

# 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 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 very rare for HIV to be transmitted through sex.*

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Canada's source for  
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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 of these approaches on the HIV epidemic, we must effectively increase awareness, uptake and proper use of them.*

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 sexual HIV transmission ranges from zero to very low.

The following statement focuses on PrEP. It begins with a simple key message followed by recommendations for service providers and a list of available tools and resources. It also provides a review of the evidence 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 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 very rare for HIV to be transmitted through sex.

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

### **RECOMMENDATIONS FOR SERVICE PROVIDERS**

PrEP is a highly effective HIV prevention strategy that is increasingly being used in Canada, with most provincial/

territorial drug plans offering coverage for PrEP. The only version of PrEP currently approved by Health Canada is the daily use of a pill containing tenofovir disoproxil fumarate (also called TDF) and emtricitabine (also called FTC). Health Canada has approved the use of oral PrEP to help prevent the sexual transmission of HIV and Canadian guidelines exist to help healthcare workers prescribe PrEP. Provincial guidelines are also available for healthcare workers in Quebec, Alberta, Saskatchewan and British Columbia.

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.

#### **1. 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.
- PrEP must only be accessed through a healthcare provider.
- PrEP requires that people are highly adherent to PrEP medications.
- People who want to start taking PrEP should first be tested for kidney function and screened for sexually transmitted infections (STIs) and hepatitis A, B and C.
- People who are taking PrEP should have regular clinic visits with a healthcare provider, once after 30 days on PrEP and every three months thereafter. During these visits they should be tested for HIV and STIs, monitored for side effects and toxicity, and given adherence and risk-reduction counselling.

PrEP should only be used by people who are HIV negative and at high risk for HIV infection. Canadian guidelines define this as:

- men or transgender women who report condomless sex with men and have any of the following:
  - Infectious syphilis or a bacterial sexually transmitted infection (STI) in the last year
  - Use of post-exposure prophylaxis (PEP) more than once
  - A high score on a valid HIV risk assessment tool
- Any person who has condomless anal or vaginal sex with a partner with HIV who is not on treatment and virally suppressed

This list includes people who are likely to be at the highest risk of getting HIV. This criteria can be used to identify PrEP candidates but should not be used to deny someone access to PrEP. Other individuals may be at risk for HIV through sex or drug use and could benefit from the use of PrEP. For example, the Canadian PrEP guideline states: “When considering PrEP for heterosexual adults on the basis of having multiple or unknown-status partners, practitioners must make decisions on a case-by-case basis, using local epidemiologic data and patient-reported risk behaviours/exposures in the partner”.

Education and counselling activities should include a discussion of a client’s level of HIV risk so that they can participate in making an informed decision about whether PrEP is right for them. 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.

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.

Some gay, bisexual or other men who have sex with men (gbMSM) 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. Studies support on-demand PrEP as a highly effective strategy to help prevent the sexual transmission of HIV in gbMSM when used consistently and correctly. On-

demand PrEP is not recommended for use by people having vaginal sex.

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.

**2. Facilitate and support appropriate 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, adhere to a pill-taking regimen and attend 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 to use this strategy consistently and correctly. You may have to offer, or link clients to, interventions and services to support medication adherence and continued engagement in medical care.

**3. 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. PrEP also 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.

#### **4. 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, 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.

#### **5. 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.

#### **6. 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.

**7. 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.

## **TOOLS AND RESOURCES**

### **CATIE resources**

PrEP Resources and Tools

Oral pre-exposure prophylaxis (PrEP) – Fact sheet

Truvada – Fact sheet

8 Questions About PrEP for Guys – Client resource available online and in print

New Canadian HIV PrEP/nPEP guidelines: public health and community perspectives – Webinar

PrEP for understudied populations: Exploring questions about efficacy and safety – *Prevention in Focus*

PrEP use among gbMSM: What does it mean for STI prevention? – *Prevention in Focus*

### **Guidelines and HIV risk assessment tool**

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

La prophylaxie préexposition au virus de l'immunodéficience humaine : Guide pour les professionnels de la santé du Québec – Ministère de la Santé et des Services sociaux du Québec (French only)

Guidance for the use of Pre-Exposure Prophylaxis (PrEP) for the prevention of HIV acquisition in British Columbia – B.C. Centre for Excellence in HIV/AIDS

HIV Incidence Risk Index for MSM (HIRI-MSM)

### **Other PrEP resources**

Truvada Product Monograph – Gilead Sciences

Ongoing and planned PrEP evaluation studies – AVAC

### **HIV disclosure**

The Criminalization of HIV Non-Disclosure in Canada: Current status and the need for change (2019) – Canadian HIV/AIDS Legal Network

Expert consensus statement on the science of HIV in the context of criminal law (2018) – *Journal of the International AIDS Society*

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 (2019) – British Columbia Prosecution Service Crown Counsel Policy Manual

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

## EVIDENCE

A large body of evidence shows that PrEP is highly effective at reducing the risk of HIV transmission when used consistently and correctly.<sup>1-8</sup> Daily oral PrEP was initially proven effective based on evidence from several large randomized controlled trials (RCTs).<sup>1-7</sup> 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, bisexual and other men who have sex with men (gbMSM), heterosexual men and women, trans women, and people who use injection drugs.

The overall reduction in HIV risk provided by PrEP in these studies ranged from zero to 86%, however these analyses did not take into account whether people were actually taking PrEP as prescribed. Some of these studies conducted adherence analyses, which compared the risk of HIV infection among participants who had PrEP detected in their blood to those who did not.<sup>1,2,5</sup> These analyses found that the use of PrEP (determined by detectable drug in the blood) can reduce the risk for sexual HIV transmission among gbMSM and heterosexual men and women by between 85% and 92%.<sup>9,10</sup>

One study, conducted in gbMSM and trans women, found no HIV infections among those who took PrEP consistently (at least four times per week).<sup>11</sup> Modelling from this study estimated that daily oral PrEP is 99% effective at reducing the risk of sexual HIV transmission among gbMSM who take it every day.<sup>12</sup>

Among all the studies and the many thousands of people now using PrEP globally (including all genders and sexual orientations), there have only been a handful of documented cases of HIV transmission in people who are adherent to PrEP.<sup>13-18</sup> In fact, in all but one of these cases, the people taking PrEP acquired a rare strain of HIV that was resistant to the drugs in PrEP. Based on all the available evidence, it is now widely accepted that the risk of getting HIV through sex is reduced by up to 99% when taking PrEP every day.

For PrEP to work optimally, drug levels in the body need to be high enough to prevent HIV infection. 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, daily dosing of oral PrEP is more important for people having vaginal sex, to maintain sufficient drug levels to help prevent HIV infection.<sup>19-22</sup>

Evidence suggests that intermittent or “on-demand” PrEP reduces the risk of HIV transmission among gbMSM. One RCT, known as IPERGAY, evaluated the use of on-demand PrEP among gbMSM.<sup>23,24</sup> 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 got HIV but neither had PrEP detected in their blood).<sup>23</sup> Men in the RCT phase of this study had sex frequently and, as a result, took four pills a week on average.<sup>23</sup> IPERGAY continued as an open-label extension with all participants offered on-demand PrEP.<sup>24</sup> Results from the open-label phase showed that one HIV transmission occurred in 362 participants, over 515 person-years of follow-up.<sup>24</sup> None of the three participants who got HIV over the entire course of the study had PrEP detected in their blood, which means they were not adherent.<sup>24</sup>

Since IPERGAY, several demonstration projects in Europe have offered participants the option of choosing on-demand or daily PrEP.<sup>25,26,27</sup> These studies have found no HIV infections among gbMSM and trans women taking on-demand PrEP. The effectiveness of on-demand PrEP has not been evaluated in populations other than gbMSM and trans women.

PrEP appears to be generally safe and well tolerated. Although oral tenofovir and emtricitabine are 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.<sup>1-6</sup> 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 changes appear to be 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 RCTs, 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.<sup>1-6</sup> 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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