Special Presentation: DoxyPEP update
TRANSLATING EVIDENCE INTO ACTION FOR PUBLIC HEALTH: THE DOXY-PEP STORY

CDC/HRSA Advisory Committee (CHAC) April 10, 2024

Stephanie Cohen, MD, MPH
Director, HIV/STI Prevention Section
SF Department of Public Health
San Francisco has higher chlamydia, gonorrhea, and syphilis rates compared to the United States overall, the state of California, Los Angeles and New York City.
Overall STI Rates and Number of HIV Diagnoses, San Francisco, 2011-2022

2014 to 2019:
- Chlamydia: 76%
- Gonorrhea: 72%
- Early Syphilis: 45%

Updated: 03.22.2024
In November 2019, US DoxyPEP study launched in San Francisco and Seattle

**Why Doxycycline (doxy)?**

- Safe, well tolerated, inexpensive oral antibiotic
- Active against chlamydia & syphilis. Approx 80% of gonorrhea strains in US susceptible
- Shown to reduce STIs in two prior studies
  - Small pilot in LA (N=30) of doxy pre-exposure prophylaxis (PrEP)
  - Ipergay study in France (N=232) of doxy post exposure prophylaxis (PEP)
- Strong interest amongst men who have sex with men (MSM)
- US DoxyPEP study, French DOXYVAC and Kenya D-PEP studies aimed to assess the impact of doxy-PEP on bacterial STIs incidence *and* on drug resistance (in STIs and other bacteria)

DoxyPEP and DOXYVAC studies demonstrated substantial reduction in risk of bacterial STIs in MSM and trans women.

*Time to first CT, GC or syphilis: DoxyPEP*¹

<table>
<thead>
<tr>
<th>Hazard Ratio:</th>
<th>0.37 (0.28-0.49), p &lt; 0.0001</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Randomization Events/Total</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard of care</td>
<td>91/180</td>
</tr>
<tr>
<td>Doxy-PEP</td>
<td>108/411</td>
</tr>
<tr>
<td>Logrank P-value</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Time to first CT or syphilis: DoxyVAC*²

| Adjusted Hazard Ratio: | 0.17 (95% CI: 0.12-0.26, p<0.0001) |

¹DoxyPEP, Luetkemeyer et al, NEJM 2023; 388:1296-1306, ²DOXYVAC, Molina et al, CROI 2024
Kenya D-PEP study did not find that doxy-PEP reduced STIs in cis women

- High self-reported adherence (≥80%)
- Median 4 doses per month (IQR 0-8)
- Low hair drug levels in women in doxycycline group suggest low adherence to doxy-PEP

Stewart, et al. *NEJM* 2023
How to implement doxy-PEP in San Francisco?

• Eligibility criteria
• Supporting roll-out and uptake
• Monitoring impacts of doxy-PEP
  – Disparities in uptake
  – STI rates
  – Antimicrobial resistance
  – Adverse events (e.g. effect on microbiome)
Who Should be Offered Doxy-PEP?

More restrictive use

- Maximize benefit-risk ratio
- Minimize excess antibiotic use
- More complex to identify candidates
- Reduced reach and impact

Broader use

- Meet patient demand
- Anti-stigma
- Greater reduction in absolute number of STIs
- More antibiotics used

Study eligibility
MSM or Transwoman and Bacterial STI in past year

Slide adapted courtesy J. Dombrowski
SFDPH: First jurisdiction in US to release guidelines for DoxyPEP

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.

Doxy-PEP
Interim Guidelines

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. 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. Results from the Kenya D-PEP study found that doxy-PEP was not effective at preventing STIs among cis women. Drug level data suggest that this may have been due to low adherence to doxy-PEP. Providers can consider offering doxy-PEP to cis women on a case-by-case basis, for example to women with a history of syphilis or women who exchange sex for money or drugs.
About Doxy-PEP

Doxy-PEP fact sheet for healthcare providers in San Francisco

Who should take Doxy-PEP?
- People who have had sexual contact with a person who has HIV infection and who have symptoms consistent with HIV infection.

How should I take Doxy-PEP?
- Follow the dosage instructions provided by your healthcare provider.
- Take with food to reduce side effects.

What about when I have a side effect?
- Common side effects include nausea, headache, and skin rash.
- If symptoms persist or worsen, contact your healthcare provider.

Counseled dosing and therapy
- Discuss the potential benefits and risks of Doxy-PEP with your healthcare provider.
- Follow up with your healthcare provider regularly.

Additional resources
- Visit www.sfcityclinic.org for more information and resources.

Doxy-PEP fact sheet for healthcare providers in San Francisco

Who should take Doxy-PEP?
- People who have had sexual contact with a person who has HIV infection and who have symptoms consistent with HIV infection.

How should I take Doxy-PEP?
- Follow the dosage instructions provided by your healthcare provider.
- Take with food to reduce side effects.

What about when I have a side effect?
- Common side effects include nausea, headache, and skin rash.
- If symptoms persist or worsen, contact your healthcare provider.

Counseled dosing and therapy
- Discuss the potential benefits and risks of Doxy-PEP with your healthcare provider.
- Follow up with your healthcare provider regularly.

Additional resources
- Visit www.sfcityclinic.org for more information and resources.
Doxy-PEP as part of a comprehensive package of sexual health services

Primary prevention
- Education
- Condoms
- Risk reduction counseling
- Contraception

Vaccines
- Hepatitis A & B
- HPV
- Mpox
- Meningococcal Vaccine (ACWY)

PEP, PrEP and TASP
- HIV PEP
- HIV PrEP (Daily, 2-1-1, LA-injectable)
  - Doxy-PEP
- 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
SF City Clinic began offering doxy-PEP in November 2022

- SF City Clinic (SFCC) is a nationally-recognized center of excellence in sexual health services
- Offers integrated HIV, STI and reproductive health care grounded in a syndemic approach
- Drop-in and appointments available
- High Volume: 17,000 visits annually
- Serve a diverse population
  - 39% B/AA or Latino, 15% Asian
  - 40% <30 years
  - 50% LGBTQ
High uptake of doxy-PEP at SFCC

• At SF City Clinic, MSM and TGW are systematically informed about doxy-PEP at PrEP initiation or PrEP follow-up

• Between November 2022 and May 2023:
  • 74% of patients with GC, CT or syphilis in prior year started doxy-PEP
  • 60% of patients with ≥ 2 sex partners, but no STI history started doxy-PEP
  • Uptake was associated with having a higher # of sex partners in prior 3 months; not with demographic factors
High uptake of doxy-PEP in San Francisco after release of guidelines

- Sentinel surveillance at 1 safety-net HIV clinic and 2 sexual health clinics
- High volume health maintenance organization and primary care clinics not included
Doxy-PEP Uptake by Race/Ethnicity at 2 Sexual Health Clinics (SHC) and 1 HIV Care Clinic
San Francisco, Oct 2022 – Dec 2023

- Uptake lower in HIV care clinic setting
- Similar uptake across racial/ethnic groups within existing clinic cohorts

% of MSM and TGW prescribed doxy-PEP

SHC-1
- 22.9
- 24.2
- 22.4

SHC-2
- 23.7
- 21.9
- 27.1
- 28.1

HIV Care Clinic
- 23.5
- 24.3

- White
- Black/African American
- Latinx/o
- Asian
- Pacific Islander
- Multiracial
Patient Experience and Adverse Events

- Patients report using doxy-PEP selectively
  - At follow-up visits, 89% of those prescribed doxy-PEP reported using it, but not with every condomless sex act

- Occasional discontinuations related to GI side effects

- Sex-positive and person-first intervention
  - Improved peace of mind and sexual pleasure
  - Decreased stigma around STI diagnosis and disclosure
  - Increased self-awareness about sexual behavior
  - Facilitates communication with partners about sexual health

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)

Fredericksen R, et al. AIDS Pt Care STDs 2024 (forthcoming)
Decline in chlamydia and syphilis among PrEP patients receiving doxy-PEP at sexual health clinics in SF

<table>
<thead>
<tr>
<th></th>
<th>CBO-run sexual health clinic 6/1/22-9/1/23</th>
<th>Municipal sexual health clinic 11/3/21-10/30/23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td><strong>67% decrease</strong> [IRR: 0.33, 95% CI: 0.23-0.46]</td>
<td><strong>90% decrease</strong> [RR: 0.10, 95% CI: 0.05-0.21]</td>
</tr>
<tr>
<td>Syphilis</td>
<td><strong>78% decrease</strong> [IRR 0.22, 95% CI: 0.09-0.54]</td>
<td><strong>56% decrease</strong> [RR 0.44, 95% CI 0.21-0.92]</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>11% decrease [IRR 0.89, 95% CI 0.69-1.15]</td>
<td>23% decrease [RR 0.77, 95% CI 0.58–1.02]</td>
</tr>
</tbody>
</table>

Scott H, CROI 2024 (abstract #126); Bacon O, CROI 2024 (poster #1151)
Decline in **citywide** chlamydia and early syphilis cases in MSM in SF after release of doxy-PEP guidelines

In Nov 2023, observed **chlamydia** cases were 50% (95% CI 38%-59%) lower than model forecasts

In Nov 2023, observed **syphilis** cases were 51% (95% CI 43%-58%) lower than model forecasts
No decline in **citywide** gonorrhea cases in MSM, and continued increases in chlamydia in cis women in SF after release of doxy-PEP guidelines.

1.8%/month decrease in gonorrhea cases in MSM in pre-period (p<0.0001)

1.8%/month increase in gonorrhea cases in MSM in post-period (p<0.0001)

Chlamydia cases increased 2.46%/month increase in cis women in post-period (p<0.01)

Sankaran M, CROI 2024 (abstract #127)
Conclusions

• SFDPH moved quickly to translate evidence from a research study into services for our community

• Remarkable citywide collaboration and our engaged community facilitated early adoption of this new tool

• Early evidence of a population-level impact of doxy-PEP on chlamydia and syphilis rates, but not gonorrhea
  • Longer follow-up and to replicate findings in other jurisdictions
  • Information about antimicrobial resistance

• Providers should support their patients in assessing their need for, interest in, and use of doxy-PEP

• Guidelines for doxy-PEP can and should evolve as evidence emerges, informed by community input
Thank You!

SF City Clinic Patients & Study Participants

Maddie Sankaran
Dave Glidden
Oliver Bacon
Trang Nguyen
Bob Kohn
Franco Chevalier
Judith Sansone
Montica Levy
Christopher Ruiz
Allyson Decker
Julia Janssen
Erin Antunez
Rebecca Shaw
Meya Harris
Jennifer Lopez
Jasmine Hawkins
Frank Strona
Ricardo Beato
Romeo de la Roca
Thu Tran
Gina Limon
Shornora Miller
Yong Chun Huang
Shai Wallace
Terry Marcotte
Bettemie Prins
Clara Shayeovich
Edward Liu
Elizabeth Faber
Sally Grant
Tony Sayegh
Tae-Wol Stanley
Yvonne Piper
Sari Bushman
Ameera Snell
Tamar Besson
Nyisha Underwood
Thomas Knoble
Hanna Hjord
Oscar Macias
Nikole Trainor
Rio Bauce
Frank Strona
Ricardo Beato
Alejandro Vigil
Grecia Sambrano
Meyana Tillman
Francisco Garcia
Johnson Mao
Tova Israel
Wendy Ho
Antonia
Guatemala
Jonathan Carlson
Amy Kwan
Rho* Torres
Anthony Taylor
Crecy James
Pearl Aine
Wanda Anderson
Veronica Aburto
Adrian Vargas
Joey Sweazy
Ki-Shawna Hampton
Ryanne Brown
Rigoberto Mendez
Alison Cohee
Melody Nasser
Dorien Cimmiyotti
Nikolas Alves da Costa E Silva
Annie Luetkemeyer
Connie Celum
Susan Buchbinder
Chase Cannon
Julie Dombrowski
Hyman Scott
Jorge Roman
Jason Bena
Matt Spinelli
Thiago Torres
Courtney Liebi
Brad Hare
Jonathan Volk
SF Getting to Zero
Doxypep study team
Susan Philip
Grant Colfax
Surveillance systems to monitor for anti-microbial resistance

- CDC supports sentinel surveillance for culture-based GC antibiotic susceptibility testing
- Need systems for monitoring non-STI pathogens, including staph aureus, strep pneumo and E. coli
- Challenging to discern specific impacts of doxy-PEP in context of overall doxycycline use in medicine and agriculture

* Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs), by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2022

DoxyPEP at a Boston Community Health Center and National Survey Data

Kenneth H. Mayer, MD
CDC-HRSA HIV/AIDS Advisory Committee
April 10th, 2024
thefenwayinstitute.org
DoxyPEP: Fenway Health

Based in downtown Boston, Massachusetts
Federally Qualified Healthcare Center, Founded 1971

**Mission** To enhance the wellbeing of the LGBTQIA+ community as well as people in our neighborhoods and beyond through access to the highest quality health care, education, research, and advocacy

Serving ≈ 35,000 patients, with approximately 2,200 PLHIV and 3,500 on PrEP.

**The Fenway Institute**
- Research, Education, Policy
- Involved in NIH and other funded HIV Prevention Research
Guidelines in the US

Local / state health departments

• First to put out recommendations after the large trials were announced

Recommendations

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.

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE

ALL RECOMMENDATIONS: DOXYCYCLINE POST-EXPOSURE PROPHYLAXIS TO PREVENT BACTERIAL SEXUALLY TRANSMITTED INFECTIONS

Biomedical Prevention of STIs

• Clinicians should offer doxy-PEP to cisgender men and transgender women who are taking HIV PEP or receiving HIV care and 1) engage in condomless sex with partner(s) assigned male sex at birth and 2) have had a bacterial STI diagnosed within the past year and are at ongoing risk of STI exposure. (A1)
• Clinicians should offer doxy-PEP to cisgender men and transgender women who are not taking HIV PEP or receiving HIV care and 1) engage in condomless sex with partner(s) assigned male sex at birth and 2) have had a bacterial STI diagnosed within the past year and are at ongoing risk of STI exposure. (A2)
• Clinicians should engage in shared decision making with cisgender men who 1) engage in condomless sex with multiple partners assigned female sex at birth and 2) have had a bacterial STI diagnosed within the past year, offering doxy-PEP on a case-by-case basis. (B3)
• When prescribing doxy-PEP, clinicians should use the dosing regimen of oral doxycycline 200 mg taken ideally within 24 to 72 hours of condomless sex (A1) and counsel patients (A*) on the key points for patient education outlined in Table 1: Considerations for Doxy-PEP Implementation.
• For individuals taking doxy-PEP, clinicians should screen for HIV, chlamydia, gonorrhea, and syphilis at least every 3 months. (A1)
• Clinicians should offer HIV PEP to individuals who do not have HIV and are initiating or using doxy-PEP. (A*)
• Clinicians should offer HIV treatment to individuals with HIV who are not on antiretroviral therapy and are initiating or using doxy-PEP. (A1)

Abbreviations: doxy-PEP, doxycycline post-exposure prophylaxis; PEP, pre-exposure prophylaxis; STI, sexually transmitted infection.
“Focused” Identification Of Doxy-PEP Candidates

Evaluation of potential impact of hypothetical doxy-PEP prescribing strategies

Most efficient prescribing strategies are based on STI history rather than HIV status or PrEP use.

Efficiency = \( \frac{\% \text{ of STIs prevented}}{\% \text{ of individuals prescribed}} \)

Traeger MW, CID 2023
DoxyPEP: Fenway Health

- Assign Male At Birth, ≥18yo
  - Plus one of the following -
    - A diagnosis of a bacterial STI in the last 12 months
    - PrEP Use, ≥2 sexual partners with condomless oral/anal sex
    - PLWH, ≥2 sexual partners with condomless oral/anal sex

- Shared Decision Making
DoxyPEP: Fenway Health

Doxycycline 100mg take two tabs by mouth within 72 hours after condomless sexual activity (#60, RF1)

What is it for?
To help prevent getting chlamydia, syphilis and gonorrhea. It is not 100% protective - but early data suggests it can decrease numbers by 60%.

How do I take it? "3-2-1"
3 - within 3 days or 72 hours
2 - take 2 tabs (or 200mg)
1 - once (limit to 1 time in one day)

- Take Doxycycline 100mg x 2 tabs (200mg together) once within 72 hours of possible exposure / risk - such as condomless oral/anal sex. It is better to take it within the first 24 hours.
- Do not take more than 200mg in one day. It is safe to take daily.
- Take with 8 oz of water and food if possible to help decrease any side-effects

Other important things to consider:
- We are still learning about the effects of DoxyPEP on "good" bacteria of the gut, changes to the bacteria that live on our skin (for example staph), and possible changes in resistance to STIs such as gonorrhea.
- Although doxycycline has been used for decades, there has been no resistance to doxycycline in chlamydia or syphilis.
- If you are having symptoms of an STI, come in to get tested and treated - otherwise continue your routine testing every 3 months.
- Doxycycline is not advised for persons that are pregnant/breastfeeding.

We may reach out to you through MyChart at some point in the next few months to see how your experience with DoxyPEP has been going. This helps us to learn, make changes, and help others.
By the end of 2023, 1712 pts received doxyPEP prescriptions
• STI testing frequency increased, while percent positive tests for syphilis and CT were decreased, c/w clinic level impact
Comparison of DoxyPEP users with other men screened for a bacterial STI (bSTI) at Fenway Health (N=4,927; >1100 doxyPEP users, Fall 2023)

<table>
<thead>
<tr>
<th>Variable</th>
<th>DoxyPEP Users</th>
<th>DoxyPEP Non-Users</th>
<th>O.R.</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrEP Users</td>
<td>73.8%</td>
<td>39.9%</td>
<td>4.25</td>
<td>3.67-4.93</td>
</tr>
<tr>
<td>Private Insurance</td>
<td>85.4%</td>
<td>71.3%</td>
<td>2.37</td>
<td>1.96-2.81</td>
</tr>
<tr>
<td>bSTI dx in 2022</td>
<td>31.3%</td>
<td>15.0%</td>
<td>1.67</td>
<td>1.42-1.98</td>
</tr>
<tr>
<td>PLHIV</td>
<td>8.6%</td>
<td>18.1%</td>
<td>0.42</td>
<td>0.34-0.53</td>
</tr>
</tbody>
</table>

DoxyPEP uptake:
- 24.1% of patients with an active PrEP prescription
- 4.8% of PLHIV
- 13.7% of those screened for a bSTI in 2022
- 24.7% of those diagnosed with a bSTI in 2022
National Survey of Antibiotic Prophylaxis (Trager et al, CROI 2024)

903 respondents recruited on MSM sex networking sites, Sept 2023

Demographics

Mean age = 42 years

866 (96%) were assigned male sex at birth
Of which 96% identified as gay or bisexual male

19% living with HIV
42% using HIV PrEP
US Survey Of MSM STI Antibiotic Prophylaxis
(Traeger Et Al)
903 MSM Recruited Via Sex Networking Apps

Almost 20% used another antibiotic besides doxycycline
Preliminary results (Traeger et al)

45% had used antibiotics before sex
72% had used it after sex

With casual sex partner in the past 12m:
47% used it some of the time
32% used it most of the time
21% used it all of the time

For DoxyPEP users
24% had used a dosage other than a single 200mg dose (recommended)

When using antibiotics around the time of sex to prevent getting an STI, which antibiotics have you used?

- **Doxycycline**: 78.1%
- **Amoxicillin**: 18.8%
- **Azithromycin**: 16.4%
- **Penicillin**: 13.3%
- **Not sure**: 7.8%
- **Erythromycin**: 4.7%
- **Ceftriaxone**: 1.6%
- **Ciprofloxacin**: 1.6%

Where did you get the antibiotics?

- A doctor or clinician prescribed them to me: 60.2%
- I had leftover antibiotics from treatment of something else: 19.5%
- A friend or partner gave them to me: 18.8%
- I bought them online WITHOUT Prescription: 11.7%
- I had leftover antibiotics from treatment of past STI: 10.2%
- I bought them online WITH a prescription: 10.2%
- Other: 5.5%
Conclusions

• DoxyPEP scale up was feasible and highly acceptable at a Boston community health center
• Attention to ensuring equity remains important
• Early suggestions that doxyPEP roll-out may be having a local population impact need further study
• National data suggest high levels of interest and some possible misuse of antibiotic prophylaxis
• Community and provider education and clear guidelines are important in order to enhance optimal uptake.
Thank You

Taimur Khan, Doug Krakower, Jess Kraft, Julia Marcus, Sy Gitin, Michael Traeger

NCSD, NACCHO and CDC (Rebekah Horowitz, Lucy Slater, Lindley Barbee)