Sexually transmitted infections in San Francisco have fallen since doxyPEP roll-out

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Professor Annie Luetkemeyer and Dr Hyman Scott at CROI 2024. Photo by Liz Highleyman.

Taking the antibiotic doxycycline after sex appears to have lowered the incidence of sexually transmitted infections (STIs) in San Francisco, according to researchers who presented some of the earliest real-world data yesterday at the <u>Conference on Retroviruses and Opportunistic Infections (CROI 2024)</u>.



Find out more: Using antibiotics to prevent STIs

In October 2022, San Francisco was the first city to recommend doxycycline post-exposure prophylaxis, or doxyPEP, for gay and bisexual men and transgender people. Over the ensuing year, chlamydia cases dropped steeply and syphilis also fell, but there was little decline in gonorrhoea. Results from clinical practice and population-wide analyses are consistent with findings from recent clinical trials, suggesting that doxyPEP is in demand and is already making an impact on STI incidence.

"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 Professor Landon Myer of the University of Cape Town said at a media briefing. "This, to my mind, seals the case."

DoxyPEP in clinical trials

DoxyPEP involves taking a single 200mg dose of doxycycline within 72 hours after sex. In 2017, Professor Jean-Michel Molina of the Paris Cité University reported that doxyPEP <u>lowered the risk of chlamydia and syphilis</u> by about 70% for gay and bisexual men in the IPERGAY pre-exposure prophylaxis (PrEP) trial, though there was not a significant reduction in gonorrhoea. Yesterday, he reported <u>final results from the DoxyVAC trial</u>, showing that doxycycline reduced the risk of chlamydia by 86% and syphilis by 79%, but gonorrhoea by only 33%;

the study also found that a vaccine did not provide significant protection against gonorrhoea.

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 PrEP. In 2022, Professor Annie Luetkemeyer of the University of California San Francisco <u>first reported</u> that HIV-positive people randomly assigned to take doxycycline after sex saw a 74% reduction in chlamydia, a 77% decrease in syphilis and a 57% reduction in gonorrhoea per quarter compared with standard care. Among HIV-negative participants on PrEP, the corresponding risk reductions were 88%, 87% and 55%.

At this year's CROI, Luetkemeyer reported results from an open-label extension of the trial, showing that STI 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 sharply 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 <u>did not offer the same</u> <u>benefits</u> for young cisgender women. There were no significant differences in chlamydia or gonorrhoea incidence between those who took doxycycline after sex and those who received standard care; syphilis was rare in both groups.

DoxyPEP in clinical practice

Last October, the US Centers for Disease Control and Prevention (CDC) <u>released the first national doxyPEP guidelines</u>, stating that the intervention should be considered for cisgender men who have sex with men and transgender women who have had an STI at least once during the past year.

The San Francisco Department of Public Health (SF DPH) was ahead of the game, <u>issuing doxyPEP recommendations a year earlier</u> and getting a head start on compiling real-world data. San Francisco's guidance goes beyond the CDC's, including trans men and non-binary people and applying to those with multiple sex partners even if they haven't recently had an STI. <u>More news from United States</u>

Dr Hyman Scott reported early results from the San Francisco AIDS Foundation's Magnet sexual health clinic, where doxyPEP has been offered to around 3000 active PrEP users starting in late November 2022. The analysis compared quarterly STI incidence before the recommendation (June through November 2022) and 30 days after doxyPEP initiation.

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 1209 people (39% of all PrEP users) by September 2023. White, Black, Asian and Latino PrEP users were about equally likely to opt for doxycycline (around 40%). However, because White gay men are much more likely to be on PrEP than Black men, with Latino and Asian men falling in between, disparities are perpetuated.

Among people who started doxyPEP, overall STI incidence fell from 18% to 8%, representing a 58% decrease. Among those who did not accept doxyPEP, incidence didn't change much, falling from 8% to 7%. As in the clinical trials, the decrease was greater for chlamydia (a 67% drop) and early syphilis (a 78% drop) than for gonorrhoea (an 11% drop that wasn't statistically significant).

DoxyPEP demonstrated a "high impact" in a real-world setting, Scott concluded. "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."

More news from CROI 2024

"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," he added in a <u>press</u> release.

In a poster at the conference, Dr Oliver Bacon and colleagues reported early data from City Clinic, San Francisco's main sexual health clinic. They compared STI incidence before (November 2021 to November 2022) and after (November 2022 to November 2023) the local doxyPEP guidelines were issued.

Among 506 PrEP users with visits during both time periods, 367 (73%) started doxyPEP. Positive chlamydia tests declined by 90% among doxyPEP users compared with 27% among non-users. Positive early syphilis tests decreased by 56% and 32%, respectively; this difference was not statistically significant, but the number of cases was small. Gonorrhoea positivity actually declined less

in the doxyPEP group (by 23% vs 32%), but this difference was also not statistically significant.

Uptake of doxyPEP was high among gay men and transgender women receiving PrEP, and those who did so "had significantly reduced chlamydia and early syphilis positivity," unlike PrEP users who did not start doxyPEP during the same period, the researchers concluded. The lack of a decline in gonorrhoea may be related to drug resistance, or adherence may have been lower compared with randomised trials, they suggested.

STIs at the population level

Epidemiologist Madeline Sankaran and colleagues assessed the impact of doxyPEP in a different way, looking at changes in STI incidence at the population level. The researchers tracked the number of people starting doxyPEP at three high-volume sexual health clinics – Magnet, City Clinic and Ward 86 at San Francisco General Hospital – as well as monthly cases of chlamydia, gonorrhoea and early syphilis before (July 2021 through October 2022) and after (November 2022 through November 2023) the release of the city guidance.

<u>Glossary</u>

<u>chlamydia</u> <u>syphilis</u>

transgender

<u>rectum</u>

cisgender (cis)

More than 3700 men who have sex with men and trans women started doxyPEP at the three clinics by the end of 2023, Sankaran reported. Citywide, chlamydia cases in this population declined by 7% per month, for a total decrease of 50% compared with predicted levels. Early syphilis decreased by 3% per month, for a total 51% drop. After 13 months of follow-up, chlamydia and syphilis rates were still going down. But again, there was no significant change in gonorrhoea cases. In contrast, chlamydia cases among cisgender women rose between the two periods, which "strengthens the conclusion" that the decline among gay men and trans women is related to doxyPEP rollout, she said.

Sankaran noted that other factors may have contributed to the observed STI trends, including disruptions in STI screening in the wake of COVID and changes in sexual behaviour in response to the 2022 mpox outbreak. <u>A CDC survey</u> found that more than half of gay men reported changing their sexual behaviour to reduce their risk for mpox, for example, having fewer sex partners. Finally, Professor Jeffrey Klausner, 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 gonorrhoea 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. 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 gonorrhoea and syphilis were already decreasing each month before the guidelines and both continued to fall at a similar rate.

Taken together, these studies provide a solid body of evidence that doxyPEP is an effective intervention for reducing new cases of chlamydia and syphilis, though it is considerably less effective – if at all – against gonorrhoea.

Luetkemeyer noted that tetracycline resistance occurs along a spectrum, and we don't yet know what level would make doxycycline ineffective. What's more, doxyPEP might work better against gonorrhoea if it's taken sooner after sex. "I think we need multiple tools for gonorrhoea prevention," she said.

References

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