HIV prevention strategies

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Abstract

Existing since the 1980s, human immunodeficiency virus (HIV) prevention strategies have developed in parallel with our understanding of HIV transmission and treatment for HIV disease. The past few years have seen exciting advancements in HIV prevention methods, with the development of new, highly effective strategies such as pre-exposure prophylaxis. This sits alongside more traditional approaches such as post-exposure prophylaxis, consistent condom use and increased access to HIV testing. Data now show that an HIV-positive person with a viral load that is undetectable for at least 6 months is not infectious to their sexual partner. Therefore, early HIV diagnosis and initiation of antiretroviral therapy also prevents transmission, referred to as 'treatment as prevention'. Additionally, in the UK and Ireland, mother-to-child transmission of HIV has been virtually eliminated. These strategies in combination are starting to impact upon the incidence of HIV, both in the UK and worldwide.

Keywords Acquired immunodeficiency syndrome; condoms; HIV infections; incidence; MRCP; post-exposure prophylaxis; pre-exposure prophylaxis; safe sex; sexual partners; viral load

Key points

- Combination HIV prevention strategies are starting to impact upon the incidence of HIV in the UK and worldwide
- HIV pre-exposure prophylaxis is a new prevention tool that is highly effective when there is good adherence
- When an HIV-positive person is on effective antiretroviral therapy and has an undetectable HIV viral load (<200 copies/ml), HIV is untransmittable
- Condoms remain the only prevention method that also prevent transmission of other sexually transmitted infections

Introduction

Focused human immunodeficiency virus (HIV) prevention efforts and increased education have led to dramatic falls in new HIV diagnoses in certain communities, such as men who have sex with men (MSM) in San Francisco and London. However, knowledge and understanding of available HIV prevention methods is still lacking in some sectors of the population who might benefit, such as women, individuals from black and ethnic minorities and trans/non-binary communities.

Individuals with an increased risk of HIV infection should be given information on HIV prevention strategies and referred to specialist sexual health services. These individuals include those with an HIV-positive partner who is not on antiretroviral therapy, plus MSM and transgender men and women having condomless anal sex.

Pre-exposure prophylaxis (PrEP)

What is PrEP?

PrEP is medication given to HIV-negative people *before* sex, to prevent infection with HIV. Daily oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) is licensed for PrEP in the UK and mainland Europe. Other drugs and formulations are in development, including long-acting injectable agents and intravaginal rings.

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When is PrEP indicated?

PrEP is indicated for HIV-negative people at substantial risk of HIV acquisition. The World Health Organization defines this as a risk of >3 per 100 person−years.

In the UK, PrEP is **recommended** for:

- HIV-negative people having condomless vaginal or anal sex with partners who are HIV-positive, unless the partner has been on antiretroviral therapy for at least 6 months and their plasma viral load is <200 copies/ml
- HIV-negative MSM, transgender men and women who are identified as being at elevated risk of HIV acquisition through condomless anal sex in the previous 3−6 months and are continuing condomless anal sex

PrEP should be **considered** for use on a case-by-case basis for:

- HIV-negative people with other current factors that might put them at increased risk of HIV acquisition. See the British HIV Association/British Association for Sexual Health and HIV (BHIVA/BASHH) PrEP guideline for further information

How effective is PrEP?

The PRe-exposure Option for reducing HIV in the UK: an open-label randomisation to immediate or deferred daily Truvada for HIV negative gay men (PROUD)[1] study in England enrolled 544 gay and bisexual MSM: 275 were randomly allocated to take daily TDF/FTC as PrEP immediately and 269 to wait for a year before starting it. Results show an 86% reduction in HIV incidence in the men who took PrEP immediately.

Looking deeper into data from PROUD and indeed all PrEP randomized controlled trials, it is clear that the efficacy of PrEP is tightly correlated with adherence.

Partners PrEP,[2] an RCT of 4747 heterosexual couples in Africa, measured adherence using plasma TDF/FTC concentrations in 29 seroconverters, comparing them with 196 randomly selected control individuals. When TDF levels were consistent with daily dosing, the estimated protective effect of PrEP against HIV was 91% (95% confidence interval (CI) 47%−98%; $p = 0.008$). It is thought that the lack of efficacy reported in two other PrEP studies in heterosexuals, was the result of insufficient plasma drug levels in participants.

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In MSM and transgender women, a substudy of a large open-label study (Initiativa Profilaxis Pre-Exposición Open-Label Extension (iPrEx OLE))[3] measured TDF concentrations in dried blood spots. The hazard ratio for HIV infection was 0.00 (95% CI 0.00–0.17) in participants with TDF concentrations compatible with the use of four to seven tablets per week (for anal sex).

In reality, people who become infected with HIV while using PrEP either have an early infection that was missed as they started PrEP, or are infected as a result of poor adherence or a break in taking PrEP. To date, there have been only three reported cases of people fully adherent to PrEP becoming infected with HIV. In two individuals, this was caused by infection with a multidrug-resistant strain of HIV. The third case is the only documented case of transmission occurring with wild-type HIV, despite adequate TDF levels. Infection occurred in an MSM with multiple risk factors. Initial HIV tests showed an atypical pattern of GP160 positivity only. As no HIV proviruses were detected in peripheral blood mononuclear cells, the HIV infection is likely to have been mucosally contained. It is postulated by some that if PrEP had been continued, or combination antiretroviral therapy commenced, the infection may have been aborted.

Starting PrEP

Exclude HIV: the most important factor when commencing PrEP is to exclude HIV infection. In an individual with a negative blood-based point-of-care test, PrEP can be started while the result from a serological fourth-generation combined HIV antibody/antigen test is awaited. The only exception is when an individual has symptoms consistent with HIV seroconversion. In this case, PrEP should be deferred until an HIV antibody/antigen *and* HIV viral load result is available.

If there has been a risk of HIV acquisition during the 4 weeks before starting PrEP, consider obtaining an HIV viral load measurement alongside the HIV antibody/antigen test. In this circumstance, the HIV antibody/antigen test should also be repeated 4 weeks after starting PrEP.

Measure renal function: TDF can cause a decline in creatinine clearance. Although this is not usually clinically significant, baseline renal function should be measured via creatinine clearance (estimated glomerular filtration rate). TDF can be used for HIV prevention when creatinine clearance is >60 ml/minute. Urinalysis should also be tested to exclude proteinuria.

Individuals with a background of renal disease, those who have medical problems with the potential for associated renal disease such as hypertension and diabetes mellitus, and those aged >40 years are more likely to develop reduced creatinine clearance when taking TDF. This group of individuals should be followed up more closely.

Assess hepatitis B status: TDF/FTC can be used both as treatment for hepatitis B and as PrEP. However, in individuals with hepatitis B, the risk of rebound viraemia and fulminant liver damage on discontinuation means that this should be carefully monitored, with advice taken from hepatologists.

How to take PrEP

The dosing schedule required for PrEP to be effective differs depending on the mucosal tissue to be protected (Table 1). An adequate amount of PrEP needs to be taken before sex to be present in the mucosa at protective levels when exposure occurs. This represents the 'lead-in time to protection'. Equally, when stopping PrEP, there needs to be an adequate amount of drug present after the last episode of sex to prevent HIV transmission.

RCTs have shown daily dosing of TDF/FTC to be effective for all populations. On demand dosing (also known as event based dosing), when PrEP is taken only when sex is anticipated, has been shown in the Ipergay study[4] to be effective for MSM having anal sex (See Figure 1).

TDF and FTC reach the rectal mucosa more quickly than the female genital tract, and TDF is present in higher concentrations in the rectum. Subsequently, dosing schedules for anal sex can be more forgiving than those for protection from receptive vaginal sex.

PrEP dosing schedules

	Lead-in time to mucosal protection	Level of adherence required for PrEP effectiveness	Doses required for protection when stopping PrEP after last episode of sex
Daily dosing – receptive vaginal sex *FTC/TDF* *one tablet once daily*	7 days	6 or 7 daily tablets of FTC/TDF per week	7 daily doses
Daily dosing – receptive anal sex FTC/TDF *one tablet once daily*	A double dose of FTC/TDF taken 2–24 hours before sex	**After having taken 7 daily doses,** at least 4 tablets of FTC/TDF per week	2 daily doses
On demand dosing NOT RECOMMENDED FOR VAGINAL SEX	A double dose of FTC/TDF taken 2–24 hours before sex (A single dose ONLY is needed if TDF/FTC has been taken in the preceding 7 days)	Continued daily until 48 hours after the last sexual risk. This can be as little as a double dose followed by 2 daily doses (4 tablets in total)	2 daily doses

Table 1

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