



PRACTICE

10-MINUTE CONSULTATION

HIV pre-exposure prophylaxis (PrEP)

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What you need to know

- PrEP is an effective and proactive form of HIV prevention, in which people who are HIV negative and have active and substantial risk factors for HIV infection take antiretroviral medication to prevent infection
- Efficacy of PrEP is highly dependent on adherence
- PrEP does not protect against other sexually transmitted infections such as chlamydia, gonorrhoea, and syphilis, therefore additional methods of protection (eg, condoms) are necessary

A 22 year old man attends a sexual health clinic. Six months previously, he completed a course of HIV post-exposure prophylaxis for anal receptive intercourse without a condom. Since then, he reports six anal receptive sexual exposures without a condom. He has been treated at another sexual health clinic for rectal gonorrhoea. He asks if you could prescribe him PrEP.

HIV pre-exposure prophylaxis (PrEP) is the use of HIV antiretroviral medicines in people without HIV to prevent infection. When taken correctly, PrEP has been shown to reduce the risk of HIV infection in numerous populations, including young women, men who have sex with men, HIV uninfected members of sero-discordant couples, and injecting drug users.¹⁻³ Based on this evidence, PrEP is recommended for people considered at high risk of acquiring HIV. However, availability of PrEP and access to expert advice and counselling about its use vary globally. For example, in England it is only available as part of a clinical trial, whereas it is available in the rest of the UK at sexual health clinics. Awareness of PrEP among at-risk groups is growing, and availability of the treatment is becoming more widespread; therefore generalists—as well as those working in sexual health services—require an awareness of the indications, efficacy, use, and potential harms of PrEP.

What you should cover

Identify risk of HIV

Ask the patient about known or potential HIV exposures in the previous six months, particularly sexual exposures or injecting drug use. **Box 1** summarises high risk groups in whom PrEP is recommended.

Box 1: Indications for PrEP^{1 2}

PrEP is recommended for

- men who are HIV negative who have condomless sex with men of unknown HIV serostatus, or with men who do not have evidence of a persistently suppressed HIV plasma viral load (<200 copies/mL) for at least six months
- transgender individuals who are HIV negative and engage in anal sex without a condom
- individuals who are HIV negative and engage in sex without a condom with those known to be HIV positive who do not have a suppressed HIV plasma viral load (<200 copies/mL) for at least six months.

Consider PrEP on a case by case basis in individuals who are HIV negative and

- engage in sex without a condom with partners of unknown HIV status, particularly in areas with a high HIV prevalence (eg, southern Africa)
- in the past 6-12 months have had bacterial sexually transmitted infections, hepatitis C infection, or have used HIV post-exposure prophylaxis, with anticipated future high risk sexual behaviour
- inject drugs and share drug injection paraphernalia
- have partners of unknown HIV serostatus and may not be able to use condoms (eg, because of poverty, threat of violence) with sexual partners—for example, in some commercial sex workers.

Sexual exposure to individuals known to be HIV positive with persistently undetectable viral loads (<200 copies/mL for greater than six months) indicates a zero to negligible risk for HIV acquisition, and PrEP benefits are unlikely to outweigh its risk for individuals in monogamous relationships with individuals who have long term and consistent virological suppression.^{1 3 4}

The risk assessment is also informed by

- the frequency and type of sex the patient is having, such as anal, oral, or vaginal sex, and receptive or insertive sex;

- number of sexual partners and knowledge of HIV serostatus of the partners, as well as whether any who are HIV positive are taking antiretroviral treatment;
- sexually transmitted infections such as syphilis, gonorrhoea, and chlamydia in the previous six months;
- how often they use barrier protection during sex;
- injecting drug use history (and, if positive, practices around sharing of drug paraphernalia);
- screening for concomitant psychiatric issues, as well drug and alcohol misuse, which may be facilitating higher risk behaviour;
- drugs used to enhance and disinhibit sexual experience (eg, “chemsex,” “party and play,” or “PNP”);
- factors that may affect sexual health autonomy, such as coercive or violent power dynamics in relationships.

Ask about renal, liver, or bone disease to assess safety of the most commonly prescribed PrEP regimen.

What you should do

If PrEP is indicated based on your assessment of the person's risk of acquiring HIV, order the necessary baseline tests. Explain the risks, benefits, and logistics of taking PrEP to help the person make an informed decision (fig 1).

Baseline tests

Before starting PrEP, exclude HIV infection, preferably using a fourth generation laboratory assay (a test for both HIV antibodies and p24 antigen). In situations where acute HIV is suspected (ie, infection within the past 2-3 weeks), perform an HIV RNA nucleic acid test. If the HIV RNA test is not available or the exposure was within the last 7-10 days (within the window period for detection of HIV with a viral load assay), guidelines recommend repeat testing with a fourth generation assay in 1-4 weeks.^{1,3} Withhold PrEP in scenarios where HIV cannot be excluded, because the regimen used for PrEP is inadequate for treatment of HIV infection, and might lead to drug resistance.

Test for chlamydia, syphilis, and gonorrhoea (urine nucleic acid amplification test, rectal and pharyngeal culture or nucleic acid amplification tests, if indicated by exposure), assays of renal and liver function, and serologies for hepatitis A, B, and C. Offer vaccination against hepatitis A and B and human papillomavirus in line with local guidelines. The tenofovir disoproxil fumarate plus emtricitabine (TDF/FTC) combination tablet is active against hepatitis B infection, so there is potential for hepatitis B reactivation should PrEP be discontinued. Use PrEP with caution in people with active hepatitis B; episodic or “on-demand” PrEP is not recommended in this group.^{1,3}

Offer a pregnancy test in women. PrEP is believed to be safe and effective in pregnancy and during breastfeeding.⁵ However, discuss the potential risks of taking PrEP in pregnant women, those who could become pregnant, or who are breastfeeding, to facilitate informed decision making.²

Discuss PrEP options

Oral PrEP is recommended as a two drug regimen of TDF and FTC, co-formulated as a single pill, and taken as one pill once daily.^{1-3,5,6} Data show very high efficacy of daily PrEP with TDF/FTC for preventing HIV acquisition among those with moderate to high adherence. In a systematic review and meta-analysis involving 18 studies (including randomised control trials, open label extension studies, and demonstration

studies), PrEP afforded a 70% relative risk reduction in HIV infection versus placebo in those with adherence levels of 70% or more.⁷ In those with low adherence rates (<40%), no difference in HIV infection rates versus placebo was found. A real world observational study of PrEP use in San Francisco found there were no new HIV infections from 657 people initiating PrEP over a mean follow-up of 7.2 months.⁸

On demand PrEP (box 2) is an alternative to once daily PrEP in men who have sex with men (MSM). On demand PrEP has been shown to reduce HIV transmission among MSM who can predict the timing of high risk exposures. It involves taking two tablets of TDF/FTC 2-24 hours before sex, then a subsequent tablet of TDF/FTC 24 hours after sex, and then again 48 hours after sex.⁶

Box 2: Daily versus on demand PrEP

- Daily PrEP involves taking one tablet of TDF/FTC once per day
- MSM or trans women using on demand PrEP take two tablets of TDF/FTC 2-24 hours before anal sex, then a subsequent tablet of TDF/FTC 24 hours and then 48 later⁶
- Patient preference may dictate daily versus on demand PrEP for MSM and trans women based on cost or frequency of use. The efficacy of on demand PrEP in people with very infrequent sexual exposures (without a condom) is uncertain, and on demand post-exposure prophylaxis (PEP) rather than on demand PrEP may be considered as an alternative in these situations⁹
- PrEP does not protect against other sexually transmitted infections, such as chlamydia, gonorrhoea, and syphilis. Even with perfect drug adherence, PrEP is not effective against infrequent circulating strains of HIV that are resistant to TDF/FTC.¹⁰ Advise patients that PrEP is not 100% protective against HIV infection but will substantially reduce their risk of acquiring HIV if taken correctly

Potential harms

PrEP has infrequent but potentially harmful side effects such as nephrotoxicity and reduction in bone mineral density.¹⁻³

Tenofovir disoproxil fumarate (TDF), one of the two components of PrEP, is contraindicated in those with glomerular filtration rates less than 60 mL/min and is associated with loss of bone mineral density.¹⁻³

Drug resistance may develop in those who initiate PrEP with unrecognised HIV infection.¹¹

When to start PrEP

Evidence is limited for the time to maximal protection once PrEP is started, and there is some variation between guidelines.¹⁻³ UK guidelines note that, for anal exposures, taking the first dose of PrEP 2-24 hours before exposure is appropriate if two tablets (a double dose) of TDF/FTC are taken. For all other sex, or in the context of injecting drug use, seven days of single dose once daily TDF/FTC is recommended before exposure.

Arrange follow-up

People taking PrEP are asked to follow up every three months.¹⁻³ Each review should include discussion of

- adherence to PrEP and side effects
- reassessment of HIV risk and discussion of risk reduction strategies
- monitoring for drug toxicity, including kidney function testing
- screening for concomitant mental health or substance abuse issues
- screening for HIV seroconversion and other sexually transmitted infections.

People in monogamous relationships with a partner with HIV can typically discontinue PrEP safely after their partner achieves virological suppression for at least six months.⁴ If someone is no longer a candidate for PrEP, for instance if they are no longer at risk, UK guidelines recommend stopping TDF/FTC two days after their last anal sexual exposure, or seven days after other types of sexual exposures.¹

Education into practice

- Think about the last few patients you saw for HIV post-exposure prophylaxis. How many had ongoing risk factors for HIV acquisition and would have been good candidates for PrEP?
- How many of your patients currently taking PrEP (either daily or on demand) have indications to continue, based on their current risk of HIV infection?

How patients were involved in the creation of this article

- Two patients at our clinic who were taking PrEP for HIV prevention provided insight for this article. Both are men who have sex with men. Both were asked how PrEP changed their views towards sex, and to provide practical PrEP tips.
- The patients noted that PrEP provided them with greater autonomy over their sexual health and reduced fear with sexual activity. One patient mentioned that he preferred daily compared to on demand PrEP as it was much easier to remember to take his tablets.

How this article was created

We based the article mainly on current guidelines and on systematic reviews.

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The authors declare the following other interests: none.

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Patient consent: patients involved were anonymised.

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Figure

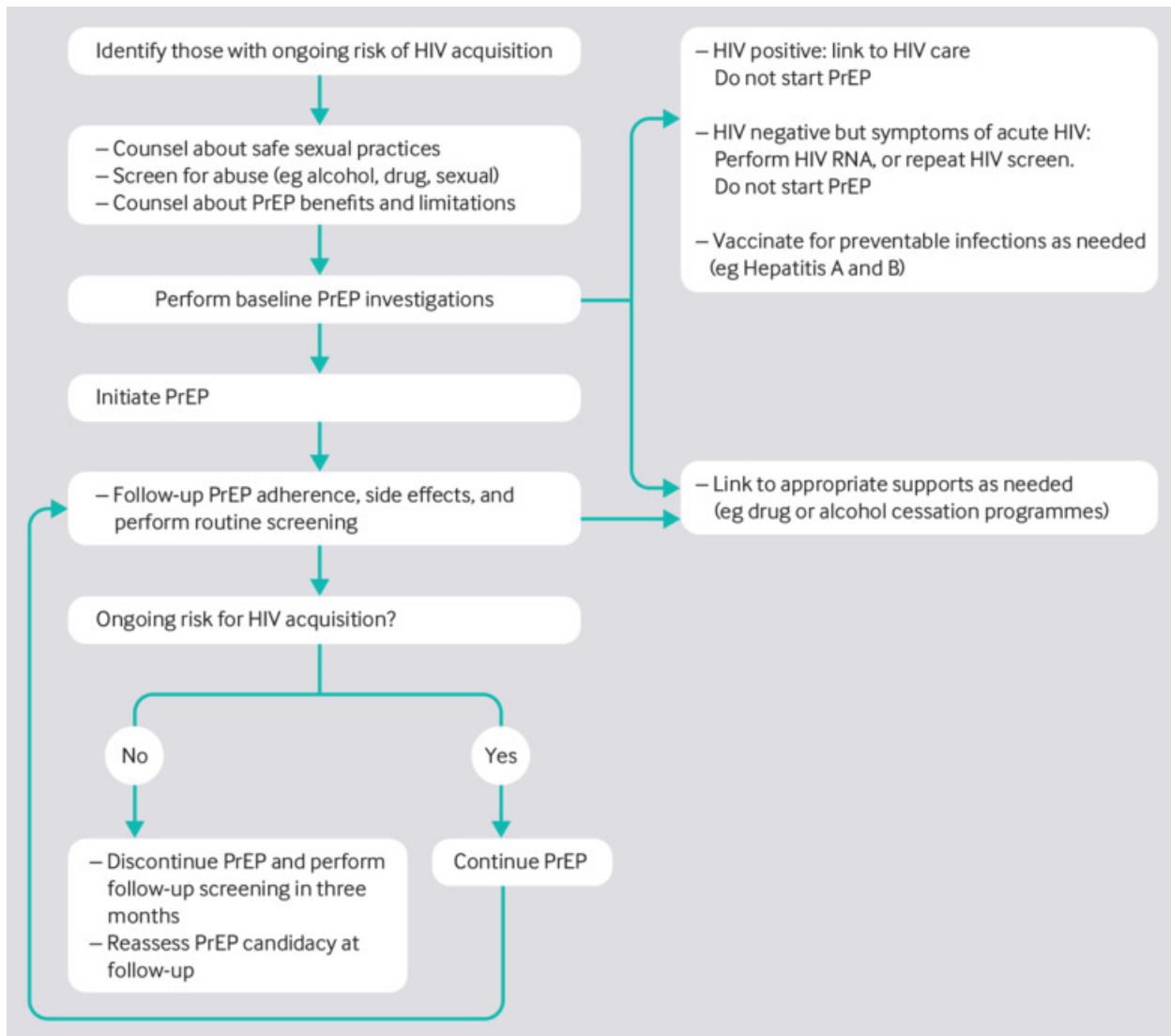


Fig 1 Decision making flowchart to guide PrEP initiation and follow-up care