

CATIE STATEMENT

on the use of oral pre-exposure prophylaxis (PrEP) as a highly effective strategy to prevent the sexual transmission of HIV

The consistent and correct use of oral Truvada as pre-exposure prophylaxis (PrEP) is a highly effective strategy to help prevent the sexual transmission of HIV. When this highly effective strategy is used consistently and correctly it is rare for HIV to be transmitted.

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Over the past several years the HIV prevention toolbox has expanded significantly. This is due to a rapid growth in our knowledge of effective approaches that help prevent the transmission of HIV. However, to maximize the impact on the HIV epidemic, we must effectively increase awareness, uptake and proper use of these approaches.

The CATIE statements summarize the best available evidence on the effectiveness of three approaches to help prevent the sexual transmission of HIV. These statements were developed to help service providers in Canada adapt their programs and incorporate this evidence into their messaging.

There are three highly effective strategies to help prevent the risk of the sexual transmission of HIV:

- The consistent and correct use of oral pre-exposure prophylaxis (PrEP)
- The consistent and correct use of condoms
- The consistent and correct use of antiretroviral treatment (ART) by people living with HIV to maintain an undetectable viral load

When any highly effective strategy is used consistently and correctly the risk for HIV transmission ranges from very low to negligible.

The following statement focuses on PrEP. A simple key message is followed by recommendations for service providers and a list of available tools and resources. A review of the evidence is also provided that service providers can use for more specific discussions with clients. Please consult the companion statements for more information on the other two highly effective strategies.

KEY MESSAGE

The consistent and correct use of tenofovir (also called TDF) and emtricitabine (also called FTC) as oral pre-exposure prophylaxis (PrEP) is a highly effective strategy to help prevent the sexual transmission of HIV. When this highly effective strategy is used consistently and correctly it is rare for HIV to be transmitted.

For more information, please see the evidence review at the end of this statement.

RECOMMENDATIONS FOR SERVICE PROVIDERS

PrEP is no longer a strategy on the horizon but one that is increasingly available and being used in Canada. Health Canada has approved the use of oral PrEP to help prevent the sexual transmission of HIV, in combination with safer sex practices, for people at high risk for HIV. Oral PrEP contains two HIV medications: tenofovir (also called TDF) and emtricitabine (also called FTC).

People working with communities at risk for or living with HIV have an important role to play in promoting PrEP as a highly effective prevention strategy.

Below are recommendations on how you might better integrate PrEP into your programming.

Improve awareness of oral PrEP as a highly effective HIV prevention strategy, including the factors important for maximizing its effectiveness.

Any educational and counselling activities provided for HIV-negative clients and for HIV-positive clients who have HIV-negative partners should include information on the prevention benefits of PrEP and how to use it consistently and correctly.

Education and counselling activities should also include discussion of other prevention strategies such as, but not limited to, condoms and the use of antiretroviral treatment (ART) to maintain an undetectable viral load. Encourage clients to choose the combination of strategies that will work most effectively for them.

Inform clients who are interested in PrEP of the factors important for maximizing its safety and effectiveness. Emphasize that PrEP::

- must only be used by people who are HIV negative
- must only be accessed through a healthcare provider
- requires that people are highly adherent to PrEP medications
- requires that people be tested for kidney function and screened for the hepatitis B virus before taking PrEP
- requires regular clinic visits with a healthcare provider every three months to test for HIV and sexually transmitted infections (STIs), to monitor for side effects and toxicity, and for adherence and risk-reduction counselling.

PrEP should only be used by people who are HIV negative and at high risk for HIV infection. Education and counselling activities should include a discussion of a client's level of HIV risk so that they can make an informed decision about whether PrEP is right for them.

The World Health Organization recommends that PrEP may be indicated for people who are HIV-negative and:

- Have a sexual partner with HIV who is not on treatment or not virally suppressed

OR

- Sexually active in a high HIV incidence/prevalence population AND any of the following:
 - Has condomless vaginal or anal sex, or
 - Has a sexual partner with one or more HIV risk factors, or
 - Has a history of STIs in the past 6 months, or
 - Use of post-exposure prophylaxis (PEP), or
 - Requesting PrEP.

Daily oral PrEP is the only type of PrEP approved for use by Health Canada. It is the most commonly prescribed type of PrEP. There is strong evidence from multiple studies to support that it is a highly effective strategy to help prevent the sexual transmission of HIV in multiple populations when used consistently and correctly.

Gay men and other men who have sex with men (MSM) may consider using an intermittent or 'on-demand' PrEP strategy. This strategy consists of two pills taken two to 24 hours before first sexual activity, followed by one pill taken daily until 48 hours after the last sexual activity. This type of PrEP is not approved by Health Canada but can be prescribed 'off-label' by physicians. One study supports on-demand PrEP as a highly effective strategy to help prevent the sexual transmission of HIV in MSM when used consistently and correctly. On-demand PrEP is not recommended for use by people having vaginal sex.

When discussing PrEP use with a client, it is important to recognize that each client has the right to decide whether or not to use it as a prevention approach, based on their own assessment of what is best for their health and well-being.

You can also lead or support efforts to improve awareness of PrEP as a prevention approach among a range of service providers in your area, including doctors, nurses, pharmacists, and non-clinical staff at community-based organizations.

Facilitate and support appropriate uptake and use of oral PrEP as a prevention strategy.

Guidelines recommend the offer of PrEP to individuals at high risk for HIV infection as part of a comprehensive prevention package that includes regular STI testing and ongoing adherence and risk-reduction counselling. PrEP is not for

everyone and you can support clients to decide whether PrEP is right for them. During discussions, help your clients consider their level of HIV risk, and the possible side effects, as well as their ability to cover the cost (i.e., insurance coverage), access a knowledgeable healthcare provider, and adhere to a pill-taking regimen and regular medical visits.

Whenever possible, be aware of – and develop partnerships with – local healthcare providers, clinics, and health centres that are willing to prescribe PrEP. Establishing these connections can ensure that clients who may benefit from PrEP (and are interested in using it) are linked to a location where it is available. Clients may need support in talking to a healthcare provider about PrEP and determining whether their provincial/territorial or private health insurance will cover the cost of the medications. Clients who start PrEP should also be supported with the consistent and correct use of this strategy. You may have to offer, or link clients to, interventions and services to support medication adherence and continued engagement in medical care.

Encourage a comprehensive plan for sexual health.

Discuss how PrEP fits into a comprehensive plan for sexual health, including regular STI testing and safer sex practices.

There are circumstances in which HIV transmission can occur while someone is on PrEP. We know that adherence to medications can be an issue for some people and that low adherence decreases the ability of PrEP to prevent transmission. As well, PrEP does not protect against strains of HIV that are resistant to the drugs in PrEP (though these strains are very rare).

It is important that clients understand these risks and the options available to them so they can make an informed decision about using PrEP as part of a comprehensive sexual health plan to further minimize the risk for HIV transmission over the long term. A comprehensive sexual health plan also helps to protect against STIs because PrEP does not provide any protection against STIs.

Address underlying risk of HIV transmission.

HIV prevention counselling offers an opportunity to engage individuals in additional services. You can help your clients address the underlying factors that may increase their HIV risk, such as depression or alcohol and other substance use; reinforce safer sex strategies; and facilitate the increased use of all appropriate prevention strategies. You may find that counselling alone is not enough. You may need to provide – or link clients to – appropriate and relevant support services.

Offer comprehensive couples-based counselling.

For couples, you may want to offer to counsel both partners in the relationship at the same time (couples-based counselling) as this may be more effective than counselling partners individually. Couples-based counselling can create a supportive space where clients can come to a consensual agreement on how to reduce their risk of HIV transmission, develop ways to support each other in using HIV prevention strategies consistently and correctly, and discuss potentially sensitive issues relevant to HIV prevention. Be prepared to discuss issues such as: what a couple wants from sex and the type of sex they enjoy most; the desire for pleasure, intimacy, conception, and monogamy or non-monogamy; and disclosure of sex outside the relationship. This counselling can also support non-monogamous clients to develop strategies or agreements to help prevent HIV or STIs from outside partners, such as the consistent and correct use of condoms when having sex outside the relationship.

Incorporate information about PrEP into all prevention programming to increase its impact.

In-person counselling is one way to convey information about PrEP as a highly effective prevention strategy. However, this information can be integrated into a variety of other communication channels, such as print publications, websites and campaigns to increase its reach and impact.

Be prepared to discuss the legal issues around HIV disclosure.

Canadian law requires that people tell their sex partners that they have HIV in certain circumstances. However, the law and its application are evolving. For the most up-to-date information on when people with HIV have a legal duty to disclose their HIV status, contact the Canadian HIV/AIDS Legal Network (www.aidslaw.ca).

TOOLS AND RESOURCES

CATIE resources

Oral pre-exposure prophylaxis (PrEP) – Fact sheet

Truvada – Fact sheet

Are you prepped for PrEP? – webinar

Truvada approved for HIV prevention in Canada – *CATIE News*

Guidelines

Canadian guidelines on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis – Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network (CTN)

Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations – World Health Organization

Oral pre-exposure prophylaxis—putting a new choice in context – UNAIDS

Preexposure prophylaxis for the prevention of HIV infection in the United States – 2017 update: A clinical practice guideline – Centers for Disease Control, US Public Health Service

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 update: Clinical Providers' Supplement – Centers for Disease Control, US Public Health Service

Interim guidance on providing HIV PrEP – Quebec Ministry of Health (French only)

Pre-exposure prophylaxis (PrEP) guidelines – B.C. Centre for Excellence in HIV/AIDS

Other PrEP resources

Providing HIV PrEP: steps to patient engagement – CTAC

Canadian Consensus Statement on the health and prevention benefits of HIV antiretroviral medications and HIV testing – CTAC, CATIE, positivelite.com

Truvada Product Monograph – Gilead Sciences

Ongoing and planned PrEP evaluation studies – AVAC

HIV disclosure

Criminal Justice System's Response to Non-Disclosure of HIV (2017) – Department of Justice, Government of Canada

Sexual Offences against Adults (2017) – Ontario Crown Prosecution Manual

Sexual Transmission, or Realistic Possibility of Transmission, of HIV (2018) – British Columbia Prosecution Service Crown Counsel Policy Manual

Criminal law and HIV non-disclosure in Canada (2014) – Canadian HIV/AIDS Legal Network

HIV disclosure to sexual partners: Question and answers for newcomers (2015) – Canadian HIV/AIDS Legal Network

HIV disclosure and the law: What you need to know (2015) – Positive Women’s Network

Legal and clinical implications of HIV non disclosure: A practical guide for HIV nurses in Canada (2013) – CANAC (Canadian Association of Nurses in AIDS Care), CATIE

EVIDENCE

Evidence from several randomized clinical trials has found that the use of daily oral tenofovir and emtricitabine significantly reduces the risk of HIV transmission.¹⁻⁷ In these trials, PrEP was provided along with a comprehensive prevention package that included regular STI testing and treatment and ongoing adherence and risk-reduction counselling. Trials were conducted in several populations, including gay men and other MSM, heterosexual men and women, and people who use injection drugs. The overall reduction in HIV risk provided by PrEP in these studies ranged from zero to 86%. Varying levels of adherence to daily pill-taking among study participants is responsible for this wide range, as some participants were only taking their pills occasionally and others were not taking their pills at all.⁸ Indeed, adherence was so low in two studies that PrEP provided no protection against HIV infection.^{3,6}

Some studies have limited their analyses of effectiveness to participants who were taking their pills consistently.^{1,2,5} These analyses compared the risk of HIV infection among those with antiretroviral drugs in their blood (which suggests they were using PrEP consistently) to those who did not have these drugs in their blood. These analyses show us that the consistent use of PrEP can reduce the risk for sexual HIV transmission among gay men and other MSM and heterosexual men and women by between 85% and 92%.⁹ A modelling study has estimated that daily oral PrEP may be up to 99% effective at reducing the risk for the sexual transmission of HIV among MSM but this has not been demonstrated in a clinical trial.¹⁰

The daily use of oral tenofovir and emtricitabine has been evaluated in “open-label” studies predominantly among MSM.^{7,11} In these types of studies, no placebo is used and participants know they are using PrEP and that it is effective against HIV infection. Several of these “open-label” studies have been completed and they support the conclusion that the daily use of oral PrEP is highly effective against HIV infection when used consistently and correctly.

The randomized clinical trials of daily oral tenofovir and emtricitabine that enrolled heterosexual men and women found no difference in the effectiveness of PrEP based on sex

when used consistently and correctly. However, there is some evidence to suggest that oral PrEP reaches maximum drug concentrations more quickly in rectal tissues compared to vaginal tissues, and that drug levels are higher in rectal tissues. For these reasons it may take longer to build up necessary protection from PrEP in the vagina, and women having vaginal sex may need to be more adherent to PrEP than men having anal sex to maintain sufficient drug levels to help prevent HIV infection.^{3,12-17}

Evidence suggests that intermittent or “on demand” PrEP reduces the risk of HIV transmission among MSM. One randomly controlled trial (RCT), known as IPERGAY, evaluated the use of on-demand PrEP among MSM.^{18,19} In the IPERGAY trial, men were to take two pills at once two to 24 hours before first sexual activity, followed by one pill taken daily until 48 hours after the last sexual activity. The RCT phase of IPERGAY found an 86% reduced risk of HIV infection among gay men in the on-demand PrEP group compared to a placebo group (two participants in the PrEP arm became infected).¹⁸ Men in the RCT phase of this study had sex frequently and – as a result – took their pills on a regular basis (four pills a week on average).¹⁸ IPERGAY continued as an open-label extension with all participants offered on-demand PrEP.¹⁹ Results from the open-label phase showed that one HIV transmission occurred in 362 participants, over 515 person-years of follow-up.¹⁹ None of the three participants who became infected over the entire course of the study had PrEP detected in their blood, which means they were likely not adherent.¹⁹ On-demand PrEP has not been evaluated in populations other than MSM.

PrEP is not effective against strains of HIV that are resistant to the drugs in PrEP (TDF and FTC). There have been two reported cases of transmission of drug-resistant HIV to men who were adherent to PrEP;^{20,21} however these are rare cases.

There has been one well-documented case of PrEP failure in a gay man enrolled in a PrEP demonstration project. He was highly adherent to PrEP but after being on PrEP for seven months he acquired a strain of HIV with no drug resistance. He had many anal sex partners where no condoms were used, experienced episodes of rectal chlamydia and gonorrhoea, and used drugs during sex, including mephedrone, GHB/GHL, ketamine, cocaine and amphetamine. However, the reason why PrEP failed in this man is unclear.²²

PrEP appears to be generally safe and well tolerated. Although oral tenofovir and emtricitabine is associated with some side effects such as headache, nausea, diarrhea and fatigue, these tend to be mild, infrequent (affecting between 1% and 10% of users), and resolve after one to two months of use.¹⁻⁶ The use of PrEP has been associated with more concerning

toxicities in a small number of people, such as small decreases in kidney, liver and bone health. Promisingly, these toxicities did not increase the risk of kidney or liver failure, or bone fracture, and the changes were reversible after stopping PrEP.

Of concern is the potential for the development of drug resistance in people who are taking PrEP. If drug resistance develops, this could limit future treatment options. In clinical trials, those who started PrEP when they were already HIV positive (their infection was missed during initial screening for HIV because they were recently infected and in the “window period”) were at high risk of developing drug resistance.^{1–6} On the other hand, those who started PrEP when they were HIV negative, and became infected while taking it, had a lower risk of developing drug resistance.

Based on studies that looked at participants who took their pills consistently and correctly, including ongoing medical care, we conclude that oral PrEP is a highly effective strategy to help prevent the sexual transmission of HIV.

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DISCLAIMER

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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