# Daily DoxyPrEP May Be Another Option for STI Prevention

Taking the antibiotic doxycycline every day—not just after sex—reduced chlamydia, gonorrhea and syphilis among gay men and women sex workers.

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Doxycycline post-exposure prophylaxis (doxyPEP) for prevention of sexually transmitted infections (STIs) has been big news at recent AIDS conferences, but for people who have sex often, daily doxycycline pre-exposure prophylaxis (doxyPrEP) may also be an effective option, according to two small studies presented at the International AIDS Conference (#AIDS2024) this week in Munich.

DoxyPEP is a single 200 milligram dose of doxycycline taken within 72 hours after anal, vaginal or oral sex. It can be taken on consecutive days if sex is repeated, but no more than one dose in a 24-hour period. DoxyPrEP, in contrast, involves taking half the dose of doxycycline (100 mg) every day.

In a study of HIV-positive gay and bisexual men in Canada, daily doxycycline reduced the risk of chlamydia, gonorrhea and syphilis by about 80% overall compared with a placebo. Another study, which enrolled women sex workers in Japan, saw a 67% reduction in these bacterial STIs.

As previously reported, the DoxyPEP trial showed that doxycycline after sex significantly reduced STI incidence for gay and bisexual men and transgender women in the United States. But a similar study in Africa found that doxyPEP did not significantly lower the risk of STIs among young women, likely due to suboptimal adherence.

The idea of taking doxycycline prophylaxis every day instead of as a morning-after pill is not new. In 2015, Jeffrey Klausner, MD, MPH, now at the University of Southern California, and colleagues reported results from a small pilot study showing that HIV-positive gay and bisexual men who used daily doxycycline were significantly less likely to test positive for chlamydia, gonorrhea or syphilis.

But the use of doxycycline for STI prevention is not without concerns, including antibiotic resistance and disruption of the microbiome, the ecosystem of healthy bacteria that normally live in the gut, vagina and elsewhere.

DoxyPrEP for Gay Men

Troy Grennan, MD, of the British Columbia Centre for Disease Control, and colleagues conducted a pilot study of doxyPrEP for HIV-positive men who have sex with men who were taking daily oral antiretroviral therapy.

The analysis included 52 men in Toronto and Vancouver with a median age of 43 years. They were randomly assigned to receive 100 mg oral doxycycline or a placebo once daily for 48 weeks. They underwent quarterly screening for chlamydia, gonorrhea and syphilis and completed questionnaires about their medication adherence and sexual behavior. In addition, nasal swabs were collected to assess the emergence of doxycycline resistance in people with Staphylococcus aureus.

“We need to provide patients with choice,” Grennan told reporters at a conference news briefing. “One of the assumptions we often make is that we know what patients will prefer, but we just don’t know that.”

Some study participants, for example, said they prefer to take a pill daily rather than as needed because they’re already taking daily meds for HIV and other conditions. Among people who have frequent sex, those who take 100 mg doxycycline daily may end up using less of the drug than those who take the 200 mg PEP dose multiples times per week. What’s more, keeping drug levels constant—rather than starting and stopping—could discourage development of resistance.

More than three quarters of the men completed the study. About 77% in both groups achieved good adherence according to pill counts, Grennan said, and blood drug level analysis is underway. There were no differences between the two groups in terms of sexual behavior, such as the number of partners or condomless sex acts.

At the end of a year, the incidence of chlamydia declined by 92%, syphilis by 79% and gonorrhea by 68% in the doxyPrEP group relative to the placebo group. Daily doxycycline was especially protective against chlamydia: There was one case in the doxyPrEP group versus 13 in the placebo group. Gonorrhea cases were also lower in the doxyPrEP group (four versus 13), which is notable because some studies have found that doxyPEP does not significantly reduce this STI, and doxycycline-resistant gonorrhea is common in Canada. Syphilis cases were low in both groups (one versus five cases, respectively).

Daily doxycycline was generally well tolerated. Adverse events were mostly mild, and their frequency was similar in both groups. Samples from three men in the doxyPrEP group and two in the placebo group showed new S. aureus doxycycline resistance. “There was no signal of concern, but the numbers were very small, so it’s really hard to draw any definitive conclusions,” Grennan said.

These findings support further investigation of doxyPrEP as STI prevention intervention, the researchers concluded.

To that end, the DISCO study is comparing doxyPrEP versus doxyPEP for gay and bisexual men. The trial should be fully enrolled with 560 participants by next summer, with full data expected in

mid-2026, Grennan said. “We really need to look at other key populations, like cisgender women and youth, who are always ignored in STI and HIV research,” he added. “And we really need to do some work on implementation of these interventions in an equitable way.”

## DoxyPrEP for Women

In the second study, Seitaro Abe, MD, of the National Center for Global Health and Medicine in Japan, and colleagues evaluated daily doxycycline prophylaxis for cisgender women sex workers, looking at its effect on STI incidence and changes in the vaginal microbiome.

The study recruited women at a private STI clinic in Tokyo. After a discussion of the potential benefits and harms, the women and their providers could opt for daily doxyPrEP based on shared decision-making. The women were tested regularly for chlamydia, gonorrhea and syphilis, and the researchers collected vaginal samples to evaluate vaginal flora and test for bacterial vaginosis and candidiasis (yeast infection).

The retrospective analysis included 40 Asian women who started 100 mg daily doxyPrEP. The median age was 29 years. Most reported that they engaged in sex work most days of the week. More than 80% were already taking HIV PrEP, and nearly 90% used contraceptive pills. At their first visit, 18% had chlamydia, 15% had gonorrhea and 57% had bacterial vaginosis; none had syphilis or candidiasis.

During follow-up, STIs declined after starting doxyPrEP, Abe reported. Overall STI incidence rate fell significantly, from 108 to 18 new cases (232.3 to 79.2 cases per 100 person-years), a 67% reduction. There was a marginally significant reduction in chlamydia, from 74 to 13 cases (159.2 to 57.2 per 100 person-years). Gonorrhea fell from 26 to five cases (55.9 to 22.0 per 100 person-years)—a 55% reduction—but this difference was not statistically significant. Syphilis dropped from eight to zero new cases. Bacterial vaginosis fell from 36 to 23 cases, and candidiasis fell from 18 to 12 cases, but neither difference was significant.

The women did get tested more often after starting doxyPrEP, but STI incidence (test positivity) still declined, and bacterial vaginosis and candidiasis still remained stable, when taking this into account.

Here, too, daily doxycycline was safe and well tolerated. About a quarter of the women reported nausea and vomiting, but there were no severe drug-related adverse events. This small study did not address drug resistance.

Among the 22 women who completed surveys, almost all said they “adhered strictly” to doxyPrEP; 73% reported no missed doses. More than 95% reported no change in condom use, according to Abe. Regarding satisfaction, 73% of the women said they felt less anxiety about acquiring STIs, and 32% said that having to take fewer days off from sex work was a benefit. On the other hand, about a third cited cost as a concern.

“DoxyPrEP significantly reduced overall STI rates in cisgender female sex workers without

increasing other vaginal infections," the researchers concluded.

It is not clear why daily doxyPrEP worked well in this study, while doxyPEP was not effective for women in Africa. It could be that daily dosing facilitates good adherence, or perhaps the Japanese sex workers perceived themselves to be at greater risk for STIs or did not face the same barriers to consistent use.

Click here to read the Canada study abstract.
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