

DOXY PEP

EVIDENCE-BASED GUIDANCE FOR HEALTHCARE PROVIDERS



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Cook County DEPT. of
Public Health

A division of Cook County Health

**BUILDING
HEALTHIER
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INTRODUCTION



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Demian Christiansen, DSc
Director, Communicable Disease
Prevention & Control Unit

Dear Colleagues:

While the sexually transmitted infection (STI) epidemic may be slowing down, STI rates remain high. Some populations are affected more commonly than others, including Black/African Americans, Hispanics/Latinos, as well as cisgender gay and bisexual men.¹

Doxycycline postexposure prophylaxis, or doxy PEP, is a novel strategy now demonstrated in several clinical trials to dramatically reduce incidence rates of chlamydia, syphilis and gonorrhea in some populations.

Doxy PEP has been shown to reduce syphilis and chlamydia infections by more than 70%, and gonorrhea by 50%. Current efficacy data apply only to adult gay, bisexual, and other men who have sex with men, and transgender women. Studies among heterosexual cisgender women are ongoing.²

This document provides information on populations for whom doxy PEP should be offered, dosing and prescribing guidance, the benefits and risk of use, and counseling messages that can be used when discussing doxy PEP with patients.

Research Studies Showing Efficacy of Doxy PEP

For many years, the primary means to prevent a bacterial sexually transmitted infection (STI) has been limited to condoms and advising people to abstain from sex or reduce the number of people with whom they have sex. Following the successes of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) for HIV infections, researchers have identified a new option for STI prevention to add to our toolbox. Doxycycline post-exposure prophylaxis (doxy PEP) offers a self-administered approach to STI prevention, potentially suitable for individuals who find consistent condom use challenging or undesirable. Many studies have demonstrated that doxy PEP reduces the incidence of syphilis, chlamydia, and gonorrhea among cisgender men who have sex with men (MSM) and transgender women (TGW) who have sex with men. While doxy PEP should not replace other prevention methods, this new tool shows promise for the prevention of STIs among select populations at higher risk for encountering an STI.

Table 1 | Some Doxy-PEP Randomized Clinical Trials Among MSM and TGW – 2015 to 2023

Study	Participating Population	STI Rate or Outcome		Relative Risk Reduction in STIs*	Absolute Risk Reduction in STIs
		Doxy-PEP	No Doxy-PEP		
IPERGAY France 2015-2016	232 MSM on HIV PrEP	37.7 per 100 person-years	69.7 per 100 person-years	47%	32 per 100 person-years
DoxyPEP US 2020-2022	327 MSM and transgender women taking HIV pre-exposure prophylaxis	10.7% per quarter	31.9% per quarter	66%	21.2 % per quarter
	174 MSM and transgender women with HIV	11.8% per quarter	30.5% per quarter	62%	18.7 % per quarter
DoxyVac France 2021-2022	502 MSM on HIV PrEP	26.1 per 100 person-years	76.7 per 100 person-years	66%	51 per 100 person-years

*Risk reduction estimates in this table refer to combined risk reductions for all STIs (syphilis, chlamydia, and gonorrhea) examined in the studies. Risk reductions for each STI individually are presented in the forthcoming sections.

The first study, IPERGAY, was conducted in France and showed a reduced risk of 70%³ for acquiring syphilis and chlamydia. There was no significant difference in gonorrhea incidence, likely due to the high prevalence of doxycycline-resistant gonorrhea in the studied population. Doxycycline currently has variable activity against gonorrhea, globally, potentially explaining variable findings of doxy PEP's efficacy for gonorrhea prevention.⁴

The next study, DoxyPEP US, showed reductions of 87% for syphilis, 88% for chlamydia, and 55% for gonorrhea among people taking HIV PrEP, and reductions of 77% for syphilis, 74% for chlamydia, and 57% for gonorrhea among people living with HIV.^{5,6}

Finally, DoxyVac, demonstrated an 84% relative risk reduction in chlamydia and syphilis infections.^{4,7} This study was distinct from the other two clinical trials as it also assessed for efficacy of the meningococcal group B vaccine to reduce gonorrhea incidence in the study population. The study did not identify efficacy in reducing gonorrhea incidence through doxy PEP provision or through vaccination.⁷

To date, doxy PEP has been proven effective only among cisgender MSM and TGW who are at increased risk for STIs. Following the findings from the primary doxy PEP clinical trials, the CDC recommends limiting doxy PEP provision to these populations. Clinicians should counsel patients in these populations about the risks and benefits of doxy PEP and allow for shared decision making as to whether or not a patient may opt for this prevention tool.

There is insufficient evidence to assess the balance of benefits and harms of the use of doxy PEP in other populations. Studies in other populations, including cisgender women are vital, and the CDC will update their guidelines as additional data are made available.⁸

Currently, primary concerns over the provision of doxy PEP have been related to the risk of organisms developing antimicrobial resistance. Direct evidence of this risk being associated with doxy PEP provision has not been definitively proven. Based on in vitro experiments and observational data, many experts have raised concerns that doxy PEP could also increase the risk of resistance in bystander bacteria like *Staphylococcus aureus*, *Streptococcus pneumoniae*, and other gram-negative bacteria in the gut.⁴

Concern for the development of resistance to tetracyclines (and thus doxycycline) among the bacteria which cause chlamydia and syphilis infections, *Chlamydia trachomatis* and *Treponema pallidum*, has also been raised. Despite this concern, resistance has never been reported for these STIs and is thought to be highly unlikely to occur. More studies are needed to understand the potential for antimicrobial resistance to be driven by doxy PEP provision but are underway⁸.

Recommendations for healthcare providers:

- CDC recommends healthcare providers discuss doxy PEP with all cisgendered MSM and TGW with a history of at least one bacterial STI (gonorrhea, chlamydia, and syphilis) in the last 12 months.
- Although not directly assessed in the cited clinical trials, providers may also wish to discuss doxy PEP with other cisgendered MSM and TGW who have not had a bacterial STI in the past year. This determination should be made if the patient will be participating in sexual activities known to pose an increased risk of infection, like condomless sex.
- Providers should engage in shared decision making with their patients by educate them on the proven benefits of doxy PEP in reducing STIs, as well as the known and unknown risks.
- Providers should still give comprehensive preventative sexual health counseling and education to all sexually active individuals. Such comprehensive counseling and education includes HIV and STI screening; education on prevention methods like doxy PEP, expedited partner therapy, HIV PrEP, and HIV PEP; vaccinations for hepatitis A/B, human papilloma virus, Mpox, and *Neisseria meningitidis*; and contraception methods.

Dosing and Prescribing Guidance

For patients currently recommended to be considered for doxy PEP, write a prescription for self-administration of doxycycline 200 mg (any formulation) within 72 hours after unprotected oral, vaginal, or anal sex. Patients should not take more than 200 mg every 24 hours. Provide enough doses until the patient's next follow-up visit.

Help patients minimize doxycycline side effects by advising that they:

1. Take doxy PEP with at least 8 ounces of water and food to reduce side effects like nausea, upset stomach, and esophageal irritation.
2. Do not lie down for one hour after taking doxycycline.
3. Do not take doxycycline within two hours of having any dairy products, antacids and supplements with iron, calcium, or magnesium.
4. Wear sunscreen or cover skin to stay protected from the sun while taking doxycycline.

Also consider the following when prescribing doxy PEP:

- Screen for and treat STIs.
- Patients who are at increased risk of encountering an STI may also be at increased risk for viral hepatitis or HIV. Consider additional screens for these conditions if it is relevant to your patient.
- For those without HIV, who are receiving HIV PrEP, screen for HIV per CDC's [HIV PrEP guidelines](#) at 3-month intervals.
- Discuss and facilitate access to PrEP for those who are HIV negative, not on HIV PrEP, and at risk for HIV.
- Discuss prevention strategies and help connect patients to other health or social services as needed.
- Review patients' medication lists, including over-the-counter medications and vitamins, to assess for potential drug interactions.
- Provide information about how to take doxy PEP.
- Provide enough doses to last until each patient's next follow-up visit, with dosing based on an individual's frequency of sexual activity.

Follow-Up Care Guidance

Schedule follow-up visits for every 3 to 6 months

- Patients on doxy PEP should test for STIs and HIV every 3 to 6 months as appropriate for the individual patient.
- Continue screening for gonorrhea, chlamydia, and syphilis. If a patient on doxy PEP tests positive for an STI, they should be treated following the most current CDC [STI Treatment Guidelines](#).
- Continue screening and testing for HIV.
- Continue to discuss other prevention strategies and connect patients to other health and social services as needed.

Assess doxy PEP side effects

- Consider hematopoietic, renal, and hepatic laboratory monitoring as clinically indicated in addition to counseling patients on standard precautions and warnings while taking doxy PEP, as outlined in the drug package insert. Caution patients on risks, including: sun sensitivity, pill esophagitis and, rarely, intracranial hypertension.
- Re-assess the need for doxy PEP, if side effects are not well tolerated by the patient.

Benefits and Risks of Doxy PEP

Patients should be counseled about both the benefits and potential risks of taking Doxycycline.

BENEFITS

- Doxycycline has been used for many years, for many conditions, ranging from bacterial infections to acne to malaria.
- Doxy PEP has been shown to be highly effective at preventing syphilis, chlamydia, and to a lesser extent, gonorrhea, among select populations. Some of the fundamental clinical trials of doxy PEP have shown a risk reduction of more than 70% for syphilis and chlamydia.
- Doxy PEP might decrease STI incidence and improve the burden in some population.
- Doxy PEP might decrease anxiety and stigma associated with STIs.

RISKS

- Some adverse effects of doxycycline can include sun sensitivity or esophagus and stomach irritation.
- Potential contribution to antibiotic resistance in the long-term, and particularly in the bacteria which causes gonorrhea, *Neisseria gonorrhoeae*, as well as bystander or commensal bacteria or microorganisms in intestinal flora. To date, the risk for resistance among *Chlamydia trachomatis* and *Treponema pallidum* bacterium, appears to be low and theoretical.⁴
- Microbiome changes: Doxy PEP may affect microorganisms that naturally live on our bodies or inside us. These changes may have long-term health effects which are currently unknown.⁸

References

1. Centers for Disease Control and Prevention. [2023 CDC data suggest the STI epidemic may be slowing, 2024](#). Accessed January 9, 2025.
2. Centers for Disease Control and Prevention. [CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024](#). Accessed January 9, 2025.
3. Molina JM, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, Capitant C, Rojas-Castro D, Fonsart J, Bercot B, Bébéar C, Cotte L, Robineau O, Raffi F, Charbonneau P, Aslan A, Chas J, Niedbalski L, Spire B, Sagaon-Teyssier L, Carette D, Mestre SL, Doré V, Meyer L; ANRS IPERGAY Study Group. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. *Lancet Infect Dis*. 2018 Mar;18(3):308-317. doi: [10.1016/S1473-3099\(17\)30725-9](#).
4. Cannon CA, Celum CL. Doxycycline postexposure prophylaxis for prevention of sexually transmitted infections. *Top Antivir Med*. 2023 Dec 5;31(5):566-575. PMID: [38198668](#)
5. Luetkemeyer AF, Donnell D, Cohen SE, Dombrowski JC, Grabow C, Haser G, Brown C, Cannon C, Malinski C, Perkins R, Nasser M, Lopez C, Suchland RJ, Vittinghoff E, Buchbinder SP, Scott H, Charlebois ED, Havlir DV, Soge OO, Celum C. Doxycycline to prevent bacterial sexually transmitted infections in the USA: final results from the DoxyPEP multicentre, open-label, randomised controlled trial and open-label extension. *Lancet Infect Dis*. 2025 Aug;25(8):873-883. doi: [10.1016/S1473-3099\(25\)00085-4](#).
6. Luetkemeyer AF, Donnell D, Dombrowski JC, Cohen S, Grabow C, Brown CE, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *N Engl J Med*. 2023;388(14):1296-1306. doi: [10.1056/NEJMoA2211934](#)
7. Molina JM, Bercot B, Assoumou L, Rubenstein E, Algarte-Genin M, Pialoux G, Katlama C, Surgers L, Bébéar C, Dupin N, Ouattara M, Slama L, Pavie J, Duvivier C, Loze B, Goldwirt L, Gibowski S, Ollivier M, Ghosn J, Costagliola D; ANRS 174 DOXYVAC Study Group. Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2 × 2 factorial design. *Lancet Infect Dis*. 2024 Oct;24(10):1093-1104. doi: [10.1016/S1473-3099\(24\)00236-6](#).
8. Centers for Disease Control and Prevention. Doxy PEP for Bacterial STI Prevention, 2024. Accessed January 9, 2025. <https://www.cdc.gov/sti/hcp/doxy-pep/index.html>

Resources

- Illinois Department of Public Health – [Dear Colleagues Letter Doxy PEP Update, October 21, 2024](#).
- Centers for Disease Control and Prevention – [Primary Prevention Methods](#).

Mandatory Reportable Sexually Transmitted Infections

Under *Illinois Administrative Code Section 693.30*, healthcare providers must report all diagnosed or treated reportable STIs to the local health department. Reports must be made within 7 days of diagnosis. Contact:

Tobi-Velicia Johnson, MPH

STI/HIV Program Manager

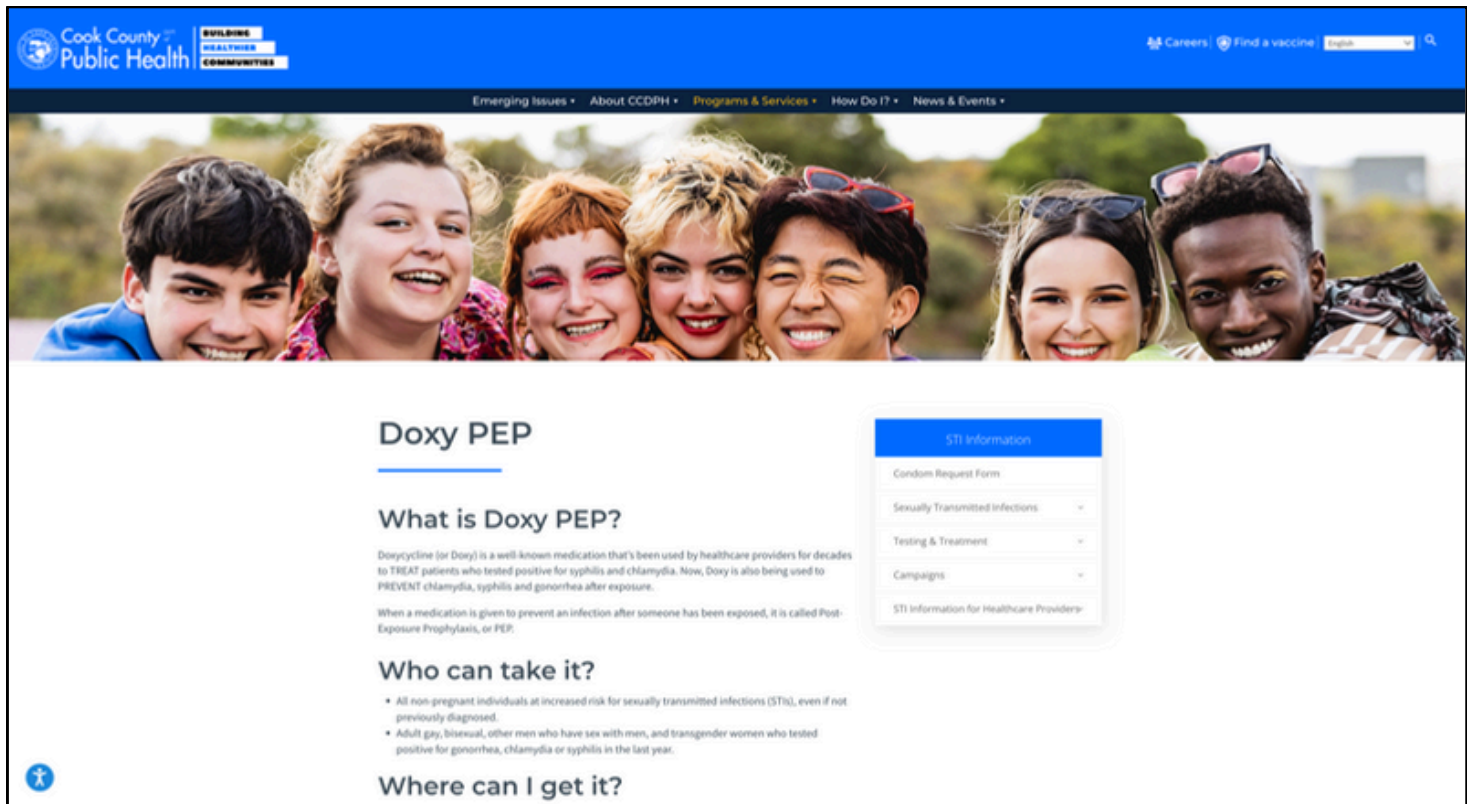
Office: 708-836-5458

Cell: 312-446-5435

Email: tjohnson@cookcountyhhs.org

Visit Our Website

Encourage patients to visit cookcountypublichealth.org for more information and to download fact sheets in English and Spanish.



The screenshot shows the Cook County Public Health website. The header includes the Cook County Public Health logo and navigation links: Emerging Issues, About CCDPH, Programs & Services, How Do It?, and News & Events. Below the header is a large image of a diverse group of young people smiling. The main content area features a section titled "Doxy PEP" with a subheading "What is Doxy PEP?". The text explains that Doxycycline (or Doxy) is a well-known medication used by healthcare providers for decades to TREAT patients who tested positive for syphilis and chlamydia. Now, Doxy is also being used to PREVENT chlamydia, syphilis and gonorrhea after exposure. It further states that when a medication is given to prevent an infection after someone has been exposed, it is called Post-Exposure Prophylaxis, or PEP. Below this, a section titled "Who can take it?" lists two bullet points: "All non-pregnant individuals at increased risk for sexually transmitted infections (STIs), even if not previously diagnosed." and "Adult gay, bisexual, other men who have sex with men, and transgender women who tested positive for gonorrhea, chlamydia or syphilis in the last year." To the right of the text is a sidebar titled "STI Information" with a list of links: Condom Request Form, Sexually Transmitted Infections, Testing & Treatment, Campaigns, and STI Information for Healthcare Providers.

Doxy PEP

What is Doxy PEP?

Doxycycline (or Doxy) is a well-known medication that's been used by healthcare providers for decades to TREAT patients who tested positive for syphilis and chlamydia. Now, Doxy is also being used to PREVENT chlamydia, syphilis and gonorrhea after exposure.

When a medication is given to prevent an infection after someone has been exposed, it is called Post-Exposure Prophylaxis, or PEP.

Who can take it?

- All non-pregnant individuals at increased risk for sexually transmitted infections (STIs), even if not previously diagnosed.
- Adult gay, bisexual, other men who have sex with men, and transgender women who tested positive for gonorrhea, chlamydia or syphilis in the last year.

Where can I get it?

STI Information

- Condom Request Form
- Sexually Transmitted Infections
- Testing & Treatment
- Campaigns
- STI Information for Healthcare Providers

