HIV PrEP and PEP in Primary Care

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February 27,2024

Outline

HIV PrEP

- Oral
- Injectable

HIV PEP

- DoxyPEP

Which of the Following Best Describes your Experience with PrEP?

A. Never heard of PrEP

B. Familiar with PrEP but have never recommended it

C. Prescribed PrEP a few times before

D. Extensive experience prescribing PrEP to patients

HIV Prevention Strategies

- Sexual behavior modification
- Condom use
- Test and treat STIs
- HIV treatment as prevention (U=U)
- PrEP: Pre-Exposure Prophylaxis
- PEP: Post-Exposure Prophylaxis
- Offer sterile, personalized injection drug use equipment for people who inject drugs

https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/20/48/the-basics-of-hiv-prevention

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Which of the following patients would benefit from PrEP?

A. A person who injects drugs, shares needles and the last injection was 2 months ago
B. A man who has sex with men (MSM), has multiple partners and inconsistent condom use
C. A heterosexual female recently diagnosed with syphilis
D. A 23 yo male who is asking for PrEP but denies any risk factors for HIV
E. A and B are correct
F. All are correct

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PrEP: Definition

- **Pre-exposure** …le at very high risk for HIV … to …
  - Help … from a sexual …
- **Medic…**
  - take … (Descovy®)

  OR
  - Ca… …ble susp…nsion (Apretude®) taken … …n injections administered one month a… …d th… every two months thereafter

PrEP is not a substitution for other HIV prevention interventions!

PrEP does not protect against other STIs!

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Why PrEP?

PrEP is highly effective

When taking oral daily PrEP the risk of acquiring HIV is reduced by:

~ 99% among men who have sex with men (MSM)	~ 74 – 84% among people who inject drugs (PWID)

https://www.cdc.gov/hiv/risk/estimates/preventionstrategies.html

PrEP Should be Offered to People Who are HIV Negative and:

- Have **had anal or vaginal sex in the past 6 mont nd**:
  - Sexu
  - Doe
  - Has
- **Inject d**
  - H
  - S example, cookers).
- **Have been prescribed non-occupational post-expos rophylaxis (PEP) and**
  - report continued risk behavior, or
  - have used multiple courses of PEP

Anyone who is at risk for acquiring HIV

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Oral PrEP

Oral PrEP

Generic Name	Trade Name	Dose	Frequency	Most Common Side Effects[109,110]
F/TDF	Truvada	200 mg/300 mg	Once a day	Headache, abdominal pain, weight loss
F/TAF	Descovy	200 mg/25 mg	Once a day	Diarrhea

Adherence and F/TDF PrEP Efficacy in **MSM**

Weekly Medication Adherence Estimated by Drug Concentration	HIV Incidence per 100 person/years
None	4.2
≤2 pills/week	2.3
2-3 pills/week	0.6
≥4 pills/week	0.0

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Baseline Labs for Oral PrEP

Renal function

Hepatitis B serology:

- Hep B Surface Ab
- Hep B Surface Ag
- Hep B Core Ab

Lipid profile (F/TAF)

HIV 1/2 Ab/Ag

- **Add on HIV RNA (Viral Load) for a**nyone who has taken oral PrEP in the last 3 months and/or has received a CAB injection in the last 12 months

Plus other STI Screening

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Time to positivity of HIV diagnostic tests

Test	Target of detection	Approximate time to positivity (days)
Enzyme-linked immunoassay		
IgG sensitive tests	IgG antibody	35 to 45
	IgG antibody	25 to 35
IgM/IgG-sensitive tests	IgM and IgG antibody	20 to 30
Ag/Ab Immunoassays	IgM and IgG antibody and p24 antigen	15 to 20
Western blot		
	IgM and IgG antibody	35 to 50 (indeterminate)
		45 to 60 (positive)
HIV viral load test		
Sensitivity cutoff 50 copies/mL	RNA	10 to 15
Ultrasensitive cutoff 1 to 5 copies/mL	RNA	5

Oral PrEP Follow-up

- **Every 3 months:**
  - Repeat HIV testing
  - Assess for signs or symptoms of acute HIV infection
  - Provide RX for no more than 90 days (until the next HIV test)
  - Assess medication adherence and risk-reduction behaviors
  - Conduct STI testing if symptoms of infection
  - Conduct STI screening for asymptomatic MSM at high risk for syphilis, gonorrhea, or chlamydia

Features	Overall (n = 375) %
Fever	75
Fatigue	68
Myalgia	49
Skin rash	48
Headache	45
Pharyngitis	40
Cervical adenopathy	39
Arthralgia	30
Night sweats	28
Diarrhea	27

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Oral PrEP Follow-up

- **Every 6 months:**
  - **eCrCl** for persons age ≥50 years or had eCrCl <90 ml/min at PrEP initiation
    - More frequently if at risk for renal diseases (e.g., hypertension, diabetes),
    - A rise in serum creatinine is not a reason to withhold treatment if eCrCl remains ≥60 ml/min for F/TDF or ≥30 for F/TAF
    - If eCrCl is declining steadily (but still ≥60 ml/min for F/TDF or ≥30 ml/min for F/TAF), evaluate for other nephrotoxic medicadions and consider nephrologist consultation
  - **Conduct STI screening** for sexually active persons (i.e., syphilis, gonorrhea, for all PrEP patients and chlamydia for MSM and TGW even if asymptomatic)
  - **Assess need for continuing or discontinuing PrEP**

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Oral PrEP Follow-up

- **At least every 12 months:**
  - Monitor eCrCl for all patients continuing on PrEP medication
  - Monitor lipid panel, and weight for patients prescribed F/TAF
  - Conduct chlamydia screening for heterosexual women and men even if asymptomatic

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Timing of Oral PrEP-associated Lab Tests

Test	Screening/Baseline Visit	Q 3 months	Q 6 months	Q 12 months	When stopping PrEP
HIV Test	X*	X			X*
eCrCl	X		If age ≥50 or eCrCL <90 ml/min at PrEP initiation	If age <50 and eCrCl ≥90 ml/min at PrEP initiation	X
Syphilis	X	MSM /TGW	X		MSM/TGW
Gonorrhea	X	MSM /TGW	X		MSM /TGW
Chlamydia	X	MSM /TGW	X		MSM /TGW
Lipid panel (F/TAF)	X			X	
Hep B serology	X				
Hep C serology	MSM, TGW, and PWID only			MSM,TGW, and PWID only	

* Assess for acute HIV infection

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Discontinuing Oral PrEP

Provider should document:

- HIV status at the time of discontinuation
- Reason for discontinuation
- Recent medication adherence and reported sexual risk behavior

Restarting PrEP requires same initial evaluation, minus the Hep B serology

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Injectable PrEP

Injectable PrEP

- Cabotegravir (CAB) 600 mg (brand name Apretude®)
- Only for prevention of HIV sexual transmission patients whose risk factors for HIV include sexual transmission only (not for PWID)
- Adults and adolescents who weigh at least 35 kg (77 lb)
- CAB injections may be a good option for PrEP for people who
  - Have problems taking oral PrEP as prescribed
  - Prefer getting a shot every 2 months instead of taking oral PrEP
  - Have serious kidney disease that prevents use of oral PrEP medications

https://www.cdc.gov/stophivtogether/library/topics/prevention/brochures/cdc-lsht-prevention-brochure-clinicians-quick-guide-what-is-injectable-hiv-prep.pdf

How Is Injectable PrEP Administered?

- **How:**
  - IM – ventro- (preferred) or dorso- gluteal – 3mL at room temp – must be given within 2 hours of drawing it up in syringe – use long enough needle based on body habitus – 1.5-2”
- **When:**
  - First dose – IM injection of CAB 600mg
  - 1 month later – IM injection of CAB 600mg
  - Every 2 months after - IM injection of CAB 600mg
- **If concern for side effects:**
  - A 4-week of 30 mg daily oral CAB prior to the first injection is optional

https://www.cdc.gov/stophivtogether/library/topics/prevention/brochures/cdc-lsht-prevention-brochure-clinicians-quick-guide-what-is-injectable-hiv-prep.pdf; https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215499s002lbl.pdf

Differences with Oral PrEP

- Careful with medications that reduce concentrations of CAB
  - Anticonvulsants: Carbamazepine, oxcarbazepine, phenobarbital, phenytoin
    Anti mycobacterials: Rifampin, rifapentine
- Side effects
  - Injection site reactions, headache, fever, fatigue, diarrhea, nausea, rash
- Tests not needed with CAB that are indicated with F/TAF or F/TDF:
  - Creatinine, eCrCl, hepatitis B serology, lipid panels
- Testing for STIs adapted to CAB injection appointments

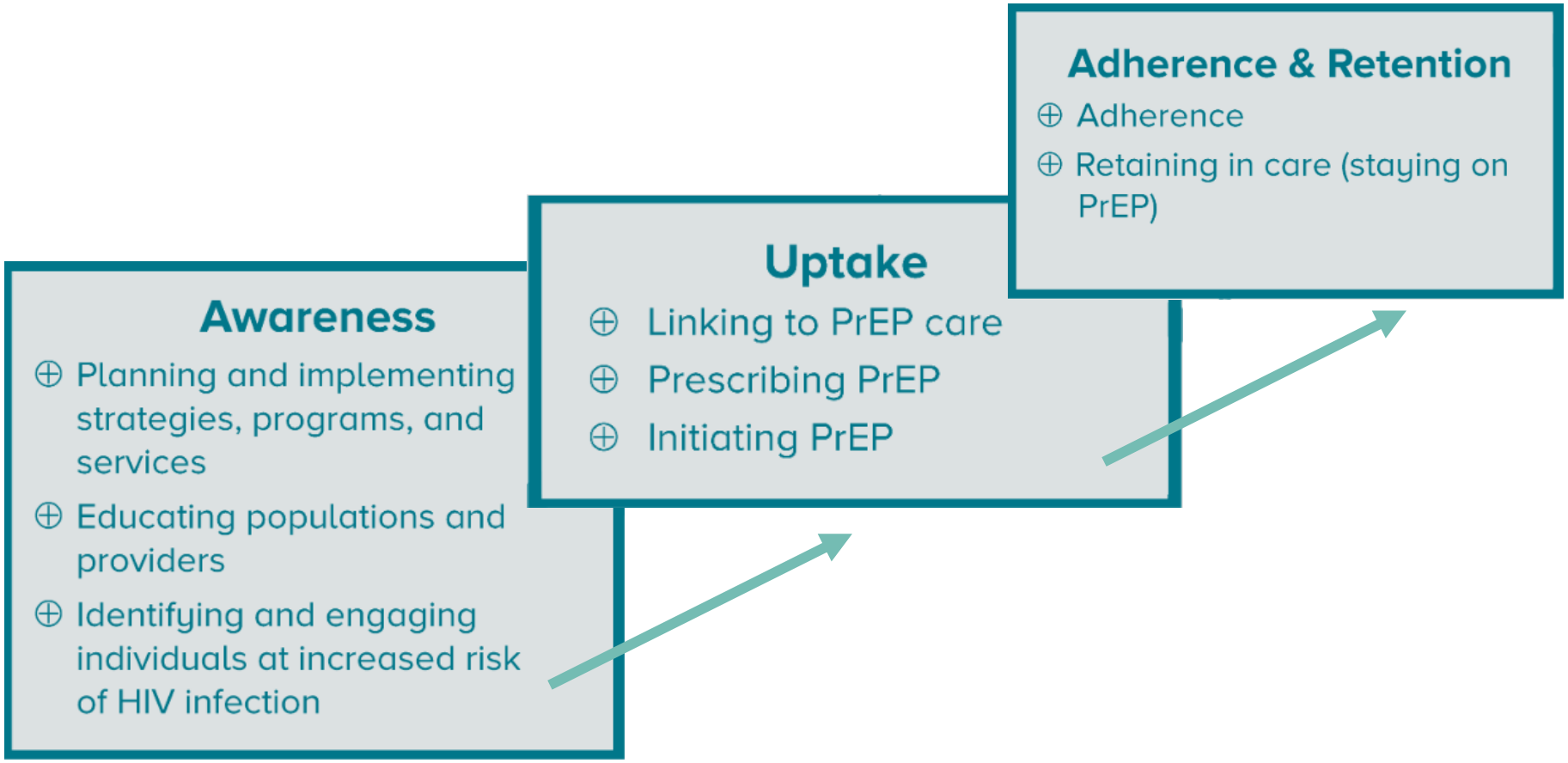
https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215499s002lbl.pdf

Discontinuing CAB

- Educate patients about the “tail” and risks during declining CAB levels
- Assess ongoing risk/indications
- If PrEP is indicated, prescribe daily oral F/TDF or F/TAF beginning within 8 weeks after last injection
- Educate about nPEP
- Continue follow-up visits quarterly for 12 months
  - Conduct HIV-1 RNA tests at each quarterly follow-up visit after discontinuing CAB injections

https://www.cdc.gov/stophivtogether/library/topics/prevention/brochures/cdc-lsht-prevention-brochure-clinicians-quick-guide-what-is-injectable-hiv-prep.pdf

PrEP Care



*Modified from Nunn, et al. Defining the HIV pre-exposure prophylaxis care continuum. *AIDS* 2017; 31(5):731-734.

If a patient tests positive (confirmed) for HIV: What now?

- Get to know the patient
- Destigmatize HIV and normalize HIV care
- Explain the basics
- Focus on the effectiveness of HIV treatment
- Get labs
- Start medication on the same day or warm hand off

Role of the PCP in PrEP

- **Consider PrEP for at-risk individuals**
  - Take a good sexual health history to find at-risk individuals
  - Ask about injection drug use
- **Discuss with the patient the principles of PrEP**
- **Offer brochures for PrEP in your office**
- **Decide:**
  - Is this something I will offer my patient?
  - If not me, who? If not now, when?

HIV Post-exposure Prophylaxis (PEP)

Exposure to HIV is an Emergency!

- Science is based on other similar scenarios, animal data and expert recommendations
- The ideal time to start PEP is within 72 hours of exposure!
  - Consider giving the first dose upon presentation
  - Can be given up to 72 hours after exposure
- After 72 hours, it should not be given

Sooner = Better

Who should be offered PEP?

Individuals who are HIV negative or unknown HIV status who:

- May have been exposed to HIV during sex
- Shared needles or other equipment (works) to inject drugs
- Were sexually assaulted
- May have been exposed to HIV at work

Determining Exposure Risk

Substantial Risk for HIV Acquisition

Exposure of
Vagina, rectum, eye, mouth or other mucous membrane, nonintact skin, or percutaneous contact

With
Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood

When
The source is known to be HIV-positive

Negligible Risk for HIV Acquisition

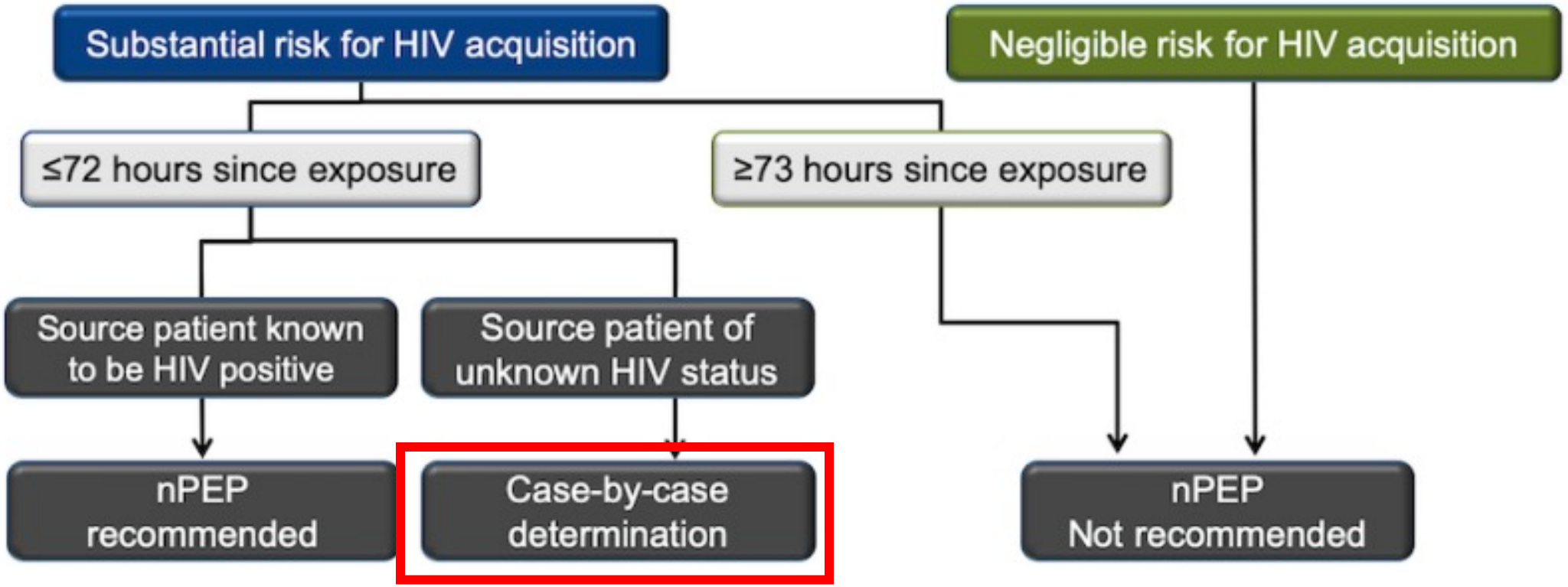
Exposure of
Vagina, rectum, eye, mouth or other mucous membrane, intact or nonintact skin, or percutaneous contact

With
Urine, nasal secretions, saliva, sweat, or tears if not visibility contaminated with blood

Regardless
Of the known or suspected HIV status of the source

https://www.hiv.uw.edu/pdf/prevention/nonoccupational-postexposure-prophylaxis/core-concept/all

Algorithm for Evaluation and Treatment of possible nonoccupational HIV exposures



HIV test at baseline, 4 weeks, and 12 weeks

https://www.hiv.uw.edu/pdf/prevention/nonoccupational-postexposure-prophylaxis/core-concept/all

Recommended Labs for nPEP evaluation

Baseline	4-6 weeks	3 months	6 months
☐ HIV Ab/Ag test	☐ HIV Ab/Ag test	☐ HIV Ab/Ag test	☐ Syphilis serology*
☐ Hep B Surface Ab	☐ Cr/AST/ALT**		☐ HIV Ab/Ag test if acquired HCV from the exposure
☐ Hep B Surface Ag	☐ Syphilis serology*		☐ Hep B serologies if not immune
☐ Hep B core Ab	☐ Gonorrhea*^		☐ Hep C Ab
☐ Hep C Ab	☐ Chlamydia*^		
☐ Cr/AST/ALT	☐ Pregnancy*		
☐ Syphilis serology*			
☐ Gonorrhea*^			
☐ Chlamydia*^			
☐ Pregnancy*			

*Sexual exposure only; ^Screen all sites of contact; **Only if taking oral PEP

Recommended PEP Regimens

Adults and adolescents aged ≥13 years with normal renal function (creatinine clearance ≥60 mL/min), including pregnant women

Preferred Regimens:

- Raltegravir (400 mg twice daily) plus tenofovir DF-emtricitabine (300-200 mg once daily)
- Dolutegravir (50 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily)

Alternative Regimen:

- Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily)

Adults and adolescents aged ≥13 years with renal dysfunction (creatinine clearance ≤59 mL/min)[+]

Preferred Regimens:

- Raltegravir (400 mg twice daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)
- Dolutegravir (50 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)

Alternative Regimen:

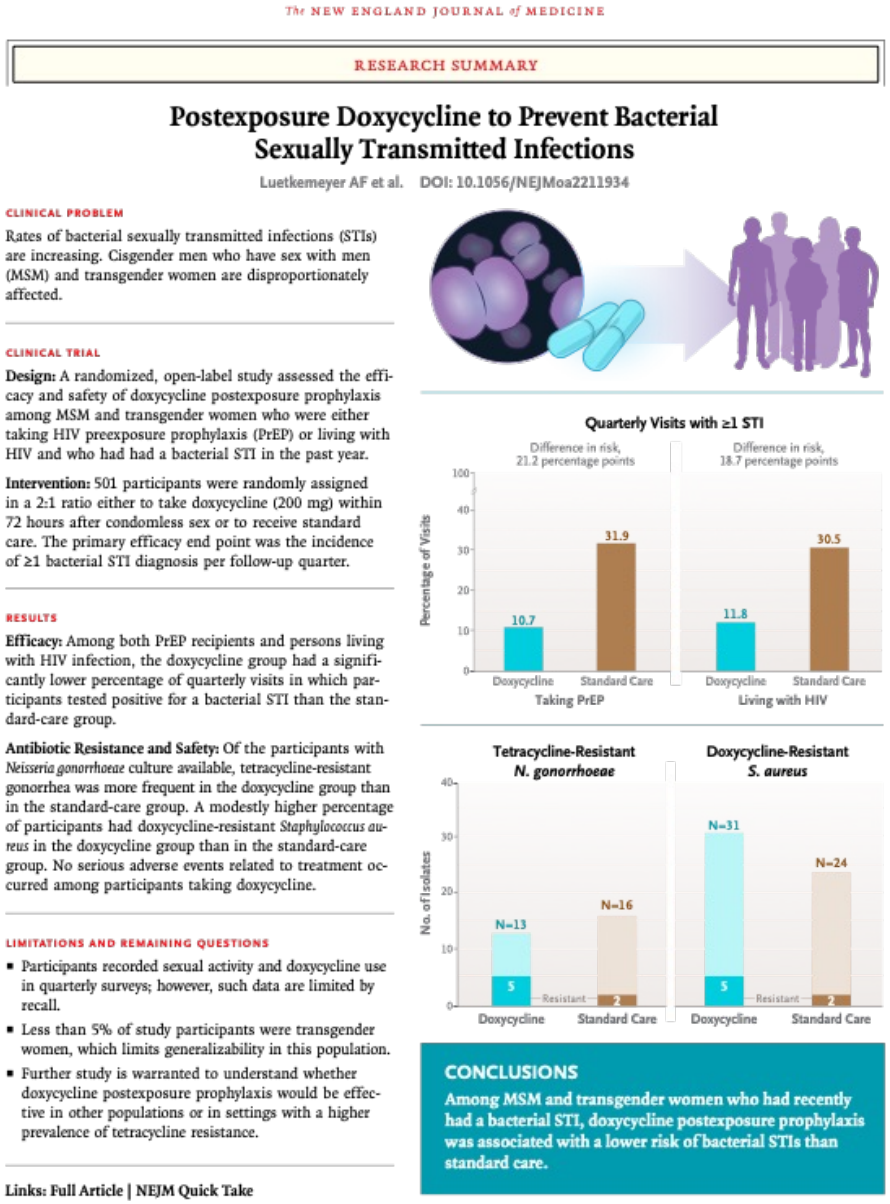
- Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)

[a]These recommendations do not reflect current Food and Drug Administration-approved labeling for antiretroviral medications listed in this table.

[b]Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir, lopinavir, and other protease inhibitors. Ritonavir is not counted as a drug directly active against HIV in the above "3-drug" regimens.

[+]The dose adjustments for zidovudine and lamivudine are made based on degree of renal function

Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Luetkemeyer AF et al. DOI: 10.1056/NEJMoa2211934

CLINICAL PROBLEM

Rates of bacterial sexually transmitted infections (STIs) are increasing. Cisgender men who have sex with men (MSM) and transgender women are disproportionately affected.

CLINICAL TRIAL

Design: A randomized, open-label study assessed the efficacy and safety of doxycycline postexposure prophylaxis among MSM and transgender women who were either taking HIV preexposure prophylaxis (PrEP) or living with HIV and who had had a bacterial STI in the past year.

Intervention: 501 participants were randomly assigned in a 2:1 ratio either to take doxycycline (200 mg) within 72 hours after condomless sex or to receive standard care. The primary efficacy end point was the incidence of ≥1 bacterial STI diagnosis per follow-up quarter.

RESULTS

Efficacy: Among both PrEP recipients and persons living with HIV infection, the doxycycline group had a significantly lower percentage of quarterly visits in which participants tested positive for a bacterial STI than the standard-care group.

Antibiotic Resistance and Safety: Of the participants with *Neisseria gonorrhoeae* culture available, tetracycline-resistant gonorrhea was more frequent in the doxycycline group than in the standard-care group. A modestly higher percentage of participants had doxycycline-resistant *Staphylococcus aureus* in the doxycycline group than in the standard-care group. No serious adverse events related to treatment occurred among participants taking doxycycline.

LIMITATIONS AND REMAINING QUESTIONS

- Participants recorded sexual activity and doxycycline use in quarterly surveys; however, such data are limited by recall.
- Less than 5% of study participants were transgender women, which limits generalizability in this population.
- Further study is warranted to understand whether doxycycline postexposure prophylaxis would be effective in other populations or in settings with a higher prevalence of tetracycline resistance.

Links: Full Article | NEJM Quick Take

CONCLUSIONS

Among MSM and transgender women who had recently had a bacterial STI, doxycycline postexposure prophylaxis was associated with a lower risk of bacterial STIs than standard care.

DoxyPEP

- Take 1 dose, **Doxycycline 200mg within 72 hours** of having condomless sex
- Repeat as needed, but no more than 1 dose within 24 hours

- Reduces the incidence of STIs
  - RR 0.45 (95% CI, 0.32 to 0.65) for gonorrhea
  - RR 0.12 (95% CI, 0.05 to 0.25) for chlamydia
  - RR 0.13 (95% CI, 0.03 to 0.59) for syphilis

Doxy PEP

- **Open-labe**l DoxyPEP US study (2022)*:
  - 501 MSM and TGW living with HIV (N=174) or on HIV PrEP (N=327) in San Francisco and Seattle
- **Randomized** to either take DoxyPEP up to once daily (intervention group) vs no medication prophylaxis (control group)
- **Primary endpoint** was incidence of at least 1 STI per follow-up quarter
- **Results**
  - **66% reduction in STIs overall** for the intervention group
  - In the intervention arm

*N Engl J Med. 2023 Apr 6;388(14):1296–306.

Doxy PEP Guidelines

- DoxyPEP after oral, anal or vaginal sex should be considered for gay, bisexual and other MSM and for transgender women who have had GC/Chlamydia or syphilis at least once during the past year.
  - This is a strong recommendation supported by data from clinical trials.

- DoxyPEP “could be considered” for MSM and TG women who have not been diagnosed with an STI if they “will be participating in sexual activities that are known to increase likelihood of exposure to STIs, e.g., during weekend events, cruises and festivals
  - No clinical trial data

Doxy PEP Guidelines

- No recommendation on the use of doxyPEP for cisgender women, cisgender heterosexual men, TG men or other queer or non-binary people

- “Doxy PEP should be implemented in the context of a comprehensive sexual health approach including risk reduction counselling, STI screening and treatment, recommended vaccination and linkage to HIV pre-exposure prophylaxis (PrEP), HIV care or other services”

Barriers to PrEP and PEP

What barriers do you have or foresee to starting PrEP at your site?

Resources

- **HIV/PrEP Warm Line: (800) 933-3413**
  - HIV/AIDS Management | National Clinician Consultation Center (ucsf.edu)
  - Clinicians are available Monday through Friday, 9:00 a.m. to 8:00 p.m. EST. Voice mail is available 24 hours a day.

- **Indian Country ECHO**
  - http://www.indiancountryecho.org
  - HIV ECHO, 2nd Wednesday of every month

    2-3 pm ET