

Recommendations for the Use of Doxycycline for Post-Exposure Prophylaxis (Doxy PEP) to Prevent Certain Bacterial STIs

Incidence of bacterial STIs, including chlamydia, gonorrhea, and syphilis, continues to increase in both Minnesota and throughout the United States. These infections disproportionately impact historically disadvantaged populations, and as a result, novel prevention and treatment approaches are required.

Evidence suggests that **a single 200 mg dose of doxycycline within 72 hours** after condomless anal, oral, or other insertive/receptive sex used as post-exposure prophylaxis (doxy PEP) can **reduce the risk of transmission of chlamydia, gonorrhea, and syphilis** among men who have sex with men (MSM) and transgender women (TGW). Because of this evidence, CDC issued [Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024](https://www.cdc.gov/mmwr/volumes/73/rr/rr7302a1.htm) (<https://www.cdc.gov/mmwr/volumes/73/rr/rr7302a1.htm>). MDH has subsequently reviewed CDC's recommendations and provides the following guidance regarding utilization of doxy PEP for prevention of STIs.

Recommendations

1. Inform MSM and TGW who have had one or more bacterial STI in the past 12 months about doxy PEP, including the efficacy, potential benefits and risks, and alternative options to prevent, diagnose, and treat STIs.
2. Consider doxy PEP for all MSM and TGW who have had one or more bacterial STI in the past 12 months.
3. Consider offering doxy PEP using shared decision-making to all non-pregnant individuals at increased risk for bacterial STIs and to those requesting doxy PEP, even if these individuals have not been previously diagnosed with an STI or have not disclosed their risk status.
 - a. Despite studies looking at efficacy of doxy PEP in cisgender women (Stewart, 2023), there is a lack of data that demonstrate efficacy for preventing bacterial STIs in this population. As such, there is no specific recommendation for this group at this time¹. In addition, there are currently no data on efficacy of doxy PEP in cisgender heterosexual men, transgender men, and other queer and nonbinary individuals.

¹ In a recent randomized trial of 449 cisgender Kenyan women who were taking HIV PrEP ([Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women \(www.nejm.org/doi/full/10.1056/NEJMoa2304007\)](https://www.nejm.org/doi/full/10.1056/NEJMoa2304007)), doxy-PEP was not shown to be protective against STIs, though pharmacologic studies suggest that doxycycline levels in vaginal fluid should be sufficient to provide such protection (Haaland, CROI, 2023). Objective measures of doxycycline use in the dPEP Kenya Study suggest that null results were due to low rates of doxycycline use (Stewart et al, NEJM, 2023). Further studies are needed to determine efficacy of doxycycline prophylaxis to prevent STIs among people assigned female sex at birth.

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- b. Providers may give particular consideration to prescribing doxy PEP to those at highest risk for bacterial STIs (e.g., those who engage in transactional sex, those with multiple previous STIs) or on an episodic basis when patients anticipate periods of higher STI risk.
4. Doxy PEP should be provided in the context of a comprehensive sexual health visit, and patients should be offered, where warranted, prevention options and strategies, including HIV and STI testing and treatment, HIV pre-exposure prophylaxis (HIV PrEP), condoms, contraception, expedited partner therapy, vaccines, and other care as indicated.
5. Counseling should include a discussion of the potential benefits as well as known and unknown harms of doxy PEP including potential side effects, and the need to take doxycycline exactly as prescribed.

The use of doxy PEP could lead to increased antibiotic resistance, both at the individual and population levels. Recent evidence² suggests that taking doxy PEP is associated with tetracycline resistant *N. gonorrhoeae*, especially in those patients taking it three times or more per month. A reduction in tetracycline susceptible *N. gonorrhoeae* among patients taking doxy PEP suggests that doxy PEP use may select for tetracycline resistant *N. gonorrhoeae* over time. Data also suggest the potential for increased tetracycline resistance among other bacteria as well, including *S. aureus*. Patients should be encouraged to inform all medical providers that they are using doxy PEP, as this could potentially inform empiric antibiotic choice for skin and soft-tissue infections (SSTIs) or community-acquired pneumonia (CAP), particularly among those taking doxy PEP three or more times per month.

Currently, there is no or low known risk of increased resistance for the bacteria that cause chlamydia and syphilis. Further studies are required to continue to evaluate the risk of the development of antibiotic resistance and understand related clinical outcomes to inform future recommendations.

Evidence

- The DoxyPEP study (Luetkemeyer, 2023) was conducted in San Francisco and Seattle and enrolled MSM and TGW who were either on HIV PrEP or were living with HIV (PLWH). In those on PrEP, doxy PEP reduced the risk of chlamydia by 88%, syphilis by 87%, and gonorrhea by 55%; in PLWH, doxy PEP reduced the risk of chlamydia by 74%, syphilis by 77% (although this did not reach statistical significance), and gonorrhea by 57%.
- The ANRS DOXYVAC study (Molina, CROI 2023) was conducted in France and enrolled MSM on HIV PrEP. Over a nine-month follow-up period, doxy PEP reduced the risk of chlamydia by 89%, syphilis by 79%, gonorrhea by 51%, and *Mycoplasma genitalium* by 45%. These

² Olusegun O Soge, Christina S Thibault, Chase A Cannon, Stephanie E McLaughlin, Tim W Menza, Julia C Dombrowski, Ferric C Fang, Matthew R Golden, [Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in *Neisseria gonorrhoeae* and Colonization with Tetracycline-Resistant *Staphylococcus aureus* and Group A *Streptococcus*, *Clinical Infectious Diseases*, 2025 \(<https://doi.org/10.1093/cid/ciaf089>\)](https://doi.org/10.1093/cid/ciaf089)

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preliminary results were presented at the 2023 Conference on Retroviruses and Opportunistic Infections in February 2023.

- The ANRS IPERGAY study (Molina, 2018) was also conducted in France, and enrolled MSM on HIV PrEP. Over a 10-month follow-up period, randomization to doxy PEP was associated with a 47% relative risk reduction in the occurrence of a new bacterial STI, 70% for chlamydia, and 73% for syphilis.
- In the three studies of MSM on HIV PrEP or living with HIV, adherence to doxycycline was high and adverse effects were minimal. In the study of cisgender women (Stewart, 2023), while there was no statistical difference in bacterial STIs found between those receiving doxy PEP versus those who did not receive doxy PEP, there was concern over medication adherence. As such, more data are needed in this population to make recommendations.
- Additional studies on effectiveness of doxy PEP on STI rates at the population level, along with the effects of doxy PEP on the microbiome are currently being conducted, and this guidance will be updated as these studies become available.

Summary of Results from Randomized Control Trials of Doxycycline PEP

Study	Participants (N)	STI Rate (Doxy PEP)	STI Rate (No Doxy PEP)	Relative Risk Reduction (RRR)	p-value
DoxyPEP	Status neutral MSM and TGW with STI in prior year (501)	10.7% per quarter	31.9% per quarter	65%	P<0.001
DoxyVac	MSM taking PrEP with STI in prior year (502)	5.6 per 100 person-years	35.4 per 100 person-years	84%	p<0.0001
IPERGAY	MSM taking PrEP (232)	37.7 per 100 person-years	69.7 per 100 person-years	47%	p=0.008
dPEP Kenya	Cisgender women taking PrEP (449)	25.1 per 100 person-years	29.0 per 100 person-years	12%	p=0.51

Note: Trials reported differing STI outcomes and time periods. Doxy PEP = gonorrhea, chlamydia, or syphilis per three months; DoxyVAC, IPERGAY, and dPEP Kenya = gonorrhea, chlamydia, or syphilis per 100 person years.

Prescribing doxycycline as PEP

Doxycycline is FDA approved for treatment of STIs (e.g., chlamydia and syphilis) and prevention of other infections. The use of doxycycline for prevention of STIs as post-exposure prophylaxis (doxy PEP) is currently included in [CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024](https://www.cdc.gov/sti/hcp/doxy-pep/index.html) (<https://www.cdc.gov/sti/hcp/doxy-pep/index.html>). Based on these national guidelines, MDH recommends:

1. Begin by taking a comprehensive sexual history as part of every routine care visit to identify the appropriate clinical course of action.

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2. **Prescribe 200 mg of doxycycline taken within 72 hours** (ideally within 24 hours or as soon as possible) **after condomless oral, anal, or other insertive/receptive sex.** Doxycycline can be taken daily depending on sexual activity, but no more than 200 mg every 24 hours.
3. Screen for both gonorrhea and chlamydia at all anatomic sites of exposure (urogenital, pharyngeal, and/or rectal), as well as test for syphilis and HIV at initiation of doxy PEP and every three months or sooner if there is a concern about STIs.
4. Counsel patients about both the benefits and potential adverse effects of taking doxycycline.

Considerations

- Doxycycline has been in use for many years and is used for many conditions, from bacterial infections to acne to malaria prophylaxis.
- Some adverse effects of doxycycline can include sun sensitivity, pill esophagitis, and gastric upset. Rarely, it can cause benign intracranial hypertension.
- Patients should take doxycycline with fluids and remain upright for 30 minutes after taking the dose. Taking with food may increase tolerability.
- Patients should not share doxycycline.
- Doxycycline has not been studied in pregnancy and is therefore not recommended in pregnancy. For patients who can become pregnant, conduct regular pregnancy testing while prescribed doxy PEP.
- Laboratory monitoring is not routinely indicated for patients on doxy PEP but should be considered periodically (complete blood count, liver function tests, renal function) in patients taking doxycycline for a prolonged period or at the prescriber's discretion.

If a patient is diagnosed with an STI or has a known exposure to syphilis while using doxy PEP, they should be treated according to standard [CDC Treatment Guidelines](https://www.cdc.gov/std/treatment-guidelines/default.htm) (<https://www.cdc.gov/std/treatment-guidelines/default.htm>).

References and Links

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11. [Seattle & King County Public Health - Guidelines, June 2023 Doxycycline Post-Exposure Prophylaxis \(Doxy-PEP\) to Prevent Bacterial STIs in Men who Have Sex with Men \(MSM\) and Transgender Persons who Have Sex with Men: \(https://cdn.kingcounty.gov/-/media/depts/health/communicable-diseases/documents/hivstd/DoxyPEP-Guidelines.ashx\)](https://cdn.kingcounty.gov/-/media/depts/health/communicable-diseases/documents/hivstd/DoxyPEP-Guidelines.ashx)

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