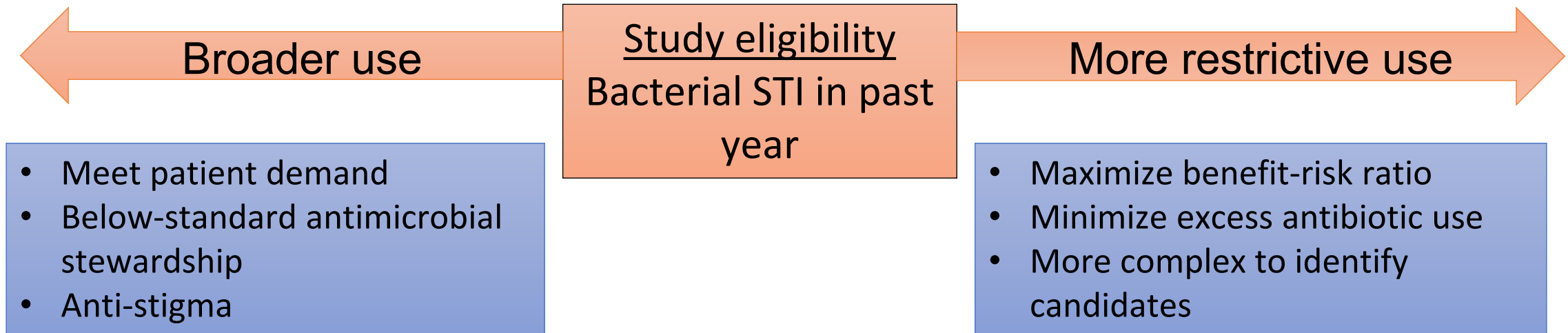
Not added to CDC STI Treatment Guidelines in July 2022

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.

Who Should be Offered Doxy PEP?



- Without a proactive approach, we risk worsening disparities
- Need to generate evidence to guide the approach (but not wait for it)
- Need to tailor to local epidemiology & resources

SFDPH released interim guidelines for Doxy-PEP



Health Update

Doxycycline Post-Exposure Prophylaxis Reduces Incidence of Sexually Transmitted Infections

October 21, 2022

Situational Update

Researchers at the San Francisco Department of Health (SFDPH), Zuckerberg San Francisco General, University of California, San Francisco, and the University of Washington recently collaborated on a randomized controlled clinical trial of post-exposure prophylaxis (PEP) of sexually transmitted infections (STIs) using a single dose of doxycycline 200 mg within 72 hours after oral, anal, or vaginal sex, in men who have sex with men (MSM) and transgender women (TGW) who were living with HIV (PLWH) or taking HIV pre-exposure prophylaxis (HIV PrEP). **The study showed that this regimen significantly reduced acquisition of chlamydia, gonorrhea, and syphilis in these populations.**

Participants randomized to doxycycline PEP (doxy-PEP) had a 66% (HIV-negative and on PrEP) and 62% (PLWH) reduction in STIs per quarter of study follow-up, compared with participants randomized to standard of care (no doxy-PEP). Taking doxycycline was also safe and well-tolerated by participants, with no drug-related serious adverse events. These [data](#) were recently presented at the 2022 International AIDS Conference in Montreal, Canada. Data are still being collected and analyzed to assess the impact of doxy-PEP on risk for drug resistance in bacterial STIs, *Staph aureus*, and commensal *Neisseria*, and on the gut microbiome.

The CDC has released [considerations](#) for doxy-PEP as an STI prevention strategy, but there is not yet detailed guidance from CDC on doxy-PEP, for which its indication is currently off-label. STIs can cause significant morbidity and reducing STI rates in San Francisco is an urgent public health priority. **Doxy-PEP is the first biomedical prevention tool that has been shown to be effective and well-tolerated, community awareness is growing, and many providers in SF are already prescribing doxy-PEP to their patients at risk for STIs.** SFDPH is providing guidance to SF clinicians on the use of doxy-PEP to reduce STI incidence in MSM and TGW at risk of bacterial STIs.



Doxycycline PEP Interim Guidelines

Health Update

Doxycycline Post-Exposure Prophylaxis Reduces Incidence of Sexually Transmitted Infections

October 21, 2022

- 1. Recommend doxy-PEP** to cis men and trans women who: 1) have had a bacterial STI in the past year and 2) report condomless anal or oral sexual contact with ≥ 1 cis male or trans female partner in the past year. These were the eligibility criteria used for the DoxyPEP study. Patients with a history of syphilis should be prioritized for doxy-PEP.
- 2. Offer doxy-PEP using shared decision making** to cis men, trans men and trans women who report having multiple cis male or trans female sex partners in the prior year, even if they have not previously been diagnosed with an STI.
- 3. Doxy-PEP not recommended for cis women** based on currently available evidence from Kenya DPEP study.



Counseling Recommendations

Health Update

Doxycycline Post-Exposure Prophylaxis Reduces Incidence of Sexually Transmitted Infections

October 21, 2022

- Review key findings from DoxyPEP study:
 - 2/3 reduction in acquiring gonorrhea, chlamydia and syphilis among MSM and TGW who had a history of STIs in the past year
 - Safe and well-tolerated
- Recommend comprehensive package of sexual health services:
 - HIV PrEP or engagement in HIV care
 - STI screening
 - Vaccines for MPX, Meningococcus, Hepatitis A and B, HPV



Counseling Talking Points

Health Update

Doxycycline Post-Exposure Prophylaxis Reduces Incidence of Sexually Transmitted Infections

October 21, 2022

- Possible drug interactions
- Risk of sun sensitivity and use of sunscreen
- Remain upright for 30 minutes after taking doxycycline to reduce the risk of pill esophagitis
- Rare risk of benign intracranial hypertension and other serious side effects
- Unknowns about long-term use of DoxyPEP:
 - Gut microbiome
 - Skin flora and other non-STI bacteria
 - Long-term safety
 - STIs and their susceptibility to doxycycline
 - Population-level rates of antimicrobial resistance

Summary: Counseling patients about DoxyPEP

- Utilize shared-decision making to support patient's choice
- Guide self-assessment of risk
- Review how to use doxy-PEP
- Acknowledge unknowns
- Offer comprehensive package of sexual health services

About Doxy-PEP



What is doxy-PEP?

- Doxy-PEP means taking the antibiotic doxycycline after sex, to prevent getting an STI. It is like a morning-after pill but for STIs. Taking doxy-PEP reduces your chance of acquiring syphilis, gonorrhea, and chlamydia by about two-thirds.



When should I take doxy-PEP?

- Two 100 mg pills of doxycycline should be taken ideally within 24 hours but no later than 72 hours after condomless sex. Condomless sex means oral, anal or vaginal/front-hole sex where a condom isn't used for the entire time.

What about when I have sex again?

- If you have sex again within 24 hours of taking doxycycline, take another dose 24 hours after your last dose. You can take doxycycline as often as every day when you are having condomless sex but don't take more than 200 mg (two 100 mg pills) every 24 hours.



How should I take doxy-PEP?

- Take doxycycline with plenty of water or something else to drink so that it does not get stuck when you swallow. If your stomach is upset by doxycycline, taking it with food may help.
- Some people are more sensitive to the sun when they take doxycycline, so wear sunscreen.
- Please do not share doxycycline with others.
- Avoid dairy products, calcium, antacids, or multivitamins 2 hours before after taking doxycycline.³⁰



About Doxy-PEP



What are we still learning about doxy-PEP?

- Does it affect normal (“good”) bacteria in our intestines?
- Could it increase or decrease the bacteria that live on our skin, or make them resistant to doxycycline (for example staph)?
- Will doxy-PEP increase doxycycline resistance in bacteria that cause STIs?
 - Although doxycycline has been used for decades, there is not resistance to doxycycline in chlamydia or syphilis.
 - About 25% of gonorrhea in the US is already resistant to doxy; doxy-PEP may not work against these strains. The DoxyPEP study and other studies will help understand whether using doxy-PEP changes resistance in gonorrhea.



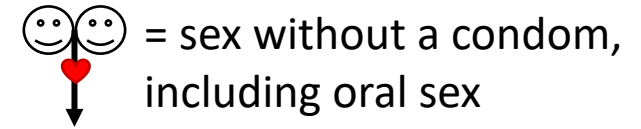
Reminders

- Call us at 628-217-6692 if you run out of doxycycline, if you are having any side effects, or if you think you may have an STI.
- Please continue to get tested for STIs every 3 months and whenever you have symptoms.
- Doxy-PEP doesn’t protect against MPX (monkeypox), HIV, or other viral infections



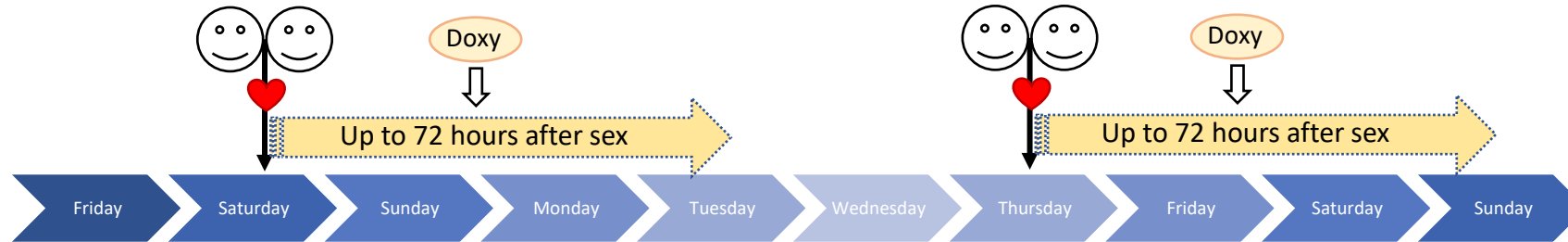
Messaging – Dosing guidance

Doxy PEP – How to Take

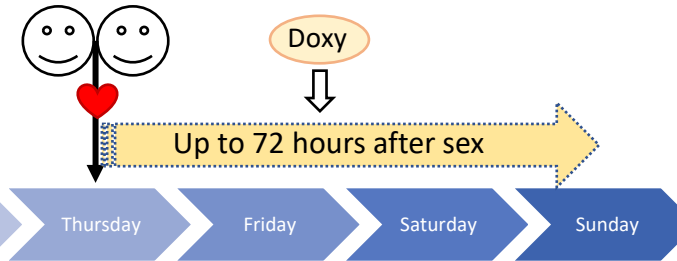


One pill of doxycycline ideally within 24 hours but no later than 72 hours after condomless sex

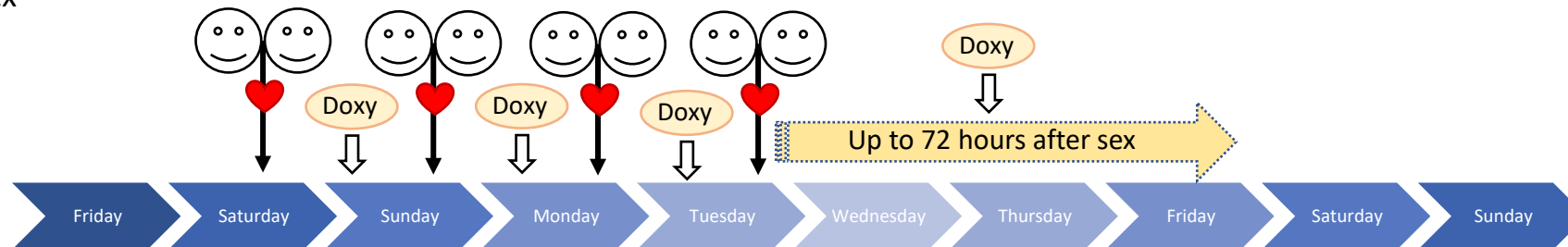
Example: Sex on Sat; take dose of doxy by Tues



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 one pill (200 mg) every 24 hours

DoxyPEP at SFCC: High uptake by persons who would benefit from it

312 persons started doxy-PEP at SFCC 11/3/22-1/6/23

- 94% MSM, 4% TWSM
- 48% with 2-5 sex partners in last 3 months
- 40% with 6+ sex partners in last 3 months
- 35% with at least 1 episode of chlamydia, gonorrhea, or syphilis in last year
- 9% reported multiple STIs in last year
- 37% White, 31% Hispanic, 15 % Asian/PI, 6% Black

SFCC doxy-PEP program overview

- Open to pts with any insurance but Kaiser or VA
- “Status neutral” - Open to pts living with HIV or not
- All patients see a clinician at doxy-PEP initiation
- Doxy e-prescribed for patients with insurance
- Doxy dispensed in clinic (no cost to patient) for uninsured and <500% FPL
- Dispense 60-100 pills (30-50 doses)
- Annual LFTs
- Biomedical HIV prevention team (PrEP navigators) provide critical support to the program
 - Determine patients coverage (eRx vs. dispense in clinic) and “pend” the prescription
 - Provide education, information and counseling
 - At follow-up visits, collect information on risk behaviors and adherence

Early insights from program

- Confusion re. dosing and how it differs from 2-1-1 PrEP or daily PrEP
- Most pts do not need refills at first quarterly continuation visit
- Most pts report taking the medication 0-5 times in prior 3 months
- Most patients are reporting “selective” use – i.e. not using it with all partners

Clinical questions/conundrums

- How to clinically manage contacts to an STI – epi treat or not?
- Frequency of STI screening?

Next steps for doxy-PEP

- Await CDC guidelines – expected by end of 2nd quarter
- Additional studies pending
 - Kenya dPEP study (doxy-PEP in cis women)
 - Studies in Canada and Australia
- Implementation science:
 - Interest, uptake, community engagement, social marketing strategies, provider education
 - Long-term impact on individual health
 - Long-term impacts on antimicrobial resistance
 - Modelling studies to assess potential impact on STI incidence

Thank you!

- DoxyPEP Participants
- DoxyPEP Study team
- SFCC team - Registration, Nursing, Clinicians, PrEP, LINCS, Research, Social work and behavioral health
- Montica Levy
- Oliver Bacon
- Stephanie Cohen