DoxyPEP Helps Reduce Sexually Transmitted Infections in California

Two real-world studies find that doxycycline after sex has contributed to lower rates of chlamydia and syphilis.

January 8, 2025 By Liz Highleyman

A dose of the antibiotic doxycycline after sex—an approach known as doxyPEP—helped reduce the risk of bacterial sexually transmitted infections (STIs) in Northern California, according to a pair of real-world studies published this week. Rates of chlamydia and syphilis notably declined, though there was less effect on gonorrhea.

“Our study suggests that doxyPEP may be turning the rising tide on chlamydia and syphilis, which had been seemingly endless, while important questions remain about gonorrhea and antibiotic resistance,” Julia Marcus, PhD, MPH, of Harvard Pilgrim Health Care Institute in Boston, the senior author of one of the reports, told POZ.

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 of chlamydia and syphilis for gay men and transgender women, with a smaller but still significant decline in gonorrhea. However, the dPEP Kenya trial, reported the following year, found that this approach did not work well for cisgender women in Africa.

Now, the newly published studies show that doxyPEP is starting to make a difference in the real world in cities that rolled it out early.

San Francisco DPH Study

In October 2022, San Francisco was the first city to recommend prophylactic doxycycline. The city’s latest guidance goes beyond the Centers for Disease Control and Prevention’s 2023 national doxyPEP guidelines, offering it for transgender men and nonbinary people as well as cisgender men who have sex with men and trans women, and including those who have not recently had an STI.

San Francisco Department of Public Health epidemiologist Madeline Sankaran, MPH, and colleagues compared monthly cases of chlamydia, gonorrhea and early syphilis before (July 2021

through October 2022) and after (November 2022 through November 2023) the city issued its guidance.

More than 3,900 men who have sex with men and transgender women started doxyPEP at three sentinel clinics—City Clinic, San Francisco General Hospital's Ward 86 and the San Francisco AIDS Foundation's Magnet clinic—by the end of 2023. This is an underestimate of citywide use, as health systems such as Kaiser Permanente and independent practitioners also provide doxyPEP.

The results, first reported at last year's Conference on Retroviruses and Opportunistic Infections (CROI) and now published in JAMA Internal Medicine, showed that, overall, STIs declined significantly after doxyPEP implementation. Citywide, there were 6,694 cases of chlamydia, 9,603 cases of gonorrhea and 2,121 cases of early syphilis among gay men and trans women during the study period. Over 13 months, chlamydia cases fell by 50% relative to predicted levels, while early syphilis decreased by 51%. However, there was a small but statistically significant increase in gonorrhea.

"This study suggests that San Francisco's doxyPEP guideline release was associated with decreases in reported cases of chlamydia and early syphilis, but not gonorrhea, among [men who have sex with men] and transgender women in San Francisco," the study authors concluded. "Supporting doxyPEP implementation for [men who have sex with men] and transgender women at risk for STIs could have a significant impact on the nationwide STI epidemic."

The researchers acknowledged that further analysis is needed to assess whether these declines in STIs will be sustained and to monitor for adverse consequences of doxyPEP use, including antibiotic resistance.

In their discussion of the findings, they noted that they "cannot definitively rule out that these declines were due to or affected by other factors." At CROI, Sankaran said that changes in STI screening in the wake of COVID-19 and sexual behavior change in response to the 2022 mpox outbreak might have influenced the results.

Nonetheless, the abrupt decrease in cases among gay men after a decade of rising STI rates, as well as the fact that there was no corresponding decline in chlamydia along cisgender women—a group not indicated for prophylactic doxycycline—suggest that doxyPEP is having a real effect.

Kaiser Northern California Study

In the second study, also published in JAMA Internal Medicine, Marcus and colleagues analyzed doxyPEP use and STI rates among people receiving HIV pre-exposure prophylaxis (PrEP) through Kaiser Permanente Northern California, an integrated health system that covers the San Francisco Bay Area and surrounding counties, including the cities of Oakland, San Jose, Santa Cruz and Sacramento. Using electronic health records, the researchers followed participants from their first recorded STI test in November 2020 or later through the end of December 2023, comparing STI rates before and after doxyPEP initiation.

“Our patients have enthusiastically embraced this proactive approach to reduce their STI risk,” study coauthor Jonathan Volk, MD, MPH, of Kaiser Permanente San Francisco, said in a news release. “After doxyPEP became available for our PrEP patients, we have seen a dramatic decline in positive STI tests and less need for treatment after STI exposures.”

Between November 2022 and December 2023, a total of 11,551 people received PrEP. Within this population, 2,253—nearly one in five—also received doxyPEP. Most doxyPEP recipients were gay or bisexual men, and nearly half had an STI during the prior year. On average, they were older and had used PrEP longer than people who did not receive doxyPEP.

Among doxyPEP recipients, quarterly STI rates dropped significantly after they started using prophylactic doxycycline. Chlamydia fell by 79% (from 9.6% to 2.0%) and syphilis declined by 80% (from 1.7% to 0.3%). The 12% decrease in gonorrhea (from 10.2 to 9.0%) was less impressive, but still statistically significant. Specifically, declines were significant for rectal and urethral gonorrhea, but not for pharyngeal (throat) gonorrhea. In contrast, no changes in STI rates were observed during the same period for people who did not use doxyPEP.

“This study found that receipt of doxyPEP was associated with substantial declines in chlamydia and syphilis incidence and modest declines in urethral and rectal gonorrhea incidence among individuals using HIV PrEP. These findings suggest that doxyPEP may offer substantial benefits for reducing population-level STI transmission with broader implementation,” the study authors concluded.

“These modest reductions in gonorrhea rates reinforce the importance of regular STI testing for patients on doxyPEP and the need for novel prevention strategies for gonorrhea prevention, like vaccines that are currently in development,” Volk added.

Study Implications

Taken together, these studies add to the growing body of evidence that doxyPEP is an effective intervention for reducing chlamydia and syphilis, although it is less effective against gonorrhea.

In an invited commentary accompanying the two reports, National Institute of Allergy and Infectious Diseases (NIAID) director Jeanne Marrazzo, MD, MPH, and Jodie Dionne, MD, MPH, of the University of Alabama at Birmingham, cautioned that the mixed results on gonorrhea and the potential for drug resistance point to the need to closely track the development of antimicrobial resistance among doxyPEP users and to include measures of drug resistance in all doxyPEP studies.

While studies so far do not suggest that doxyPEP has caused an increase in drug-resistant STI bacteria, the fact that resistant Neisseria gonorrhoeae is already common may help explain why prophylactic doxycycline does not work as well against gonorrhea as it does against chlamydia and syphilis. Among people at high risk for STIs, those who use doxyPEP may actually end up using less antibiotics than people receive a full course of treatment after becoming infected.

“These reports are part of the crucial scientific process of translating clinical research to implementation at scale,” Marrazzo said in a NIAID news release. “DoxyPEP is proving to be an important intervention in our effort to decrease STI incidence while we continue to invest in research to develop safe and effective preventive vaccines and next-generation antibiotics.”

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