# Doxycycline Postexposure Prophylaxis for Sexually Transmitted Infection Prevention

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**Consider prescribing doxycycline as prophylaxis for bacterial sexually transmitted infections (STIs) in certain clinical scenarios. New data suggests that a one-time dose of 200 mg doxycycline taken within 72 hours of an unprotected sexual encounter may reduce transmission of syphilis, gonorrhea and chlamydia by a combined two thirds in a high-risk population. ( J Am Board Fam Med 2024;37:1140–1142.)**

***Keywords:*** **Antimicrobials, Doxycycline, MSM, PEP, Public Health, sexually transmitted infections**

## Strength of Recommendation: B

***Based on Data of an Open Label, Randomized Controlled trial.***[1]

## Illustrative Case

A 29 year old man who has sex with men (MSM) presents to your clinic the morning after an unprotected sexual encounter with another man. He does not know the last time his sex partner was tested for sexually transmitted infections (STIs). He was diagnosed with and treated for syphilis earlier this year and is trying his best to remain disease-free. He is already on pre-exposure prophylaxis (PrEP) therapy for HIV prophylaxis. He wants to know whether there is any medication he can take to reduce his risk of developing a bacterial STI from this encounter.

## Clinical Context

The rates of bacterial sexually transmitted infections (STIs) are increasing across the US; gonorrhea, syphilis, and chlamydia incidence all increased year over year according to the 2021 CDC STD Surveillance report.[2] The rate of increase within gay and bisexual male cohorts is among the highest rates across all populations.[2] Pre and postexposure prophylaxis for HIV have been crucial in the battle against HIV, as they can significantly lower HIV transmission risk by 74% if taken properly.[3] There is new data, however, that suggests that using pre-exposure prophylaxis may actually increase rates of unprotected sex and, in turn, predispose persons using HIV PrEP to increased rates of bacterial STIs.[4,5] This raised the scientific question of antibiotics as pre-exposure prophylaxis of bacterial STIs.

The "IPERGAY" trial was 1 of the first to confront this dilemma.[6] In this French study, 232 MSM on HIV pre-exposure prophylaxis were given doxycycline within 24 hours of condomless sexual encounters. Over the 9-month duration of the study, the investigators found a 20% reduction in the incidence of bacterial STIs (gonorrhea, syphilis, and chlamydia) in the doxycycline arm. Researchers in Kenya attempted to answer the question whether the positive findings in that study could be extrapolated to different population subgroups. They found that doxycycline prophylaxis provided no benefit in preventing bacterial STIs in cisgender women on HIV PrEP.[7]

## Methods

This article was identified as a potential PURL through the standard systematic methodology.[12] An additional literature search was conducted by searching PubMed with the terms "doxypep," "doxycycline STI prophylaxis," "doxycycline pep," and

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"bacterial STI prophylaxis" to find additional literature to place this research into the context of current clinical practice.

### *Study Summary*

DoxyPEP is a 2023 open label, randomized controlled trial by Luetkemeyer et al evaluated the effectiveness of single-dose doxycycline in preventing bacterial STI transmission in their study population and found this intervention efficacious.[1] DoxyPEP was a randomized controlled trial (n = 501) funded by the National Institutes of Health investigating efficacy of postexposure doxycycline prophylaxis in MSM who are on pre-exposure prophylaxis (PrEP) or are living with HIV (PLWH) who had been diagnosed with an STI within the past 12 months. The study was conducted at 2 HIV clinics and 2 sexual health clinics in San Francisco and Seattle. The intervention group (n = 327) self-administered doxycycline DR 200 mg 24 to 72 hours after sexual activity, postexposure prophylaxis (doxyPEP). The control group received standard of care per CDC guidelines at the time that the study was conducted. Of the 501 eligible participants, 94% had at least 1 follow-up visit. A total of 18 participants discontinued the study early though results were reported through a modified intention to treat analysis. In the PrEP cohort, an STI was diagnosed in 61 of 570 quarterly visits (10.7%) in the doxycycline group and 82 of 257 quarterly visits (31.9%) in the standard-care group, for an absolute difference of −21.2 percentage points (NNT = 5) and a relative risk of 0.34 (95% confidence interval [CI], 0.24 to 0.46). In the PLWH cohort, an STI was diagnosed in 36 of 305 quarterly visits (11.8%) in the doxycycline group and 39 of 128 quarterly visits (30.5%) in the standard-care group, for an absolute difference of −18.7 percentage points (NNT = 5) and a relative risk of 0.38 (95% CI, 0.24 to 0.60). The incidences of the 3 evaluated STIs were lower with doxycycline than with standard care; in the PrEP cohort, the relative risks were 0.45 (95% CI, 0.32 to 0.65; NNT = 10) for gonorrhea, 0.12 (95% CI, 0.05 to 0.25; NNT = 9) for chlamydia, and 0.13 (95% CI, 0.03 to 0.59; NNT = 43) for syphilis, and in the PLWH cohort, the relative risks were 0.43 (95% CI, 0.26 to 0.71; NNT = 9), 0.26 (95% CI, 0.12 to 0.57; NNT = 9), and 0.23 (95% CI, 0.04 to 1.29; NNT = 59), respectively. There were low total numbers of new syphilis cases overall in the PLWH group which led to the insignificant confidence interval. There were no meaningful differences between the groups in adverse events or antimicrobial resistance. DoxyPEP, doxycycline DR 200 mg administered within 24 to 72 hours after sexual activity, is an effective treatment for reducing incidence of STI (chlamydia, gonorrhea, syphilis) in MSM who are taking PrEP or are living with HIV who have been diagnosed with an STI within the past 12 months compared with the standard of care.

### *What Is New*

Doxycycline is effective in postexposure prevention of bacterial STIs in select populations. The CDC has drafted a proposed guideline to recommend the use of doxycycline prophylaxis for the prevention of bacterial STIs in these populations.[8]

### *Caveats*

The long-term effects of taking doxycycline frequently are not well established. While the study did not demonstrate significant antimicrobial resistance, this was studied over 12 months and the effects of continuing to take doxycycline past this are unknown. Other studies have demonstrated concerns for antimicrobial resistance and changes to the microbiome.[9–11] In addition, demographic data and differences in study site were not provided which could demonstrate confounding variability.

### *Challenges to Implementation*

The challenge to implementation is similar to that of any outpatient prescription medication which requires adequate patient education and compliance for therapeutic benefit.

*To see this article online, please go to: http://jabfm.org/content/37/6/1140.full.*

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