

# Interim Recommendations for the Use of Doxycycline for Post-Exposure Prophylaxis (doxy PEP) for the Prevention of Certain Bacterial Sexually Transmitted Infections (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. Recent evidence suggests that a single 200mg dose of doxycycline within 72 hours after condomless anal, oral, or other insertive/receptive sex 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). While the Centers for Disease Control and Prevention (CDC) has released interim draft considerations for doxy PEP as a strategy to prevent bacterial STIs, the guidance has not been finalized.

## During this period, the Minnesota Department of Health (MDH) is issuing the following interim recommendations:

- Inform men who have sex with men (MSM) and transgender women (TGW) who have had  $\geq 1$  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.
- Doxy PEP should be considered for all MSM and TGW who have had  $\geq 1$  bacterial STI in the past 12 months.
- 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.
  - 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 time<sup>1</sup>. In addition, there are currently no data on efficacy of doxy PEP in cisgender heterosexual men, transgender men, and other queer and nonbinary individuals.

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<sup>1</sup> 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://doi.org/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.

- 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.
- 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.
- 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. This includes the potential for increased resistance in certain bacteria, including *Neisseria gonorrhoeae*, *Staphylococcus aureus* and other staph infections, *Mycoplasma genitalium*, and the bacteria that cause certain respiratory infections. There is no or low known risk of increased resistance for the bacteria that cause chlamydia and syphilis. Further studies are required to evaluate 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 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.

## 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
IPEGAY	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

\*Trials reported differing STI outcomes and time periods. Doxy PEP = gonorrhea, chlamydia, or syphilis per three months; DoxyVAC, IPEGAY, 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 is not currently included in national guidance. However, CDC has released draft guidance considerations for doxy PEP as an STI preventative strategy.

1. Begin by taking a comprehensive sexual history as part of every routine care visit in order to identify the appropriate clinical course of action.
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 GC and CT at all anatomic sites of exposure (urogenital, pharyngeal, and/or rectal), as well as test for syphilis and HIV (if not known PLWH) at initiation of doxy-PEP and every three months or sooner if there is a concern about STIs.
4. Patients should be counseled about both the benefits and potential adverse effects of taking doxycycline.
  - a. Doxycycline has been in use for many years and is used in a number of conditions, from bacterial infections to acne to malaria prophylaxis.
  - b. Some adverse effects of doxycycline can include sun sensitivity, pill esophagitis, and gastric upset. Rarely, it can cause benign intracranial hypertension.
  - c. Patients should take doxycycline with fluids and remain upright for 30 minutes after taking the dose. Taking with food may increase tolerability.
  - d. Patients should not share doxycycline.

5. 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.
6. 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 \(www.cdc.gov/std/treatment-guidelines/default.htm\)](http://www.cdc.gov/std/treatment-guidelines/default.htm).

## References and Links

1. Molina JM, Charreau I, Chidiac C, et al. 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.
2. Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure doxycycline to prevent bacterial sexually transmitted infections. *N Engl J Med*. 2023 Apr 6;388(14):1296-1306.
3. Jean-Michel Molina, Beatrice Bercot, Lambert Assoumou, Algarte-Genin Michele, Emma Rubenstein, Gilles Pialoux, et al. ANRS 174 DOXYVAC: An Open-Label Randomized Trial to Prevent STIs in MSM on PrEP. CROI [Internet]. 2023 Feb 19;Seattle, Washington. CROI ANRS 174 Doxyvac: [CROI ANRS 174 Doxyvac: CROI ANRS 174 Doxyvac: An Open-Label Randomized Trial to Prevent STIs in MSM on PrE \(www.croiconference.org/abstract/anrs-174-doxyvac-an-open-label-randomized-trial-to-prevent-stis-in-msm-on-prep/\)](http://www.croiconference.org/abstract/anrs-174-doxyvac-an-open-label-randomized-trial-to-prevent-stis-in-msm-on-prep/)
4. Stewart J, Oware K, Donnell D, et al. Doxycycline prophylaxis to prevent sexually transmitted infections in women. *N Engl J Med*. 2023 Dec 21;389:2331-2340.
5. [California Department of Public Health - Doxycycline Post-Exposure Prophylaxis \(doxy-PEP\) for the Prevention of Bacterial Sexually Transmitted Infections \(STIs\) \(www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/CDPH-Doxy-PEP-Recommendations-for-Prevention-of-STIs.pdf\)](http://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/CDPH-Doxy-PEP-Recommendations-for-Prevention-of-STIs.pdf)
6. [New York City Department of Health and Mental Hygiene - Doxycycline Post-Exposure Prophylaxis \(Doxy-PEP\) to Prevent Bacterial Sexually Transmitted Infections \(www.nyc.gov/assets/doh/downloads/pdf/std/dear-colleague-doxy-PEP-to-prevent-bacterial-STI-11092023.pdf\)](http://www.nyc.gov/assets/doh/downloads/pdf/std/dear-colleague-doxy-PEP-to-prevent-bacterial-STI-11092023.pdf)
7. [City of Chicago - doxy-PEP for Bacterial STIs \(www.chicago.gov/city/en/depts/cdph/provdrs/infectious\\_disease/supp\\_info/doxy-peg-for-bacterial-stis.html\)](http://www.chicago.gov/city/en/depts/cdph/provdrs/infectious_disease/supp_info/doxy-peg-for-bacterial-stis.html)
8. [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)

9. [Centers for Disease Control and Prevention - Guidelines for the Use of Doxycycline Post-Exposure Prophylaxis for Bacterial STI Prevention \(www.cdc.gov/std/treatment/guidelines-for-doxycycline.htm\)](https://www.cdc.gov/std/treatment/guidelines-for-doxycycline.htm)
10. [Centers for Disease Control and Prevention - 2021 STI Treatment Guidelines \(www.cdc.gov/std/treatment-guidelines/default.htm\)](https://www.cdc.gov/std/treatment-guidelines/default.htm)

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