CDC Issues First DoxyPEP Guidelines

The federal agency recommends doxycycline after sex to reduce the risk of STIs among gay men and transgender women.

October 4, 2023 By Liz Highleyman

The Centers for Disease Control and Prevention (CDC) has issued its first proposed guidelines for using the antibiotic doxycycline as post-exposure prophylaxis to prevent bacterial sexually transmitted infections (STIs), an approach known as doxyPEP. The guidelines, published in the Federal Register on October 2, will be open for public comment for 45 days.

"Doxy PEP is moving STI prevention efforts into the 21st century," Jonathan Mermin, MD, MPH, director of CDC's National Center for HIV, Viral Hepatitis, STD, and TB Prevention, said in a statement. "We need game-changing innovations to turn the STI epidemic around, and this is a major step in the right direction."

The proposed guidelines state that a single 200 milligram dose of oral doxycycline taken within 72 hours after oral, vaginal or anal sex should be considered for gay, bisexual and other men who have sex with men and for transgender women who have had gonorrhea, chlamydia or syphilis at least once during the past year. This is a strong recommendation supported by data from clinical trials.

The draft also says that doxyPEP "could be considered" for men who have sex with men and transgender women who have not been diagnosed with an STI if they "will be participating in sexual activities that are known to increase likelihood of exposure to STIs, e.g., during weekend events, cruises and festivals," although this has not been directly assessed in trials.

Due to a lack of supporting evidence, however, the guidelines state that "no recommendation can be given at this time" on the use of doxyPEP for cisgender women, cisgender heterosexual men, transgender men or other queer or non-binary people.

According to the guidelines, doxyPEP "should be implemented in the context of a comprehensive sexual health approach including risk reduction counseling, STI screening and treatment, recommended vaccination and linkage to HIV pre-exposure prophylaxis (PrEP), HIV care or other services, as appropriate."

DoxyPEP Research

The draft guidelines are supported by results 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.

The participants were randomly assigned to receive a single dose of oral doxycycline within 72 hours after condomless sex or the standard of care, which is regular testing and treatment following an STI diagnosis.

The study, scheduled to run until May 2023, was halted a year early 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 DoxyVAC trial also showed that doxycycline after sex reduced the risk of acquiring the three STIs. In both studies, adherence was good and doxycycline was generally safe and well tolerated, though the drug can cause side effects including gastrointestinal symptoms, irritation of the esophagus and sensitivity to sunlight.

However, a study of cisgender women in Kenya found that taking doxycycline after sex did not significantly reduce the risk of STIs in this population. Although the drug appeared to reach adequate concentrations in vaginal and cervical tissue, many participants reported that their adherence was "imperfect," suggesting that doxyPEP still might have the potential to protect women if they use it more consistently.

"It is really essential to have national guidelines to make providers aware of doxyPEP, who may benefit from this new prevention tool, and how to approach providing it safely," Annie Luetkemeyer, MD, of the University of California at San Francisco, who led the DoxyPEP trial, told POZ. "Guidelines are an important first step to address equitable access for those who are most impacted by recurrent STIs and who may be at risk for lack of access, given existing health disparities."

Who Can Benefit From DoxyPEP?

The CDC guidelines recommend doxyPEP for cisgender men who have sex with men and transgender women with a history of STIs, the group with the strongest evidence of benefit, but "they leave the door open for other populations," according to Luetkemeyer.

"We don't have data for men who have sex with women, and we don't have data to support its use in cisgender women yet. However, clinicians can use the guidance to have a case-by-case discussion with people who aren't included in the recommendation to decide if doxyPEP makes sense while we are learning more," she said. "The CDC could have stated that doxyPEP should not be given to anyone outside of the recommendation, but that would be overly narrow."

In October 2022, San Francisco was the first city to issue doxyPEP guidelines. Since then, more than 3,000 residents have used the new prevention tool, according to the San Francisco

Department of Public Health.

San Francisco's recommendation is broader than the CDC's proposal, including transgender men along with cisgender gay and bisexual men and transgender women. It also includes people in these groups who have had multiple male sex partners during the past year, even if they have not previously been diagnosed with an STI.

The California Department of Public Health's guidance recommends doxyPEP for men who have sex with men and transgender women who have had at least one STI during the past year, but also advises providers to offer doxyPEP using shared decision-making for "all non-pregnant individuals at increased risk for bacterial STIs and to those requesting doxyPEP, even if these individuals have not been previously diagnosed with an STI or have not disclosed their risk status."

Howard Brown Health Center in Chicago has also been offering doxyPEP ahead of the CDC guidance to people assigned male at birth who have been diagnosed with at least one bacterial STI and have had condomless sex with at least one assigned-male partner during the past year.

Preventive use of doxycycline is not without concerns. One is that widespread use of antibiotics could lead to drug resistance. This is especially worrisome with regard to gonorrhea, which is already resistant to many medications. 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. The CDC guidance states that these risks will need to be closely monitored.

Speaking to reporters at this year's Conference on Retroviruses and Opportunistic Infections, where she presented drug resistance data from the DoxyPEP trial, Leutkemeyer called the findings reassuring. "We didn't see a marked increase in antimicrobial resistance associated with doxyPEP use," she said. "We need larger and longer studies of what happens to common bugs," but this must be weighed against the benefits of a substantial reduction in STIs.

Jean-Michel Molina, MD, of the University of Paris Cité, who presented findings from the DoxyVAC trial, noted that doxycycline and related drugs have been used for years unhampered by resistance, and he didn't expect that a small amount of additional use by gay men would change that.

In fact, using doxyPEP to prevent STIs—rather than treating them after they occur—could reduce the overall prevalence of gonorrhea, chlamydia and syphilis, giving the bacteria less opportunity to circulate and develop resistance.

Equitable access will also be an issue in the implementation of doxyPEP. Inexpensive generic doxycycline is widely available, but the cost could add up if people take it frequently. What's more, everyone who could potentially benefit from this new prevention tool may not have access to sex-positive providers who know about the intervention and will offer it without stigma.

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