# CDC Finalizes DoxyPEP Guidelines

CDC recommends doxycycline after sex for gay men and transgender women at high risk for STI, but others may benefit too.

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The Centers for Disease Control and Prevention (CDC) has issued clinical guidelines for using the antibiotic doxycycline as post-exposure prophylaxis after sex to prevent sexually transmitted infections (STIs), an approach known as doxyPEP. This is a finalized version of draft guidelines released last October.

The CDC recommends that healthcare providers discuss the use of doxyPEP with all gay, bisexual and other men who have sex with men and transgender women who have had chlamydia, gonorrhea or syphilis at least once within the past year. For other groups, providers are urged to use clinical judgement and shared decision-making.

“The new CDC implementation guidance on doxycycline for STI prevention is an important and timely confirmation of the science behind doxyPEP,” Jeffrey Klausner, MD, MPH, of the University of California Keck School of Medicine, told POZ. “Federal guidelines help support widespread use, reimbursement and access, hopefully ensuring no one is left behind.”

STIs are a growing concern in the United States and worldwide. While cases of chlamydia have leveled off in the U.S. after rising for decades, and gonorrhea cases appear to have declined, syphilis cases continue to surge.

“Doxy PEP represents the first new STI prevention tool in decades, at a time when innovation in the nation’s fight against STIs is desperately needed,” said Jonathan Mermin, MD, MPH, director of the CDC’s National Center for HIV, Viral Hepatitis, STD, and TB Prevention.

DoxyPEP involves taking a single 200-milligram dose of doxycycline 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. It is safe to use with oral or injectable HIV pre-exposure prophylaxis (PrEP). Because it’s an antibiotic, doxycycline does not prevent viral STIs such as human papillomavirus (HPV), herpes simplex or mpox (formerly monkeypox).

The new guidelines are supported by findings from the DoxyPEP trial, first presented at the 2022 International AIDS Conference. The study enrolled more than 500 men and transgender women who have sex with men at public health clinics in San Francisco and Seattle. About a third were

living with HIV and the rest were taking PrEP. They were randomly assigned to receive a single dose of oral doxycycline within 72 hours after condomless sex or standard care, which is regular testing and treatment after an STI diagnosis.

The study was halted ahead of schedule after an interim analysis showed that doxyPEP significantly reduced STI incidence. For people with HIV, doxycycline reduced the risk of acquiring gonorrhea by 57%, chlamydia by 74% and syphilis by 77%. For those taking PrEP, the risk reduction was 55%, 88% and 87%, respectively. The French IPERGAY and DoxyVAC studies also showed that doxycycline reduced the risk of chlamydia and syphilis, though the medication and a vaccine were less effective against gonorrhea. DoxyPEP failed to significantly reduce the risk of STIs in a study of cisgender women in Kenya. Although doxycycline appeared to reach adequate concentrations in vaginal and cervical tissue, many participants reported suboptimal adherence.

Earlier this year, public health experts from San Francisco—which issued the first local doxyPEP guidelines in October 2022—reported that implementation has already contributed to a reduction in STIs in the real world.

But preventive use of doxycycline is not without concerns. One is that widespread use of antibiotics could lead to drug resistance. This is especially worrisome for gonorrhea, which is already resistant to many medications. So far, however, researchers have not seen a marked increase in antibiotic resistance associated with doxyPEP. Another is that frequent antibiotic use could disrupt the microbiome, the ecosystem of healthy bacteria that normally live in the gut and elsewhere in the body. Microbiome studies are currently underway.

## Who Can Benefit From DoxyPEP?

According to the new guidelines, published in the June 6 Morbidity and Mortality Weekly Report, providers should offer gay and bisexual men and trans women with a recent history of STIs a prescription for doxycycline so they can self-administer it after sex. The prescription should include enough doses to cover anticipated sexual activity until the next visit. Clinicians should review a patient's other medications and check for drug interactions with doxycycline. People prescribed doxyPEP should be tested for bacterial STIs before starting and then every three to six months. The ongoing need for doxyPEP should be reassessed on the same schedule.

Although it has not been directly assessed in trials, the guidelines say that doxyPEP also could be discussed with men who have sex with men and trans women who have not had an STI within the past year if they expect to participate in sexual activities that are known to increase the likelihood of STI exposure.

The pharmacokinetics of doxycycline and its effectiveness for STI treatment suggest that doxyPEP should work for other groups, including cisgender women, cisgender heterosexual men, transgender men and other queer and nonbinary people, according to the guidelines. But because data from formal studies are lacking, providers "should use their clinical judgement and shared decision-making to inform use of doxyPEP with populations that are not part of CDC

recommendations."

Some local and state guidelines are broader than the CDC's. San Francisco's guidance includes transgender men along with cisgender gay and bisexual men and trans women, and it applies to those who have multiple male sex partners even if they have not recently had an STI. The California Department of Public Health goes further, saying providers can offer doxyPEP to all nonpregnant people at increased risk for STIs and to those who request it even if they have not previously been diagnosed with an STI or have not disclosed their risk status. Seattle's guidelines say providers can consider prescribing doxyPEP on an episodic basis for people who anticipate periods of higher risk. New York state includes men who have condomless sex with multiple female partners—an important consideration given that STI complications can be more severe for women and congenital syphilis in newborn babies is rising.

The inclusion of cisgender women "makes sense because doxycycline is highly effective in treating chlamydia and syphilis in females and a single dose of doxycycline reaches very high tissue levels in female genitalia," Klausner said.

The new guidelines were finalized after careful consideration of comments on the draft version from the public and experts, as well as consideration of the available scientific evidence, according to Mermin and Laura Bachmann, MD, MPH, acting director of the CDC's Division of STD Prevention. They added that the CDC will be providing guidance to funded STI programs across the nation to help them determine how best to use their CDC resources to support doxyPEP implementation.

"We believe this is the right step for right now to protect the nation's health, although we are constantly learning more about how to prevent STIs. We will continue to adjust our recommendations as additional data are available," Bachman and Mermin wrote in a letter to colleagues. "Important questions remain about the effectiveness of this approach for other populations as well as potential long-term development of antimicrobial resistance and impacts on the microbiome. Looking ahead, we will leverage existing data systems to monitor the uptake of doxyPEP and how this impacts bacterial STI rates, understand national doxycycline prescribing rates and identify trends in antimicrobial resistance. As always, we will provide updates as we learn more."

The guidelines authors emphasized that doxyPEP "should be implemented in a context of a comprehensive sexual health approach, including risk reduction counseling, STI screening and treatment, recommended vaccination and linkage to HIV PrEP, HIV care or other services as appropriate."

The new guidelines have generally been well received, but some have concerns about implementation and equitable access.

"Doxycycline is inexpensive, easily tolerated and widely available. However, questions remain regarding who will benefit most from doxyPEP and how to implement this strategy broadly in a

way that will ensure equitable access, especially given the lack of data for cisgender women," Mitchell Warren of AVAC told POZ. "As with any new prevention option, it is essential for advocates to insist on and engage with user-centered, comprehensive and collaborative implementation programs and policies to help make sure the new CDC guidelines are translated into public health impact."

Click here for the full CDC doxyPEP guidelines.

Click here for more news about STIs.

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