

Literature Review

National STD Curriculum Podcast

Recent Research on the Impact of Doxy PEP

May 13, 2026

Season 6, Episode 5

This episode reviews four recently published studies about the impact of doxycycline post-exposure prophylaxis (doxy PEP) on *Neisseria gonorrhoeae* isolates with tetracycline resistance, *Staphylococcus aureus*, Group A streptococcus, and syphilis.

Topics:

- Doxy-PEP
- STIs
- Gonorrhea
- Staph Aureus
- Syphilis

Meena S. Ramchandani, MD, MPH
Associate Editor
Associate Professor of Medicine

Division of Allergy and Infectious Diseases
University of Washington

[Disclosures](#)

Disclosures for Meena S. Ramchandani, MD, MPH
Consulting Fee: Innoviva Specialty Therapeutics

References

[Paper #1](#) [Paper #2](#) [Paper #3](#) [Paper #4](#)

Transcript

Read along with the audio or jump to a particular chapter.

In this episode:

- [Intro & Background](#)
- [Paper #1](#)
- [Paper #2](#)
- [Paper #3](#)
- [Paper #4](#)
- [Summary](#)
- [Credits](#)

[intro--background](#)**[00:00] Intro & Background**

Hello, everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STI [sexually transmitted infections] literature review for health care professionals who are interested in remaining up to date on the diagnosis, management, and prevention of STIs.

A few health care providers asked to learn more about doxy PEP, and it would be good to review some recently published articles on this topic. Doxy PEP, which is also known as doxycycline post-exposure prophylaxis, is a biomedical intervention to reduce the incidence of chlamydia, syphilis, and, to a lesser extent, gonorrhea in patients who are taking this medication.

The medication is taken as 200 milligrams of oral doxycycline within 72 hours after sex. It's recommended to discuss doxy PEP with certain populations at higher risk of acquiring an STI, for example, MSM [men who have sex with men] who have had a bacterial STI in the last year. The studies I'll review in this episode will provide some information that might be important for your patient population, practice, or public health program. Let's review the recent literature on this topic.

[paper-1](#)**[01:11] Paper #1**

Luetkemeyer AF, Donnell D, Cohen SE, et al. 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. [\[PubMed Abstract\]](#)

The first article to review was published in *[The] Lancet* in August 2025 by Dr. Luetkemeyer and colleagues. It is titled "Doxycycline to prevent bacterial sexually transmitted infections in the USA: Final results from the DoxyPEP multicenter, open-label, randomized controlled trial and open-label extension."

1. This group looked at the effect of STI incidents, as well as some features of antimicrobial resistance in participants taking doxy PEP for up to 12 months follow-up. The authors measured the quarterly incidents of bacterial STIs, which included chlamydia, gonorrhea, and syphilis, and then compared them to participants not taking the medication.
2. 637 participants, the majority of which were MSM, with at least one bacterial STI in the past year, were enrolled in the randomized trial. There was a randomized phase in which participants received doxy PEP or standard of care, which was *no* doxy PEP, and an open-label extension in which all participants received doxy PEP after efficacy of the medication was known.
3. Greater than 95% of participants were MSM. The median age was around 36, and the participants reported a median of nine sexual partners in the three months prior to enrollment. During the randomized period, quarterly STI incidence was 31% in the standard care group, and this was compared to 12% in those who were taking doxy PEP. In the open-label extension, quarterly STI incidence was 13% among those participants who continued taking doxy PEP, which indicates a sustained effect.
4. In the open-label extension for those participants who were initially randomized to the standard of care but then started doxy PEP during the open-label extension, they found a reduction in quarterly STI incidence from 31% to 17%. And this reduction in STI incidence occurred despite a doubling of sexual partners, as well as a doubling of condomless anal sex acts in this group. Those taking doxy PEP took about 5 to 6 doses a month during the randomized period, as well as the open-label extension.
5. The authors also evaluated *Staphylococcus aureus*, which I'll say *Staph aureus* for short. They evaluated *Staph aureus* colonization and the anterior nares, as well as oropharynx of participants. They found that there was a decrease in colonization of *Staph aureus* in both groups over time, in

those taking doxy PEP and those not taking doxy PEP.

6. Participants taking doxy PEP were not significantly more likely to clear *Staph aureus* colonization than those with no doxy PEP use. But they did find an increase in doxycycline-resistant *Staph aureus* during doxy PEP use. They had five culture results for *Chlamydia trachomatis* and doxy PEP users, and they found that all were susceptible to tetracycline.

This study shows a sustained efficacy of doxy PEP to reduce bacterial STIs in a large number of participants. The majority of which were MSM who had a bacterial STI in the past year. The authors found a similar reduction in STIs in the open-label extension, despite reported increases in number of sexual partners as well as condomless sex. Doxycycline-resistant *Staph aureus* did increase with doxy PEP use, which might be expected, but I can't explain the overall trend in a decrease of *Staph aureus* colonization in both groups over time, in those taking doxy PEP, as well as those not taking doxy PEP.

[paper-2](#)[04:43] Paper #2

Soge OO, Thibault CS, Cannon CA, et al. Potential impact of doxycycline post-exposure prophylaxis on tetracycline resistance in *Neisseria gonorrhoeae* and colonization with tetracycline-resistant *Staphylococcus aureus* and Group A streptococcus. Clin Infect Dis. 2025 Jul 18;80(6):1188-1196. [[PubMed Abstract](#)]

The second article we will discuss was written by Dr. Soge and colleagues and published in *Clinical Infectious Diseases* in July 2025. It is titled "Potential impact of doxycycline post-exposure prophylaxis on tetracycline resistance in *Neisseria gonorrhoeae* and colonization with tetracycline-resistant *Staphylococcus aureus* and Group A streptococcus."

1. In King County, Washington, the guidance on the use of doxy PEP was issued around June of 2023, so about the middle of the year. The authors evaluated trends in *Neisseria gonorrhoeae* tetracycline resistance from 2017 through 2024, and they looked at the association of resistance with doxy PEP use in MSM attending the sexual health clinic.
2. They found that tetracycline resistance in *Neisseria gonorrhoeae* and MSM was relatively stable from 2017 to the beginning of 2023 at around 27% of isolates, and then increased every quarter to 70% in 2024, so a huge number. *Neisseria gonorrhoeae* with high-level tetracycline resistance, which they defined as a tetracycline minimum inhibitory concentration (or MIC) of at least 16 micrograms per milliliter, trended downwards from 2017 to 2021, and then increased from 2% in 2021 to 65% in 2024.
3. So, what they found is that the prevalence of high-level tetracycline resistance began increasing in MSM before the release of the doxy PEP guidelines and widespread doxy PEP use in Seattle and King County. MSM who took 1 to 3 doses of doxy PEP were not more likely than non-users (or those not taking doxy PEP) to have *Neisseria gonorrhoeae* tetracycline resistance. But those patients taking more than 3 doses of doxy PEP per month was associated with the *Neisseria gonorrhoeae* tetracycline resistance.
4. The authors evaluated *Staphylococcus aureus*, as well as Group A streptococcus. I'll also say Group A strep for short. They evaluated *Staph aureus* and Group A strep colonization in doxy PEP users because doxycycline is sometimes used to treat skin and soft-tissue infections. It's also used to treat other infections with *Staph aureus*, and long-term doxycycline use has been associated with an increase in oropharyngeal Group A strep colonization in prior studies.
5. Specimens were collected from the nares as well as the pharyngeal area. And what they found is that while overall *Staph aureus* colonization was less common among those using doxy PEP compared to non-users, tetracycline-resistant *Staph aureus*, as well as Group A strep colonization, was more common among doxy PEP users. 82% of all Group A strep were tetracycline resistant, but this didn't vary between doxy PEP users and non-users.

This article highlights how the proportion of *Neisseria gonorrhoeae* isolates with tetracycline resistance greatly increased from 2023 to 2024 in MSM in King County, Washington. This increase coincided with the rollout of doxy PEP guidance. Although doxy PEP might not fully explain *Neisseria gonorrhoeae* tetracycline

resistance in the community, because the authors found high-level tetracycline resistance among MSM increased *prior* to widespread doxy PEP use. And it's possible that the shift of using doxycycline—to treat NGU (or non-gonococcal urethritis) as well as chlamydia infections—in place of azithromycin might be one of these causes of the increasing resistance that's seen in the community. In 2024, 65% of the *Neisseria gonorrhoeae* isolates in MSM had high-level tetracycline resistance, and they also found an increase in doxycycline-resistant *Staph aureus* and Group A strep colonization in doxy PEP users, demonstrating some effect of doxy PEP on the microbiome.

[paper-3](#)[08:40] Paper #3

Menza TW, Berzkalns A, Cannon CA, Balkus J, Kerani RP, Dombrowski JC, Golden MR. The population-level impact of doxycycline post-exposure prophylaxis on syphilis in King County, WA: an interrupted time series analysis. Clin Infect Dis. 2026 Mar 26:ciag209. [[PubMed Abstract](#)]

Dr. Menza and colleagues published the next article we will review in *Clinical Infectious Diseases* in March 2026. It is titled “The Population-level impact of doxycycline postexposure prophylaxis on syphilis in King County, Washington: An interrupted time series analysis.” I do realize many of the studies we are reviewing in this episode are from Seattle and King County, but this was not intentional.

Let's go over some background. Data published from San Francisco showed that doxy PEP has a population-level effect on syphilis among MSM, which is promising. Doxy PEP implementation led to a 51% decrease in syphilis among MSM in San Francisco. Now, in King County, doxy PEP was quickly utilized among MSM, and within one year of the release of the guidelines, 45% of MSM attending the sexual health clinic reported recent doxy PEP use in 2024.

1. Dr. Menza and colleagues analyzed the population-level effect of doxy PEP in King County, Washington, using public health surveillance data. Now, in King County, doxy PEP is recommended and primarily used by MSM.
2. There are around 10,000 syphilis cases during the study period of 102 months. The mean was 98 syphilis cases per month. There were around 7,800 cases in men and 1,800 cases in women.
3. Doxy PEP implementation resulted in around 3,000 fewer total syphilis cases for a relative difference of -52%. The relative difference of syphilis in men was -53%, which was similar to what was seen in San Francisco.
4. Surprisingly, there was an effect of fewer syphilis cases in women, despite the absence of recommendations and limited doxy PEP use in women in King County. The relative difference of syphilis in women was -47% after doxy PEP implementation.
5. Despite the decrease in syphilis in men and women, syphilis in pregnant women and congenital syphilis cases increased from 2017 to 2024 in King County.

In summary, following doxy PEP implementation in King County, syphilis cases had a dramatic decline in men, but also in women. Although doxy PEP is not recommended for women in King County, it's possible that the decrease in syphilis among women could be due to a decreased transmission through shared sexual networks, for example, men who have sex with both men and women. Unfortunately, cases of syphilis in pregnant women and congenital syphilis continued to increase during the study period, and it's not clear why this is the case. The authors note that it's possible pregnant women may not benefit from the indirect effects of shared sexual networks or that the effects of doxy PEP may lag in this population, and they might see those effects later on. It's also possible that the decrease in syphilis seen in King County may not be completely related to doxy PEP. Doxy PEP may be responsible for part of the trend, but there has also been increased public health efforts that may contribute to a decline in some populations. I'm sure there will be more to come on this topic.

[paper-4](#)[11:44] Paper #4

Tantalo LC, Luetkemeyer AF, Lieberman NAP, et al. In vitro exposure of *Treponema pallidum* to subbactericidal doxycycline did not induce resistance: Implications for doxycycline postexposure prophylaxis. J Infect Dis. 2025 Mar 17;231(3):729-733. [\[PubMed Abstract\]](#)

Next, I'd like to briefly review a report published in the *Journal of Infectious Diseases* in March of 2025 by Lauren Tantalo and colleagues. It is titled "In vitro exposure of *Treponema pallidum* to subbactericidal doxycycline did not induce resistance: Implications for doxycycline postexposure prophylaxis."

1. This group propagated the *Treponema pallidum* SS14 strain and then exposed the treponemes to doxycycline both intermittently over seven months, as well as continuously for 10 weeks. They used a concentration of doxycycline that exerts antibiotic pressure but is not bactericidal, so it doesn't kill the organism.
2. Treponemes were recovered from culture plates and then evaluated by whole genome sequencing, and they found that no resistance developed in *T. pallidum*.
3. In the culture exposed to intermittent doxycycline, they saw cell numbers recovered faster after the last two exposure cycles.
4. No treatment-emergent mutations in 16S rRNA were recovered, and they did not find evidence of a doxycycline-resistant strain.
5. This group plans to do future experiments to evaluate this response to doxycycline exposure over time.

In this report, genetic resistance to doxycycline was not induced in vitro when *T. pallidum* was exposed to intermittent or continuous doxycycline that was below the concentration for killing *T. pallidum* organisms. This is reassuring since the widespread use of macrolides resulted in *T. pallidum* strains with resistance to macrolides in the US. Future studies are needed to evaluate the accelerated response to recovery of treponemal cultures following that fifth and sixth exposure to doxycycline.

[summary](#)**[13:31] Summary**

To conclude, I'd like to summarize some key points from this session.

1. Doxy PEP was effective in reducing bacterial STIs in MSM at risk for STIs, including during an open-label extension where doxy PEP efficacy was known.
2. Increasing antimicrobial resistance in other organisms, such as *Staph aureus*, is a concern for those using doxy PEP.
3. High-level tetracycline resistance among *Neisseria gonorrhoeae* isolates is widespread among MSM in King County, Washington, which is likely related to increasing doxycycline use for both STI treatment as well as prevention.
4. There was an association between doxy PEP use and increasing colonization with Group A strep, as well as tetracycline-resistant *Staph aureus*.
5. Doxy PEP implementation in MSM may have had a population effect in King County, Washington. There was a 53% decrease in syphilis among men and a 47% decrease in women after doxy PEP implementation.
6. Genetic resistance to doxycycline was not induced in vitro when *T. pallidum* SS14 strain was exposed to intermittent or continuous doxycycline that was below the concentration for killing *T. pallidum* organisms.

[credits](#)**[14:48] Credits**

This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by the Centers for Disease Control and Prevention. Transcripts and references for this podcast series can be found on our website, the National STD Curriculum, at www.std.uw.edu. Thank you for listening, and have a wonderful day.

