



CLINICIAN'S INFORMATION GUIDE

Doxy PEP for STI Prevention

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ABOUT THIS INFORMATION GUIDE

This information guide is intended for health care professionals involved in care of persons interested in or receiving doxycycline postexposure prophylaxis (doxy PEP) for STI prevention. The information in this guide pertains to the use of doxy PEP for STI postexposure prophylaxis. This guide was created and produced by the University of Washington Infectious Diseases Education & Assessment (IDEA) Program as part of the federally-funded *National STD Curriculum* and *National HIV PrEP Curriculum* projects.

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LAST UPDATED

This educational guide was last updated *October 28, 2024*.

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GENERAL INFORMATION

What is doxy PEP?

- Doxycycline postexposure prophylaxis (doxy PEP) is a preventive strategy using the antibiotic doxycycline to reduce the risk of developing bacterial sexually transmitted infections (STIs) – chlamydia, gonorrhea, and syphilis – after potential sexual exposure.
- Doxy PEP consists of taking 200 mg of doxycycline (typically two 100 mg tablets or capsules), ideally within 24 hours after sex has occurred and not longer than 72 hours after sex has occurred. This includes oral, vaginal, or anal sex.

Need for doxy PEP?

- Doxy PEP can help prevent bacterial STIs by targeting the bacteria responsible for chlamydia, gonorrhea, or syphilis.
- By preventing infection in exposed individuals, doxy PEP reduces the risk of further transmission to sexual partners.
- In high STI prevalence areas, or during outbreaks of STIs, doxy PEP may be part of broader public health initiatives to reduce the transmission of these infections.

Who is eligible to receive doxy PEP?

- Men who have sex with men (MSM) and transgender women (TGW) with a history of a bacterial STI (chlamydia, gonorrhea, or syphilis) in the last year.
- MSM and TGW who have not had a bacterial STI in the last year may be considered for doxy PEP if they anticipate participating in activities associated with elevated risk of STI exposure.
- Data do not currently support the use of doxy PEP in persons assigned female at birth (including cisgender women, transgender men, and other queer/nonbinary persons assigned female at birth).

Effectiveness of doxy PEP?

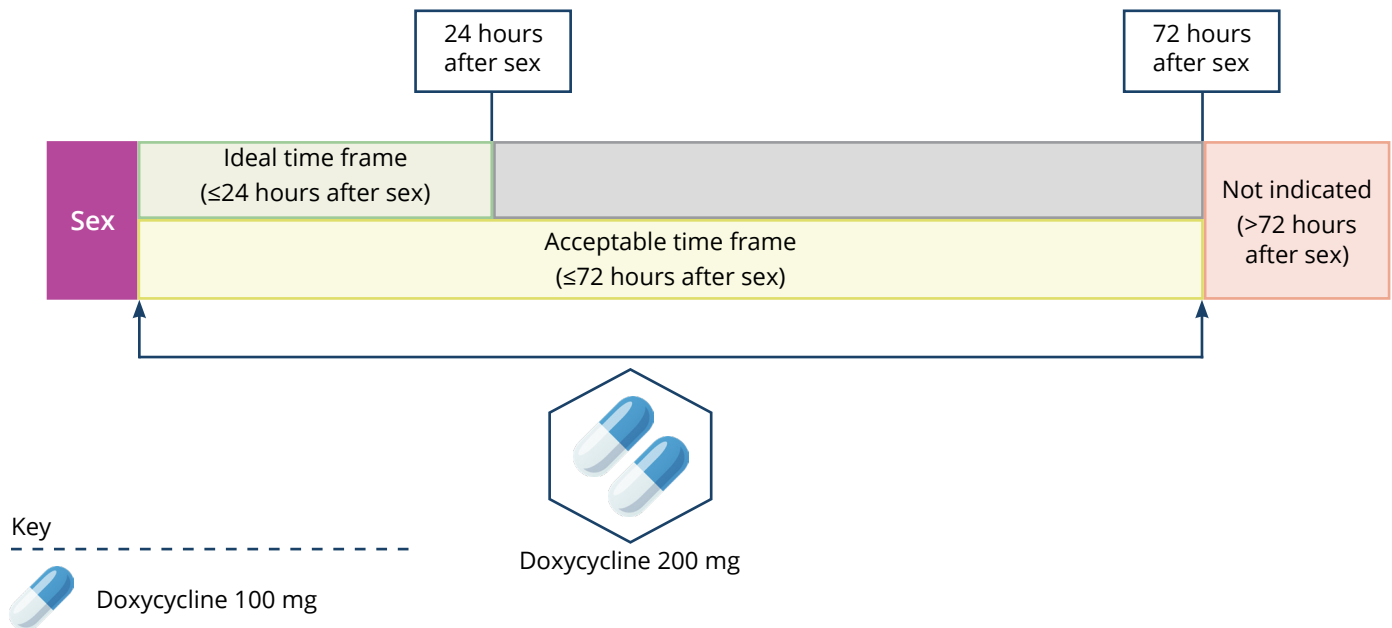
- Syphilis and chlamydia infections estimated to be reduced by approximately 70%.
- Gonorrhea infections estimated to be reduced by approximately 50%.

EDITOR'S NOTES

1. For people without HIV, if they are a candidate for doxy PEP, evaluate whether they are also candidates for HIV PrEP.

DOXY PEP DOSING

Single Sexual Event



- Patients should not take more than 200 mg of doxycycline per 24 hours.
- Patients should take doxy PEP as soon after sex as possible, but no later than 72 hours.

Doxy PEP with More than One Sex Event in 72-Hour Period[^]

With more than one sex event during a 72-hour period, it is important that all exposures are covered by a 200 mg dose of doxy PEP taken within 72 hours of the sex contact, but the individual should not take more than 200 mg of doxycycline within a 24-hour period.

PRESCRIBING

Suggested prescribing practices for patient taking doxy PEP

Prescription	Number of Pills per Month	Number of Refills
Take one 200 mg dose of doxycycline (typically two 100 mg pills or capsules) as soon as possible within 72 hours after oral, vaginal, or anal sex. Do not exceed 200 mg in 24 hours	Based on patient's anticipated sexual activity. Do not exceed 30 doses (a dose is 200 mg) per month	Sufficient refills to last until next visit
Providers should reassess the need for doxy PEP at each visit, including any anticipated changes in sexual activity and desired monthly number of doxy PEP pills prescribed.		

LABORATORY EVALUATION AND MONITORING

Table based on 2024 CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention

Laboratory Evaluation in Persons Taking Doxy PEP

Test	Initial visit	Follow-up screening (every 3-6 months)
 HIV Antigen/ Antibody	✓ # *	✓ # *
 Syphilis Serology	✓	✓
 Gonorrhea [^]	✓	✓
 Chlamydia [^]	✓	✓
 Hepatitis B Serology ⁺	✓	
 Hepatitis C Serology ⁺	✓	

LEGEND:

Do not screen for HIV if person is already known to have HIV

* For persons without HIV receiving HIV preexposure prophylaxis (PrEP), screen per [CDC HIV PrEP guidelines](#) (view the National HIV PrEP Curriculum [Laboratory Monitoring Guide](#))

[^] Recommended screening is based on anatomical site exposure (e.g., pharynx, anorectal, and urogenital)

⁺ One-time screening recommended for all adults in the United States. Give hepatitis B immunization if nonimmune. Repeat annual hepatitis C screening should be performed for persons receiving HIV preexposure prophylaxis (PrEP), for persons with HIV, and persons who inject drugs.

EDITOR'S NOTES

1. Provide immunizations for hepatitis A virus (HAV), hepatitis B virus (HBV), mpox, and human papillomavirus (HPV) if indicated.
2. All persons receiving doxy PEP who do not have HIV should be offered HIV preexposure prophylaxis (PrEP).

COUNSELING

Suggested counseling for patients taking doxy PEP

Initial Visit

- Discuss benefits of doxy PEP, including estimated 70% reduction in syphilis and chlamydia infection and 50% reduction in gonorrhea infection. Patients should be made aware that doxy PEP is not 100% effective against these bacteria and that it does not protect against sexually transmitted viral infections including herpes simplex virus, human papillomavirus, mpox, and HIV. Although doxycycline has activity against *Mycoplasma genitalium*, there are insufficient data for prevention of *M. genitalium* at this time.
- Discuss potential harms of doxy PEP, including side effects such as gastrointestinal distress, sun sensitivity, pill esophagitis, potential for antimicrobial resistance, and changes in gut microbiome.
- Advise on methods for mitigating side effects, including taking doxycycline with a full glass of water, avoiding lying down for 1 hour after doxycycline ingestion, and consistent use of sun protection when outside.
- Advise spacing doxycycline by 2 hours before or after using dairy products, antacids, and supplements that contain calcium, iron, magnesium, or sodium bicarbonate.
- Assess for drug interactions with patient's current medications.
- Review doxycycline dosing guidelines, including the recommendation to take doxy PEP as soon as possible after sex, but no later than 72 hours, and to take no more than 200 mg doxycycline per 24 hours.
- Review when doxy PEP should be used, including after receptive or penetrative vaginal, oral, or anal sex.
- Counsel on other risk-reduction strategies, if indicated.
- Offer HIV PrEP to persons without HIV.
- For patients of childbearing potential, invite discussion of their pregnancy intention and provide access to contraception if desired. These individuals should receive counseling that the use of doxy PEP during pregnancy is not recommended.

Subsequent Visits

- Discuss patient experience with doxy PEP, including confirming appropriate use and offering the opportunity to answer patient questions.
 - Re-assess ongoing need and desire for doxy PEP.
 - Assess for doxycycline side effects and new drug interactions.
 - Provide risk-reduction counseling and condoms if desired.
 - Consider initiation of HIV PrEP for patients without HIV.
 - For patients with HIV, confirm engagement in care.
 - For patients of childbearing potential, invite discussion of their pregnancy intention and facilitate contraception if desired.
 - As needed, refer for mental health and substance use treatment services (as well as other services that may be appropriate).
-

DoxyPEP

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections in MSM and TGW with and without HIV

Summary

Among men who have sex with men (MSM) and transgender women (TGW) who had a recent sexually transmitted infection (STI), the combined incidence of gonorrhea, chlamydia, and syphilis was lower by two thirds with doxycycline postexposure prophylaxis (doxy PEP) than with standard care.

Study Design

Open-label, randomized study conducted in San Francisco, CA and Seattle, WA

Participants

501
Adults



482 MSM



19 TGW



All participants had gonorrhea, chlamydia, or syphilis at least once in the past year



67% White 11% Asian or Pacific Islander
7% Black 30% Hispanic or Latino
(15% multiple races)

Cohorts

(2:1 randomization)



People without HIV
Taking HIV PrEP*

(n = 327)



People with HIV

(n = 174)

Interventions

Doxy PEP
One 200 mg tablet,
within 72 hours of sex

Standard Care
No doxy PEP

Doxy PEP
One 200 mg tablet,
within 72 hours of sex

Standard Care
No doxy PEP

Results[^]

Any new STI
(quarterly incidence)

10.7%

31.9%

11.8%

30.5%

New gonorrhea infections
(quarterly incidence)

9.1%

20.2%

8.9%

20.3%

New chlamydia infections
(quarterly incidence)

1.4%

12.1%

3.9%

14.8%

New syphilis infections
(quarterly incidence)

0.4%

2.7%

0.7%

2.3%

Antimicrobial resistance

Gonorrhea culture was available in 13 participants; after study enrollment, tetracycline-resistant gonorrhea was identified in 5 of 13 (38%) in the doxycycline groups and 2 of 16 (13%) in the standard-care groups. Doxycycline resistance rates for *Staphylococcus aureus* isolates were similar in the doxycycline groups (5%) when compared with the standard-care groups (4%).

[^]Differences in STI incidence in the doxy PEP and standard care were statistically significant for all results listed in this table.

Source: Luetkemeyer AF, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *N Engl J Med* 2023;388:1296-1306. [PMID: 37018493]

*Abbreviations: PrEP = preexposure prophylaxis

ANRS DOXYVAC

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections in MSM taking HIV PrEP

Summary

Among men who have sex with men (MSM) taking HIV preexposure prophylaxis (PrEP) with a recent history of a sexually transmitted infection (STI), use of doxycycline postexposure prophylaxis (doxy PEP) reduced the combined incidence of new chlamydia or syphilis infection by 83%.

Study Design

Multicenter, open-label, randomized trial conducted in Paris, France

Participants



545
MSM taking
HIV PrEP



Ages ranged from
34 - 49 years



88% White
2% Black
2% Asian



All participants had a history of an STI
within the past 12 months



Median number of condomless sex
acts in the past 4 weeks: 4

Interventions

Doxy PEP

One 200 mg tablet,
within 72 hours of
condomless sex



(n = 362)

No Doxy PEP

(n = 183)

Results[^]

	Events (Incidence per 100 person-years)	Events (Incidence per 100 person-years)	Hazard Ratio
Chlamydia or Syphilis (first episode)	8.8	53.2	0.17
Chlamydia (first episode)	5.9	42.1	0.14
Syphilis (first episode)	2.9	14.5	0.21
Gonorrhea (first episode)	45.5	68.4	0.67

Resistance

All tested gonorrhea isolates in both arms were resistant to tetracycline at baseline and during follow-up. There was no difference in detection of nasopharyngeal methicillin-resistant *Staphylococcus aureus* (MRSA) or extended-spectrum beta-lactamase producing *E. coli* in either group.

[^] Differences in STI incidence per 100 person-years in the doxy PEP and no doxy PEP groups were statistically significant for all results listed in this table.

Source: Molina JM, Bercot B, Assoumou L, et al. 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 x 2 factorial design. *Lancet Infect Dis*. 2024;S1473-3099(24)00236-6. [PMID: 38797183]

IPEGAY-DoxyPEP

Doxycycline Postexposure Prophylaxis in Adult Men Who Have Sex with Men and Who are Taking HIV PrEP

Summary

Among adult men who have condomless sex with men and who are taking HIV preexposure prophylaxis (PrEP), the use of doxycycline postexposure prophylaxis (doxy PEP) was associated with a 47% relative reduction in risk of new sexually transmitted infection (STI) acquisition compared to no doxy PEP.

Study Design

Multicenter, open-label, randomized study conducted in France

Participants

 **232**
adult MSM
taking HIV
PrEP



Most patients 30+ years of age



95% White 5% Other



All participants engaged in condomless anal sex with 2+ different partners in the last 6 months

Interventions

Doxy PEP

One 200 mg tablet,
within 72 hours of
condomless sex



(n = 116)

No Doxy PEP

(n = 116)

Results

	Total Incidence	Total Incidence	Relative Risk Reduction
Occurrence of new STI	28	45	47%
Occurrence of Chlamydia	7	21	70%
Occurrence of Syphilis	3	10	73%
Occurrence of Gonorrhea	22	25	No significant risk reduction

Source: 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 IPEGAY trial. Lancet Infect Dis. 2018;18:308-17. [\[PMID: 29229440\]](https://pubmed.ncbi.nlm.nih.gov/29229440/)

dPEP KENYA

Doxycycline Postexposure Prophylaxis in Cisgender Women

Summary

Among cisgender women in Kenya, the use of doxycycline postexposure prophylaxis (doxy PEP) after condomless sex did not significantly lower the incidence of sexually transmitted infections (STIs). Interpretation of these findings is limited due to low adherence with doxy PEP in the study participants.

Study Design

Open-label, randomized, controlled trial

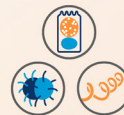
Participants



449

nonpregnant women taking HIV preexposure prophylaxis (PrEP)

Conducted in
Kisumu, Kenya



17.9% of participants had an STI (gonorrhea, chlamydia, or syphilis) at enrollment



Ages ranged from 18 - 30 years

Interventions

Doxy PEP¹

One 200 mg tablet, within 72 hours of condomless sex

(n = 224; total visits = 854)



Standard Care

No doxy PEP

(n = 225; total visits = 886)

Results²

	STIs Across Quarterly Visits	STIs Across Quarterly Visits	Relative Risk	95% CI
Any STI ³	50	59	0.88	0.60-1.29
Any chlamydia infection	35	50	0.73	0.47-1.13
Any gonorrhea infection	19	12	1.64	0.78-3.47
Adherence	Among 50 randomly selected participants in the doxy PEP group, doxycycline was detected in 58 of 200 hair samples (29.0%) across all quarterly visits.			
Resistance	100% of gonorrhea isolates in both arms at baseline and follow-up were resistant to doxycycline			

¹Doxycycline withdrawn in the event of pregnancy (80 women became pregnant during the study, including 44 in the doxy PEP group and 36 in the standard care group)

²This study was not powered to assess syphilis prevention independently due to low incidence of syphilis in western Kenya

³There were 8 instances of dual infection with chlamydia and gonorrhea

Source: Stewart J, Oware K, Donnell D, et al. Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women. *N Engl J Med.* 2023;389:2331-40. [PMID: 38118022]

FREQUENTLY ASKED QUESTIONS

1. What are the common side effects of doxycycline and what strategies can be used to reduce these side effects?

Doxycycline is generally well tolerated. The most common side effects reported in study populations were gastrointestinal, including nausea or diarrhea. Taking doxycycline with food can help to reduce nausea, but stomach upset and loose stools may be a problem, particularly for people who have receptive anal sex (bottom). Doxycycline can also cause esophagitis, or irritation of the throat, and it is recommended that patients take the medication with a full glass of water and avoid lying down for at least 1 hour following the dose. Doxycycline is associated with sun sensitivity, and all patients should be counseled on the use of sun protection. The absorption of doxycycline is impaired by dairy products, antacids containing aluminum, calcium, or magnesium, bismuth subsalicylate and iron-containing preparations. Doxycycline should be spaced by at least 2 hours from ingestion of these substances.

2. What should I do if my patient has a known STI exposure to gonorrhea or chlamydia while taking doxy PEP?

All individuals who have had sexual contact in the prior 60 days with a person with known gonorrhea or chlamydia infection should undergo testing for both gonorrhea and chlamydia at all exposed anatomic sites (urogenital, oropharyngeal, and/or rectal). Prior to the roll-out of doxy PEP, CDC guidelines recommended presumptive treatment for any person who had sexual contact with a partner diagnosed with gonorrhea or chlamydia within 60 days of symptom onset or the gonorrhea/chlamydia diagnosis. However, it is estimated that only about one-third of sexual contacts of MSM with gonorrhea/chlamydia will end up acquiring the same infection. With appropriate use of doxy PEP, the estimated likelihood of acquiring gonorrhea or chlamydia after potential exposure is even lower (approximately 15% for gonorrhea) and (approximately 6-7% for chlamydia). Thus, in this setting, it may be reasonable to delay treatment until receipt of test results. Providing presumptive STI treatment to people taking doxy PEP who have a known gonorrhea or chlamydia exposure may be considered on a case-by-case basis. The decision should be based on shared decision-making with the patient, taking into consideration patient preferences, risks of antimicrobial resistance and overuse, and the patient's ability to follow up with their health care provider for treatment if testing is positive.

3. What should I do if my patient has a known STI exposure to syphilis while taking doxy PEP?

Although appropriate use of doxy PEP by people having condomless sex is associated with >75% decreased risk of syphilis acquisition overall, the likelihood of acquiring syphilis in the setting of appropriate doxy PEP use and a verified exposure to syphilis is unknown. There is also theoretical concern that intermittent exposure of doxycycline as PEP could affect the natural history and kinetics of syphilis serologies, making it more challenging to diagnose new syphilis. Since current CDC guidelines for doxy PEP do not address how to manage syphilis exposures, the approach to managing contacts to syphilis should continue to be based on existing CDC STI Treatment Guidelines. Irrespective of doxy PEP use, sexual contacts of a person diagnosed with syphilis should undergo an assessment of any clinical signs or symptoms and serologic testing for syphilis.

- Exposure within Past 90 Days to a Partner Diagnosed with Early Syphilis: Obtain blood for syphilis serologic evaluation. If the person being evaluated has clinical signs or symptoms of syphilis, then treat promptly based on the diagnosed clinical stage of syphilis. If no syphilis-related manifestations, then treat as a contact to early syphilis (2.4 million units of benzathine penicillin IM x 1), even if serologic results are negative.

FREQUENTLY ASKED QUESTIONS

- Exposure Greater than 90 Days Before a Partner Diagnosed with Early Syphilis: Obtain blood for syphilis serologic evaluation. If the person being evaluated has clinical signs or symptoms of syphilis, then treat promptly based on the diagnosed clinical stage of syphilis. If no syphilis-related manifestations, then base treatment on likelihood of follow-up and serologic results (if available). If serologic results are available and are negative, no treatment is indicated. If serologic results are not available and follow-up is uncertain, then presumptively treat as a contact to early syphilis (2.4 million units of benzathine penicillin IM x 1).
- Exposure to Partner Diagnosed with Late Syphilis: Sexual contacts with a partner with late syphilis should be evaluated with syphilis serologies and clinical exam, then treated based on findings of that evaluation.

4. What should I do if my patient is diagnosed with a new STI while on doxy PEP?

If a person is newly diagnosed with a sexually transmitted infection while taking doxy PEP, they should be treated for that infection according to CDC STI Treatment Guidelines. If the patient's recommended STI treatment regimen includes doxycycline (e.g., chlamydia, *Mycoplasma genitalium*, or syphilis in a person who is allergic to penicillin), they should be instructed to hold doxy PEP while they are taking doxycycline treatment to avoid excess dosing. If available, gonorrhea culture should be considered for antimicrobial resistance monitoring; resistance testing is not commercially available for other bacterial STIs. All patients should be advised to abstain from sex until after completion of treatment for chlamydia, gonorrhea, or syphilis and symptoms resolve (if present). They may resume taking doxy PEP no sooner than 24 hours after their last dose of doxycycline for the STI treatment.

5. How many doxycycline pills should I prescribe at one time?

The number of pills prescribed monthly should be based on the patient's anticipated sexual activity. It is recommended that enough refills be provided to last until the patient's next visit. No more than sixty 100 mg pills (or 30 of the 200 mg pills) should be prescribed each month as patients should never exceed doses of 200 mg per 24 hours.

6. Can my patient take doxy PEP at the same time as HIV preexposure prophylaxis (PrEP)?

Yes! Doxy PEP and HIV PrEP may be taken together safely. Since doxy PEP is meant to be used after sex, it is highly recommended that any patient without HIV who is prescribed doxy PEP also be considered for and counseled on the use of HIV PrEP. Indeed, all the doxy PEP clinical trials included participants who were also taking HIV PrEP. For more information on the use of HIV PrEP, please refer to the [National HIV PrEP Curriculum](#).

7. How often should I reassess my patient's need for doxy PEP?

Patients' ongoing need for doxy PEP should be reassessed every 3-6 months. This may also be a good opportunity to discuss any anticipated changes in sexual activity, monthly number of doxy PEP pills prescribed and/or potential side effects.

FREQUENTLY ASKED QUESTIONS

8. What other counseling should I provide for my patient who is taking doxy PEP?

Doxy PEP should be offered as part of a comprehensive package of services for reducing risk of exposure to sexually transmitted infections and HIV. All patients should be offered routine screening for gonorrhea, chlamydia, syphilis, and HIV (if not already diagnosed with HIV) at baseline and every 3-6 months. Persons without HIV receiving doxy PEP should be considered for counseling on and initiation of HIV PrEP, noting that more intentional counseling may be necessary for persons using 2-1-1 (or on-demand) PrEP to mitigate confusion with dosing schedules for doxy PEP. Gonorrhea and chlamydia testing should include urogenital nucleic acid amplification testing (NAAT), and consideration of additional oropharyngeal and rectal testing for patients participating in oral and anal sex, respectively. In addition, hepatitis A and B serologic screening should be performed once at baseline, and patients who are nonimmune to hepatitis A and/or B should be offered vaccination to protect against acquisition of these viruses. Hepatitis C serologic screening should be performed at baseline and yearly thereafter for persons on PrEP, persons living with HIV, and persons who inject drugs; individuals who test positive for active hepatitis C should receive treatment. Patients who have not received mpox immunization should be offered the JYNNEOS smallpox/mpox vaccine series (2 doses given at least 28 days apart). Patients should also be informed and counseled on other risk-reduction strategies, including condom use if desired. For more information on the use of HIV PrEP, please refer to the [National HIV PrEP Curriculum](#). Patients of childbearing potential should be invited to discuss their pregnancy intention and provided access to contraceptive methods if desired. They should also be made aware that use of doxycycline is not recommended in pregnancy.

9. For patients taking doxy PEP, what is the risk of developing doxycycline resistance in STI pathogens?

The exact risk of doxycycline resistance in STI pathogens associated with the use of doxy PEP is still an area of active research. Doxycycline has historically been used as standard of care for treatment of chlamydia infection and for treatment of early or late syphilis in nonpregnant adults when penicillin cannot be used. In addition, doxycycline has been used for other conditions, such as to treat acne, respiratory tract infections, tickborne diseases, and skin and soft tissue infections. Tetracycline resistance (which is often used as a surrogate for doxycycline resistance) has never been described in the bacteria that cause chlamydia and syphilis. In contrast, approximately 20% of gonorrheal isolates are tetracycline resistant in the United States, and this rate is greater than 50% in Europe. Although several of the doxy PEP trials have attempted to evaluate doxycycline resistance in patients taking doxy PEP, evaluation of drug resistance patterns in chlamydia and gonorrheal isolates has been made challenging by low culture yield of these organisms. Three doxy PEP studies conducted outside of the United States noted substantial rates of high- or intermediate-level doxycycline resistance among gonorrhea samples both at baseline and at follow-up (77-100%) with no significant difference in resistance between the doxy PEP and no doxy PEP groups. The one randomized control trial conducted in the United States found that 27% of gonorrhea isolates were doxycycline resistant at baseline, compared to 38% (5/13) in the doxy PEP group and 12% (2/16) in the no doxy PEP group after enrollment. Statistical significance could not be calculated due to small sample size. No doxycycline resistance was detected among chlamydia samples in any study either at baseline or at follow up. Overall, the risk of tetracycline (doxycycline) resistance among sexually transmitted bacteria for patients taking doxy PEP remains an area of active research. Patients should receive counseling regarding the potential for doxy PEP to increase their risk of developing antimicrobial resistance.

FREQUENTLY ASKED QUESTIONS

10. For patients taking doxy PEP, what is the impact on non-STI pathogens and the gut microbiome?

Because doxycycline may impact the skin flora and the gut microbiome, there has been concern that persons taking doxy PEP may develop resistance in non-sexually transmitted bacteria and potentially have changes in the gut microbiome. Two studies, the DOXYVAC and DoxyPEP trials, evaluated rates of resistance in non-sexually transmitted bacteria, including *Staphylococcus aureus*. In the DOXYVAC study, the rates of detection of methicillin-resistant *Staphylococcus aureus* (MRSA) by nasopharyngeal swab were not significantly different between doxy PEP and no doxy PEP groups. In the DoxyPEP study, *S. aureus* was isolated by nasopharyngeal swab at baseline in 45% of participants, with 13% of these isolates demonstrating tetracycline resistance. At one year into the study, tetracycline resistance was found in 16% of *S. aureus* isolates from the doxy PEP group and 8% from the no doxy PEP group (not statistically different). Also, *S. aureus* carriage was found to be 40% lower in the doxy PEP group compared to the no doxy PEP group at one year. Ongoing research is needed to better understand this risk over time with wider adoption of doxy PEP among qualifying populations and to define whether significant changes occur in the gut microbiome. Patients should receive counseling regarding the potential for doxy PEP to cause changes in the gut microbiome.

11. Is doxy PEP appropriate for patients having daily or very frequent potential STI exposures?

Yes. Doxy PEP is recommended for all gay, bisexual, or other men who have sex with men and transgender women who have been diagnosed with one or more sexually transmitted infections within the last 12 months. This includes people having sexual encounters on a daily, or multiple times per day, basis. It is recommended that patients do not take more than 200 mg of doxycycline per 24 hours. For patients having anticipated daily, or multiple times per day, sexual encounters, it may be easiest for them to take a dose of doxycycline at the end of the day, after all sexual encounters have been completed, or alternatively, a single dose within 72 hours to cover the preceding sexual encounters within that period (see dosing guidance above). Though the use of doxycycline for postexposure STI prophylaxis is relatively new, the use of chronic, daily doxycycline is already standard of care for patients with a variety of other medical conditions. Though data are more limited and from smaller studies, there is evidence to support doxycycline preexposure prophylaxis whereby doxycycline 100 mg is taken daily to prevent bacterial STI. Further research is ongoing and this strategy has not yet been recognized or endorsed by CDC. Regular doxycycline use is generally well tolerated (see Question 1), though ongoing research is required to understand the risks of antimicrobial resistance associated with chronic doxycycline use.

12. Can doxy PEP be used to prevent STIs in cisgender women or other persons assigned female at birth?

The dPEP Kenya clinical trial did not find that doxy PEP was an effective intervention for cisgender women, and data are otherwise lacking for transgender men or other queer and nonbinary persons assigned female sex at birth (AFAB). The CDC notes that providers should use their clinical judgement and shared decision-making when considering doxy PEP for populations not included in their recommendation. Additional studies to evaluate doxy PEP use in cisgender women are forthcoming. Doxycycline is contraindicated in pregnancy.

13. Can doxy PEP be used to prevent STIs in cisgender, heterosexual men?

Data to support use in cisgender heterosexual men are also limited, and thus cisgender heterosexual men are not included in the CDC's guidelines for doxy PEP. The CDC notes that providers should use clinical judgement and shared decision-making to inform doxycycline use in populations in whom doxy PEP has not yet been studied.

FREQUENTLY ASKED QUESTIONS

14. If your patient stops taking doxy PEP, can they start taking it again at a later time?

Yes! Doxy PEP is a dynamic intervention. Use should reflect recent and anticipated risk and be reassessed every 3 to 6 months. Stopping doxy PEP does not preclude someone from restarting later. If planning to stop doxy PEP, patients should be counseled not to use leftover quantities of medications for treatment or prevention of any other conditions.

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DISCLOSURES

Dr. Fessler, Dr. Hunt, Dr. Cannon, and Dr. Spach have no disclosures. Dr. Dombrowski has received research funding from Hologic, Cepheid, and Mayne Pharmaceuticals.



ACKNOWLEDGEMENT

The authors would like to thank Peter Harrison, MPH and Carol Kono-Noble for their design and production work, Christine M. Johnston, MD, MPH for review of this guide, and Mary F. Annese for copy editing.

FUNDING

The National STD Curriculum and the National HIV PrEP Curriculum are supported by the Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services (HHS) as a part of a financial assistance award totaling \$625,000 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by CDC, HHS, or the U.S Government. This project is led by the University of Washington Infectious Diseases Education & Assessment (IDEA) Program.

