

DoxyPEP Effectiveness Against Gonorrhea Is Declining

DoxyPEP protection fell as antibiotic resistance rose in a Southern California study.

May 13, 2026 By [Liz Highlyman](#)

DoxyPEP is becoming less effective against gonorrhea as antibiotic resistance rises, even as protection against chlamydia and syphilis remains durable, according to study results published in [The Lancet Infectious Diseases](#).

“We report a rapid loss of effectiveness of doxycycline PEP for prevention of gonorrhea in male individuals living with HIV or receiving HIV PrEP or PEP in Southern California,” the authors wrote, noting that their findings might merit revision of guidelines recommending doxyPEP for gonorrhea prevention.

[DoxyPEP](#) refers to taking a single dose of doxycycline—an antibiotic related to tetracycline—as post-exposure prophylaxis within 72 hours after sex to prevent sexually transmitted infections (STIs). Clinical trials and real-world evidence have shown that doxyPEP dramatically reduces the risk of [chlamydia](#) and [syphilis](#) among gay and bisexual men and transgender women, though its effectiveness against [gonorrhea](#) is modest at best.

The [first large trial of doxyPEP](#), which enrolled more than 500 men and transgender women who have sex with men in San Francisco and Seattle, showed that it reduced the likelihood of chlamydia and syphilis by about 75% for HIV-positive participants and by nearly 90% for those on HIV pre-exposure prophylaxis (PrEP), while gonorrhea declined by about 55% in both groups.

At the 2024 Conference on Retroviruses and Opportunistic Infections, researchers with the San Francisco Department of Public Health reported that the early rollout of doxyPEP contributed to [a citywide decline in STIs overall](#), though there was no significant change in gonorrhea.

[Another recent study](#) found that syphilis cases in Seattle dropped by 52% overall after the implementation of doxyPEP for gay men and transgender women. But the number of pregnant women diagnosed with syphilis increased between March 2023 and June 2025, and the number of cases of congenital syphilis transmitted from mother to child rose from 0 to 23, suggesting that cisgender women and their babies could benefit from doxyPEP as well.

[Antibiotic resistance](#) limits the effectiveness of doxyPEP for preventing gonorrhea, and the growing

use of doxycycline for STI prevention may be contributing to [an increase in drug resistance](#). For example, a study described in [The New England Journal of Medicine](#) found that the proportion of U.S. gonorrhea samples carrying a gene variant called tetM, which confers resistance to tetracycline, rose from less than 10% in 2020 to over 30% in the first quarter of 2024, coinciding with the rollout of doxyPEP.

In the new study, Matan Yechezkel, PhD, of the University of California Berkeley, and colleagues assessed the durability of doxyPEP effectiveness against gonorrhea after its implementation in Southern California.

This retrospective analysis included 26,582 people at Kaiser Permanente Southern California who were assigned male at birth, were either living with HIV or using HIV PrEP and had at least one STI test between January 2023 and June 2025. Of these, 2,262 (about 9%) used doxyPEP.

Throughout the study period, doxyPEP was 67% effective against chlamydia and 61% effective against syphilis, but there was no protection against gonorrhea. The effectiveness of doxyPEP against gonorrhea declined from 42% before the statewide doxyPEP rollout to -15% in 2025, in association with a rapid increase in the presence of gonorrhea carrying tetM. DoxyPEP effectiveness was 47% during periods when about a quarter of *Neisseria gonorrhoea* samples had the resistance variant, falling to -9% when half or more were resistant. Negative effectiveness means people who used doxyPEP were actually more likely to be diagnosed with gonorrhea.

“Whereas we report sustained doxycycline PEP effectiveness against chlamydia and syphilis more than two years after doxycycline PEP implementation, our findings suggest protection against gonorrhea might not be durable,” the study authors wrote. “Risk-benefit considerations for doxycycline PEP implementation strategies should assume limited or transient benefits associated with gonorrhea prevention and address potential consequences of antimicrobial resistance expansion in *N. gonorrhoeae*.”

The researchers estimated that doxyPEP effectiveness against gonorrhea reached 0% between March and June 2024, or 11 to 14 months after implementation of doxyPEP in

California. Despite low overall uptake, doxyPEP recipients may “wield outsized influence on broader sexually transmitted infection transmission dynamics,” they suggested.

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