DoxyPEP Rollout Leads to Drop in STIs in San Francisco

Results from clinical practice and population analyses confirm that doxyPEP prevents chlamydia and syphilis but has less effect on gonorrhea.

March 5, 2024 By Liz Highleyman

Taking doxycycline after sex helped reduce the incidence of sexually transmitted infections (STIs) in San Francisco, according to real-world studies presented this week at the Conference on Retroviruses and Opportunistic Infections (CROI 2024) in Denver.

Doxycycline post-exposure prophylaxis—better known as doxyPEP—involves taking a single 200 milligram dose of the antibiotic within 72 hours after sex. In October 2022, San Francisco was the first city to recommend doxyPEP for gay and bisexual men and transgender people. Over the next year, chlamydia cases dropped steeply and syphilis also fell, but the decline in gonorrhea was minimal. The new results from clinical practice and population-level analyses are consistent with findings from recent clinical trials.

Hyman Scott and Madeline Sankaran at CROI 2024Liz HIghleyman

“The evidence now overwhelmingly supports the use of doxyPEP for STI prevention, and we see benefits of an aggressive rollout to the populations who are most likely to benefit,” said San Francisco Department of Public Health (SF DPH) researcher Hyman Scott, MD, MPH. “Despite reservations about widespread adoption, including concerns about antimicrobial resistance, the proactive distribution of doxyPEP stands poised as a powerful tool to prevent STIs across our communities.”

DoxyPEP Clinical Trials

In 2017, Jean-Michel Molina, MD, of the University of Paris Cité, reported that doxyPEP lowered the risk of chlamydia and syphilis by about 70% for gay and bisexual men in the French IPERGAY trial, but there was not a significant reduction in gonorrhea. At CROI, he reported final results from the DoxyVAC trial, showing that doxycycline reduced the risk of chlamydia by 86% and syphilis by 79%, while gonorrhea fell by only 33%.

The DoxyPEP trial enrolled more than 500 gay and bisexual men and transgender women in San Francisco and Seattle who were either living with HIV or taking pre-exposure prophylaxis (PrEP). At the 2022 International AIDS Conference, Annie Luetkemeyer, MD, of the University of California San Francisco first reported that people randomly assigned to take doxycycline after sex saw about an 80% reduction in chlamydia and syphilis and about a 55% reduction in gonorrhea compared with standard care.

At CROI, she reported results from an open-label extension of the trial, showing that risk reduction was sustained among participants initially assigned to doxycycline. Among those initially assigned to standard care and offered doxyPEP after the study was unblinded and its effectiveness was known, STI incidence fell steeply even though their number of sex partners and condomless sex acts doubled in the short term.

In contrast, the dPEP Kenya trial found that doxyPEP did not offer the same benefits for young cisgender women in Africa. There were no significant differences in chlamydia or gonorrhea incidence between those who took doxycycline after sex and those who received standard care; syphilis was rare in both groups. The researchers suggested this was likely due to suboptimal adherence, though a high prevalence of drug-resistant gonorrhea may have also played a role.

DoxyPEP in Clinical Practice

In October 2023, the Centers for Disease Control and Prevention (CDC) released the first national doxyPEP guidelines, recommending that doxycycline should be considered for cisgender men who have sex with men and transgender women who have had an STI in the past year.

In keeping with its history of leading the fight against HIV, SF DPH was ahead of the game, issuing its own doxyPEP recommendations a year earlier. The city’s guidance goes beyond the CDC’s and includes trans men and nonbinary people as well as people with multiple sex partners who haven’t recently had an STI.

“San Francisco has long been a center of innovation, and our early implementation of doxyPEP is an excellent example of public health experts, researchers and community coming together and taking the lead in addressing our most critical health issues,” San Francisco health officer Susan Philip, MD, MPH, said in a news release.

Scott reported early results from the San Francisco AIDS Foundation’s Magnet sexual health clinic, where doxyPEP was offered to about 3,000 active PrEP users starting in late November 2022. The clinic gives clients an initial supply of doxycycline and provides more if they can’t afford it. “We don’t want insurance and access to be a barrier,” he said.

Gay and bisexual men in San Francisco were early adopters of HIV PrEP, and the same is true for doxyPEP. Doxycycline use ramped up steadily, reaching 1,209 people (39% of all PrEP users) by September 2023. Although most recipients were cisgender men, transgender women (42%) and nonbinary people (44%) also had high uptake; about 25% of trans men opted for doxyPEP. Scott said the clinic does not refuse to give doxyPEP to cisgender women, but they are counseled that data so far are discouraging. White, Black, Latino and Asian PrEP users were about equally likely to opt for doxycycline. But due to disparities in PrEP use, doxyPEP uptake is still not equitable (33% white, 26% Latino, 16% Asian and 4% Black).

This analysis compared quarterly STI incidence before the guidelines (June through November 2022) and 30 days after doxyPEP initiation. Among people who started doxyPEP, overall STI incidence fell by 58%. Among those who decided against doxyPEP—presumably a group at lower risk—the incidence didn’t change much, falling from 8% to 7%. But as in the clinical trials, the decrease was greater for chlamydia (67%) and early syphilis (78%) than for gonorrhea (a nonsignificant 11% drop).

DoxyPEP demonstrated a “high impact” in a real-world setting, according to Scott. “When we opened this up and offered it as part of routine sexual health services, there was a strong demand,” he told reporters. “We’ve been really impressed by how much our community wanted this, how many people took it when it was available and what the impact of it was, both quite dramatic and quick.”

“For so long, we have only been able to rely on condoms for STI prevention—and we know that condoms don’t work for everyone,” Jorge Roman, Magnet’s senior director of clinical services, said in a news release. “It is exciting to have a new tool that we can make available for STI prevention.”

In a poster at the conference, SF DPH researcher Oliver Bacon, MD, MPH, and colleagues reported early data from City Clinic, San Francisco’s main public sexual health clinic. They compared STI incidence before (November 2021 through November 2022) and after (November 2022 through November 2023) the local doxyPEP guidelines were issued.

Among 506 PrEP users with visits during both time periods, 73% started doxyPEP. Positive chlamydia tests declined by 90% among doxyPEP users compared with 27% among nonusers. Positive early syphilis tests decreased by 56% and 32%, respectively; this difference was not

statistically significant, but the number of cases was small. Gonorrhea positivity actually declined less in the doxyPEP group (by 23% and 32%, respectively), but this difference was also not significant.

The lack of a decline in gonorrhea may be related to drug resistance, or adherence may have been lower compared with the randomized trials, the researchers suggested. According to Luetkemeyer, tetracycline resistance occurs along a spectrum, and we don't know what level would make doxycycline ineffective. What's more, doxyPEP might work better against gonorrhea if it's taken sooner after sex.

Population-Level Trends

Two other studies assessed the impact of doxyPEP in a different way, looking at changes in STI incidence at the population level.

SF DPH epidemiologist Madeline Sankaran and colleagues tracked the number of people starting doxyPEP at three high-volume sexual health clinics—Magnet, City Clinic and San Francisco General Hospital's Ward 86. They looked at changes in monthly cases of chlamydia, early syphilis and gonorrhea before (July 2021 through October 2022) and after (November 2022 through November 2023) the release of the city guidance.

More than 3,700 men who have sex with men and transgender women started doxyPEP at the three clinics by the end of 2023. Citywide, chlamydia cases among this population declined by 50% relative to predicted levels, while early syphilis decreased by 51%. But again, there was no significant change in gonorrhea cases. At the same time, chlamydia cases among cisgender women rose, which "strengthens the conclusion that the decline in chlamydia and early syphilis cases [among gay men and trans women] is related to doxyPEP rollout," Sankaran said.

Other factors may have contributed to the observed STI trends, including disruptions in screening in the wake of COVID-19 and behavior change in response to the pandemic and the 2022 mpox outbreak, Sankaran noted. A CDC survey found that more than half of gay men reported changing their sexual behavior to avoid mpox—for example, by having fewer sex partners.

"STIs are preventable, and having another tool to protect the sexual health of San Franciscans is a huge step forward," said Stephanie Cohen, MD, MPH, SF DPH's director of HIV/STI prevention. "We will continue to carefully monitor citywide trends in STIs to confirm that these early promising findings result in sustained declines and to better understand additional factors contributing to STI rates."

Finally, Jeffrey Klausner, MD, MPH, medical student Andy Liu and colleagues from the University of Southern California assessed STI trends by reviewing publicly available monthly reports on rectal chlamydia, rectal gonorrhea and syphilis cases among men in San Francisco. They looked at data from April 2020 through July 2023, attempting to account for the effects of COVID-19. All three STIs rose from April 2020 through December 2021. After that, rectal chlamydia was stable until the city guidelines were issued, at which point it declined sharply. Rectal gonorrhea and syphilis were

already decreasing each month before the guidelines, and both continued to fall.

Taken together, these studies provide a solid body of evidence that doxyPEP is an effective intervention for reducing new cases of chlamydia and syphilis, although it is less effective against gonorrhea.

“It’s not often in public health that you have population level surveillance in concordance with clinical service delivery in concordance with clinical trial results, all at the same time,” CROI chair Landon Myer, MD, of the University of Cape Town, said at the media briefing. “This, to my mind, seals the case.”

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