Studies Show Longer-Term Benefits of DoxyPEP for STI Prevention

San Francisco clinic sees significant drop in sexually transmitted infections despite quite low adherence to doxycycline prophylaxis over time.

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A growing body of research confirms that taking the antibiotic doxycycline after sex—an approach known as doxyPEP—reduces the risk of sexually transmitted infections (STIs). Two studies presented at the recent Conference on Retroviruses and Opportunistic Infections (CROI 2025) looked at longer-term doxyPEP use in San Francisco, the city that rolled it out first.

Doxycycline post-exposure prophylaxis involves taking a single 200 milligram dose of the antibiotic within 72 hours after sex. Results from the DoxyPEP trial, first presented at the 2022 International AIDS Conference, showed that it lowered the risk for chlamydia and syphilis among gay men and transgender women who were either living with HIV or on pre-exposure prophylaxis (PrEP); results showed a smaller but still significant decline in the risk for gonorrhea. However, the dPEP Kenya trial, reported the following year, found that this approach did not work well for cisgender women in Africa.

The two new studies looked at doxyPEP implementation at the San Francisco AIDS Foundation's Magnet sexual health clinic in the Castro neighborhood, which primarily serves gay and bisexual men and gender-diverse people.

In October 2022, San Francisco was the first city to recommend doxyPEP. As reported at last year's CROI and in JAMA Internal Medicine, prophylactic doxycycline appears to have contributed to a 50% decline in chlamydia and syphilis citywide, though there was little effect on gonorrhea.

DoxyPEP and STI Rates

Hyman Scott, MD, MPH, medical director at the San Francisco AIDS Foundation, and colleagues evaluated the sustained impact of doxyPEP on STI incidence over a two-year period. He previously reported one-year data at CROI 2024.

[Update: The latest data were published in Clinical Infectious Diseases in May.]

Magnet began rolling out doxyPEP in November 2022, offering it to all clients who received HIV

PrEP or other sexual health services at the clinic. The reception was enthusiastic, and initial doxyPEP demand and uptake were high.

This analysis included 2,524 people who were prescribed doxyPEP at any time through September 2024—about double the number in last year's report—along with 2,068 nonusers. For users, the researchers included data from up to five quarters before and after the initial prescription; for nonusers, they looked at data for up to five quarters before and after April 2023.

About 90% were cisgender men, about 10% were transgender or nonbinary and the median age was 35 years. About a third were white, 24% were Latino, 16% were Asian, 13% were multiracial and 4% were Black. (For comparison, San Francisco's population is approximately 38% non-Hispanic white, 37% Asian, 16% Latino and 6% Black.) Demographic characteristics were similar between the two groups. More than 90% were on HIV PrEP, mostly daily pills.

Before starting doxyPEP, users had nearly a fourfold higher risk of STIs compared with nonusers. In the pre-doxyPEP period, STIs were rising steeply among users and falling among nonusers. In the post-doxyPEP period, there was a substantial drop in STIs among doxyPEP users while nonusers saw an ongoing shallow decline, so the difference between the two groups diminished.

Among doxyPEP users, syphilis declined by 89%, chlamydia by 81% and gonorrhea by 44%. All three reductions were statistically significant and sustained throughout the follow-up period. Scott noted that this is the first real-world data showing a nearly 50% decline in gonorrhea, in line with the DoxyPEP trial.

"DoxyPEP uptake continues to increase, and bacterial STI incidence among doxyPEP users declined significantly overall and for each STI, including gonorrhea, demonstrating sustained high impact of this intervention in a real-world setting," the researchers concluded. These findings indicate that those who could benefit most from doxyPEP are choosing it, according to Scott.

Asked why this study showed better efficacy against gonorrhea than others, Scott suggested that longer follow-up may play a role. In addition, although doxyPEP guidelines say doxycycline can be taken up to 72 hours after sex, Magnet advises that clients take it within 24 hours—as the "last load of the night"—when it's more likely to be effective.

DoxyPEP Care Continuum

In the second study, Michael Barry, PhD, MPH, and colleagues at the SF AIDS Foundation looked at the doxyPEP continuum of care among Magnet clients who were eligible for doxycycline prophylaxis according to San Francisco Department of Public Health guidelines and had at least two visits between December 2022 and December 2024.

Among the 7,436 clients with a doxyPEP indication, 59% received a prescription, according to their medical records. Of these, 61% (or 36% of the total eligible group) reported taking at least one dose of doxycycline. Of those, 61% (or 22% of the eligible group) reported high adherence,

defined as consistent use within 72 hours after sex since their last visit.

The researchers saw some notable demographic differences across the continuum. Among people eligible for doxyPEP, those between ages 36 and 44 were more likely to receive a prescription than those ages 14 to 29 (64% versus 53%). Transgender women were most likely to be prescribed doxyPEP (69%) and trans men the least likely (39%). While 60% of people with stable housing were prescribed doxyPEP, this fell to 48% for those who were unstably housed or homeless. HIV-negative PrEP users were more likely to receive doxyPEP than the smaller groups of HIV-negative people not on PrEP or HIV-positive people (71%, 44% and 56%, respectively).

Among those prescribed doxyPEP, the 36–44 age group was more likely to take it at least once compared with younger people (66% versus 57%). White people were more likely to start doxyPEP compared with Black people (63% versus 55%), stably housed people were more likely to do so than those without stable housing (62% versus 47%), and HIV-negative people on PrEP were more likely to do so than HIV-positive people (62% versus 50%).

Among those who took at least one dose of doxycycline, those ages 45 and older were more likely to maintain high adherence compared to the youngest group (68% versus 58%), as were HIV-negative PrEP users compared to HIV-positive people (63% versus 50%).

Looking at the total population with a doxyPEP indication, high adherence was less likely among young people (17%), Black people (19%), unstably housed or homeless people (13%) and people living with HIV (14%).

Barry noted that the dramatic declines in STIs reported by Scott occurred despite “somewhat low adherence” to doxyPEP over time. “We’re seeing population-level impacts very likely due to doxyPEP uptake, but it could be even higher,” he said. “To ensure equitable population-level impacts of doxyPEP, we might consider giving these patients special consideration.”

After the presentation, researchers in the audience discussed how best to define good adherence to doxyPEP, as it might not be needed for all sexual encounters. For example, someone might use doxyPEP after a sex party but not after sex with a regular partner.

“I think our patients are very savvy at knowing which partners or which situations or which encounters will benefit from using this medication,” Barry said at a conference news briefing.

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