Oral pre-exposure prophylaxis (PrEP)

Summary

Oral pre-exposure prophylaxis, or PrEP, is a way for an HIV-negative person who is at risk of HIV infection to reduce their risk of getting HIV by taking antiretroviral drugs. The daily use of oral PrEP is approved by Health Canada to reduce the risk of the sexual transmission of HIV for people at high risk of HIV infection. Use of oral PrEP involves regular medical appointments for monitoring and support. Oral PrEP is a highly effective HIV prevention strategy when used consistently and correctly. It is generally safe and well tolerated, and is available by prescription in Canada.

What is oral PrEP?

Oral PrEP is a prescription pill that contains antiretroviral drugs, which are also used for HIV treatment. An HIV-negative person can reduce their risk of getting HIV by taking oral PrEP regularly.

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). This has been approved to reduce the risk of sexual HIV transmission in people at high risk for HIV infection.

How does oral PrEP work to help prevent HIV?

PrEP interferes with the pathways that HIV uses to cause a permanent infection. For HIV to cause infection the virus must gain entry into the body, infect certain immune cells, make copies of itself (replicate) within these immune cells, then spread throughout the body.

When oral PrEP is taken consistently and correctly, antiretroviral drugs get into the bloodstream and genital and rectal tissues. The drugs work to help prevent HIV from replicating within the body’s immune cells, which helps to prevent a permanent infection.

For PrEP to help stop HIV replication from happening, drug levels in the body must remain high. If pills are not taken consistently as prescribed there may not be enough medication in the body to reduce the risk of HIV infection.
**How well does daily oral PrEP work?**

A large body of evidence shows that PrEP is highly effective at reducing the risk of HIV transmission when used consistently and correctly. Daily oral PrEP was initially proven effective based on evidence from randomized controlled trials (RCTs) conducted in gay, bisexual and other men who have sex with men (gbMSM), transgender women, and in heterosexual men and women. In addition, limited evidence from one RCT found that daily oral PrEP (with tenofovir alone), is effective at reducing the risk of HIV transmission among people who inject drugs when used consistently and correctly. In all the RCTs, PrEP was provided as part of a comprehensive prevention package that included regular testing and treatment for sexually transmitted infections (STIs), free condoms and ongoing behavioural counselling.

The overall reduction in HIV risk provided by PrEP in the RCTs ranged from zero to 86%, but these analyses did not take into account whether people were actually taking PrEP as prescribed. Adherence (taking medications exactly as prescribed) is crucial for oral PrEP to work. The evidence shows that higher adherence is associated with greater protection. To demonstrate the importance of adherence, some of these studies conducted adherence analyses that compared the risk of HIV infection among participants who had PrEP detected in their blood to those who did not. These analyses found that the use of PrEP (determined by detectable drug in the blood) reduced the risk of sexual HIV transmission by between 85% and 92% among gbMSM and heterosexual men and women.

One study, conducted in gbMSM and trans women, found no HIV infections among those who took PrEP consistently (at least four times per week). 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.

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 sexual HIV transmission in people who are adherent to PrEP. 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.

Although PrEP does not work 100% of the time, reports of PrEP failure are very rare events considering the large number of people taking PrEP worldwide. In all documented cases of HIV transmission on PrEP, the men who became HIV positive were able to diagnose their HIV early and get on treatment immediately because they were having regular medical check-ups.

For people who inject drugs, only one RCT has evaluated the use of oral PrEP (with tenofovir alone). This study found a 49% overall risk reduction in people who inject drugs, however HIV risk was reduced by 84% among people who used tenofovir consistently compared to those who did not. There is otherwise limited data available on PrEP use by people who inject drugs, but the Canadian PrEP guideline recommends that PrEP can be considered for use by people who inject drugs if they are at high risk for HIV.

**Does on-demand PrEP work?**

Evidence shows that intermittent, or on-demand, PrEP reduces the risk of HIV transmission among gbMSM. A few studies have evaluated the use of on-demand PrEP among gbMSM, but no studies have been conducted to evaluate its effectiveness in other populations.

In an RCT called IPERGAY, gbMSM were to take two pills 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 gbMSM in the on-demand PrEP group compared to those in a placebo group (two participants in the PrEP arm got HIV but neither had PrEP detected in their blood). Men in the RCT phase of this study had sex frequently and, as a result, took four pills a week on average. IPERGAY continued as an open-label extension with all participants offered on-demand PrEP. Results from the open-label phase showed that one more HIV transmission occurred in 362 participants, over 515 person-years of
follow-up (equivalent to following 515 people for one year). 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.

Since IPERGAY, several demonstration projects in Europe have offered participants the option of choosing on-demand or daily PrEP. These studies have found no HIV infections among gbMSM and trans women taking on-demand PrEP consistently and correctly.

The Canadian PrEP guideline states that on-demand PrEP can be considered as an alternative form of PrEP for gbMSM only. On-demand PrEP has only been evaluated in gbMSM and is not recommended for people who have vaginal sex or people who inject drugs.

Does oral PrEP work as well for vaginal sex as for anal sex?

Evidence from RCTs suggests that daily oral PrEP is equally effective for vaginal and anal sex when used consistently and correctly, but that adherence may be more important for people having vaginal sex. For PrEP to work optimally, drug levels in the body need to be high enough to prevent HIV infection. There is some evidence showing that the drugs in PrEP take longer to reach maximum levels in vaginal tissues compared to rectal tissues, and that drug levels are lower in vaginal tissues. This suggests that daily dosing of oral PrEP may be more important for people having vaginal sex to maintain sufficient drug levels to help prevent HIV infection.

Who should take PrEP?

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

- men or trans women who report condomless sex with men and have any of the following:
  - Infectious syphilis or 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
- People who share injection drug use equipment

The above 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”.

What else is involved with taking oral PrEP?

Oral PrEP is part of a comprehensive HIV prevention strategy that includes safer sex practices and routine medical appointments.

The first step is to make sure a person is HIV negative before starting PrEP. They will also be tested for STIs and hepatitis A, B and C, and have their kidney function checked.

A person using oral PrEP needs to take it as prescribed by their healthcare provider. They must also attend regular doctor’s appointments, once after the first 30 days on PrEP and every three months thereafter. These regular visits are necessary in order to be tested for HIV and other STIs, monitored for drug side effects, and receive ongoing adherence and risk-reduction counselling.

Is PrEP intended to replace condoms and other HIV prevention strategies?

Canadian guidelines recommend that PrEP be used in combination with safer sex practices and harm-reduction strategies to optimally reduce the risk of HIV infection. Although oral PrEP is highly effective when used consistently and correctly, we know that
it is not 100% effective. Oral PrEP is one of several highly effective HIV prevention strategies, and everybody should be able to choose a strategy that works best for them.

PrEP only helps to prevent HIV and does not offer protection against STIs (such as herpes, chlamydia, gonorrhoea or syphilis) or blood-borne infections such as hepatitis C. Other prevention strategies (such as using condoms or new injection equipment) are needed to reduce the risk of all other infections that can be passed through sex or sharing of injection drug use equipment.

What are the advantages of PrEP?
The main advantage of oral PrEP is that it adds another highly effective HIV prevention option to the growing list of prevention strategies. For example, PrEP may provide another method to help protect people who are unable to negotiate condom use with their partner(s), people who inject drugs but are not able to obtain new injection equipment, or people who do not use condoms or new injection equipment consistently for whatever reason.

For people who have trouble negotiating condom use, PrEP may be especially beneficial because it is a prevention strategy that a person can control without their sexual partners knowing that they are using it. For people who worry about getting HIV during sex, PrEP can help to alleviate anxiety about getting HIV. Another advantage is that oral PrEP use can be started during periods of higher risk and stopped during periods of lower risk.

What are some of the safety concerns associated with taking PrEP?

Drug resistance
A person can develop resistance to the drugs in PrEP if they are HIV positive (and unaware of their positive status) when starting oral PrEP. Drug resistance can limit a person’s future treatment options, so it is important to ensure that they are HIV negative before starting oral PrEP.

A person can also develop drug resistance if they become HIV positive while taking oral PrEP. In clinical trials, the risk of developing drug resistance was low for people who were HIV negative when they started taking PrEP.

Regular HIV testing is necessary while taking oral PrEP. If a person using PrEP gets HIV, PrEP must be discontinued as soon as possible, to reduce the risk of developing drug resistance. If a person’s HIV becomes resistant to the drugs in PrEP, those same drugs may not work to treat HIV.

Side effects
Although TDF and FTC are generally better tolerated than some of the other drugs used to treat HIV, they are still capable of causing side effects. Some of the possible side effects include nausea, vomiting, diarrhea, headache and dizziness. Side effects caused by oral PrEP may negatively affect a person’s quality of life and ability to adhere to their medication schedule.

In clinical trials these side effects were generally mild, temporary, and only affected between 1% and 10% of participants. 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.

Although research suggests that the use of oral PrEP is generally safe and well tolerated, the long-term effects of using PrEP are less well known.

How can people at high risk of HIV infection access PrEP?
An HIV-negative person who wants to take PrEP needs to get a prescription from a doctor who is willing to provide the necessary medical follow-up in a safe and informed way. PrEP does not need to be prescribed by an HIV specialist, but not all doctors are knowledgeable about PrEP and it may be difficult for clients to find a doctor who is willing to prescribe PrEP.

Health Canada has approved the prescription of TDF and FTC as daily PrEP for reducing the risk of HIV infection through sex; however, it can be
prescribed in other ways. Healthcare providers can prescribe PrEP for daily use by people who inject drugs, or for on-demand use by gbMSM. This is possible because the drugs have already been approved for reducing the risk of sexual HIV transmission and for treatment of HIV. When an approved drug is prescribed for an unapproved use, this is called an “off-label” prescription. These types of prescriptions are legal and – for some types of drugs – common.

The cost of PrEP is covered by most public and some private health insurance plans in Canada. Without coverage, daily PrEP costs about $250 a month.

What other types of PrEP are out there?

A newer version of oral PrEP containing a different antiretroviral drug combination (tenofovir alafenamide, also called TAF, combined with FTC) has been approved for use as PrEP in the United States but not yet in Canada. Research has shown that PrEP with TAF + FTC is just as effective as PrEP with TDF + FTC. The TAF formulation is generally associated with a reduced risk of bone thinning and a reduced risk of kidney injury; however, TAF is currently much more expensive.

Other types of PrEP, including vaginal or rectal gels, intravaginal rings and long-lasting injections are currently in experimental stages. No other forms of PrEP have been approved for use by any regulatory agency in the world, and we do not expect them to be available for use in Canada in the near future.

Resources

PrEP Resources and Tools

PrEP to prevent HIV: Your questions answered–CATIE

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

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

Low rate of drug resistance to medications used for pre-exposure prophylaxis in a Canadian cohort of people with HIV – CATIE

Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational post-exposure prophylaxis

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 – BC Centre for Excellence in HIV/AIDS

2018 Alberta HIV Pre-Exposure Prophylaxis (PrEP) Guidelines – Alberta Health Services

Pre-exposure prophylaxis: Guideline review for primary care practitioners in Saskatchewan – Saskatchewan HIV Collaborative

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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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