Providing HIV preexposure prophylaxis

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Transmission of HIV is an ongoing concern in Canada. Since 1990, there have been approximately 2000 to 2500 Canadians diagnosed with HIV per year.[1] Most of these infections are diagnosed among those identifying as gay, bisexual, or men who have sex with men (MSM), although regional differences exist.[1] Preexposure prophylaxis (PrEP) is a proactive HIV prevention strategy for HIV-negative individuals at increased ongoing risk. Preexposure prophylaxis involves taking medication before and after potential HIV exposure to prevent transmission. Other risk reduction strategies such as frequent HIV testing, condom use, and opioid agonist therapy can be used in combination with PrEP. Canadian guidelines on HIV PrEP and other resources are available; however, recent data suggest that many MSM who could benefit from this strategy are not currently using PrEP.[2-4] Family physicians are trusted by their patients and thus well situated to offer PrEP to those who may benefit. This article will outline considerations when prescribing PrEP for MSM.

Identifying individuals at risk of acquiring HIV

Individuals who are HIV negative and at elevated risk of HIV acquisition can be identified by taking a detailed sexual and drug use history. Both past and anticipated future risk should be considered. A trauma-informed, individualized approach should be followed based on sex, culture, and ethnic background. Prescribers may use the HIV Incidence Risk Index for MSM (HIRI-MSM) assessment tool to estimate an individual's HIV risk.[5] Validated in a Vancouver-based study, the HIRI-MSM tool found that scores of 10 or higher were associated with a 2% per year incidence of HIV, while scores of 25 or higher represented a 7% per year incidence of HIV.[6] A Canadian guideline on HIV PrEP endorses the HIRI-MSM assessment tool and considers PrEP to be indicated for MSM with a risk score of 11 or greater.[2] A low HIRI-MSM score means HIV acquisition is unlikely; however, PrEP may still be offered if benefits outweigh risks for the individual.

In addition, an individual may be at increased risk of HIV acquisition if they have required nonoccupational post-exposure prophylaxis (approximately 7% per year incidence of HIV) or have a history of sexually transmitted infections (STIs) (approximately 5% per year incidence of HIV).[6,7]

Case description

Thomas (a pseudonym), a 31-year-old man, is new to your family practice. Thomas tells you he recently moved to the area, does not have any known medical diagnoses, and considers himself healthy. You seek permission to ask Thomas some questions about his sexual history as part of your routine care. Thomas agrees to this.

Doctor: "To start with, do you have any questions about your sexual health?"

Thomas: "It's been a while since I had an STI test. Should I get tested more often now that my boyfriend and I decided to have an open relationship? We know we should wear condoms, but it doesn't always happen."

Doctor: "I recommend STI screening at least every 3 months given that you are sexually active. Since you have male partners, can I ask you some questions about your HIV risk? This will help me determine if a medication to prevent HIV transmission is worth considering, since many men underestimate their HIV risk."

You use the HIRI-MSM assessment tool, and based on Thomas' age (31 years, score of 5), number of male sexual partners (6 to 10 partners, score of 4), condomless receptive anal sex (1 or more times, score of 10), and use of poppers (alkyl nitrites; score of 3), you calculate his cumulative score to be 22. According to a Canadian guideline on HIV PrEP,[2] he has an indication for PrEP and could consider this strategy to protect himself from acquiring HIV.

Bringing evidence to practice: combination medications

Currently, there are 2 medications indicated for the prevention of HIV in MSM in Canada (**Table 1**). In a randomized controlled trial, participants receiving a combination of 200 mg–300 mg emtricitabine–tenofovir disoproxil fumarate daily reduced the relative incidence of HIV by approximately 50% in males at high risk compared with placebo over 1.2 years (event rate=3% vs 5.8%; number needed to treat=36; hazard ratio=0.53, 95% CI 0.36 to 0.78).[8] Relative risk was reduced by 92% (95% CI 40% to 99%) in a subgroup analysis of those with detectable drug levels, highlighting the importance of adherence.[8] The prodrug formulation emtricitabine–tenofovir alafenamide, taken daily, was found to be noninferior to emtricitabine–tenofovir disoproxil fumarate taken daily for prevention of HIV in MSM.[9] Efficacy was also demonstrated in an open-label pilot study involving MSM.[10] Preexposure prophylaxis taken daily is an effective strategy to decrease the risk of HIV transmission.

Preexposure prophylaxis is generally well tolerated. In randomized controlled trials, only 2% of participants permanently discontinued therapy because of adverse events.[8,9] Individuals may experience nausea with PrEP, especially within the first 4 weeks of therapy (event

Table 1. PrEP combination medications available in Canada for MSM

GENERIC NAME (BRAND NAME)	TABLET STRENGTH	PrEP DOSING FOR MSM	COVERAGE AND COST PER 30 TABLETS
Emtricitabine–tenofovir disoproxil fumarate (Truvada)	200 mg–300 mg	Continuous daily method • 1 tablet by mouth daily (on label) On-demand method • 2 tablets taken together 2-24 h before sexual activity, then 1 tablet daily until 2 d after last sexual activity (off label)	Universal coverage among most provinces and territories; $250 for generic medication; $860 for brand-name medication
Emtricitabine–tenofovir alafenamide (Descovy)	200 mg–25 mg	Continuous daily method • 1 tablet by mouth daily (on label)	Nonformulary among most provinces and territories; $860 for brand-name medication (no generic available)

MSM—men who have sex with men, PrEP—preexposure prophylaxis.

rate=9% vs 5%; number needed to harm=25; $P<.0021$).[8] However, tolerance developed after 1 to 2 weeks, with nausea rates decreasing similar to placebo.[8] Some individuals may experience diarrhea (4% to 16%) or headache (2% to 4%); these adverse events were similar to placebo.[8,9]

Preexposure prophylaxis does not usually lead to more risky sexual practices. Multiple trials have shown no difference in STI incidence for participants taking PrEP compared with placebo.[8,10] One trial found a reduction in participants' number of receptive anal intercourse partners from approximately 12 partners to 6 partners, and an increase in condom use from approximately 50% to 75%.[8]

Emtricitabine–tenofovir disoproxil fumarate may impact kidney function (approximately 1 mL/min/year estimated glomerular filtration rate [eGFR] decrease compared with placebo) and may minimally decrease bone mineral density.[2] Both changes are usually reversible upon discontinuation. Experts suggest minimizing nephrotoxins such as nonsteroidal anti-inflammatory drugs, avoiding volume depletion, and managing kidney-related comorbidities (eg, hypertension and diabetes).[2] Emtricitabine–tenofovir alafenamide appears to have less impact on kidney and bone surrogate biomarkers and may be an alternative for those with an eGFR less than 60 mL/min or previous fracture.[9]

When PrEP is initiated, kidney function testing, along with all other investigations outlined in **Table 2**, are required at baseline and periodically to ensure ongoing effectiveness and safety. Baseline bone mineral density testing is not recommended unless there is another compelling indication.[2,3,11] Individuals with an eGFR less than 60 mL/min, with a history of fractures, or who are pregnant should be referred to an HIV or infectious disease specialist for further management.

Back to Thomas

You discuss Thomas' risk of acquiring HIV and explain the benefits of PrEP. Thomas is interested but does not know much about PrEP beyond having a few friends who currently take it. You show Thomas a PrEP infographic (available from **CFPlus***) and provide information about PrEP.

Doctor: "PrEP, or preexposure prophylaxis, is a way to prevent you from getting HIV. It is 1 pill that contains 2 medications typically taken once daily. This is called the continuous dosing method. The short-term and long-term effects of this medication are well known because it has been used for years as a component of HIV treatment. In studies, it has been shown to be effective, safe, and well tolerated when taken as prescribed."

Thomas: "I'm still not sure. Can you tell me about the side effects?"

Doctor: "Most people do not have side effects, but some may experience mild stomach upset or headaches after starting. If these occur, they typically resolve in about 1 to 2 weeks as you adjust to the medication. If you take PrEP daily for many years, it may minimally impact kidney function and bone mineral density. Because of this, we check your kidney function before starting, as well as every 3 months along with HIV tests. Monitoring bone density is not required for most individuals since this effect occurs gradually over many years and appears to be reversible when PrEP is discontinued."

See **Box 1** for further counseling tips. After your discussion, Thomas agrees to start PrEP and you order bloodwork as per **Table 2**.

Follow-up via telephone, 1 week later

Thomas' baseline bloodwork results are within the normal range and he is HIV negative. He is advised to initiate the medication for at least 7 days before sexual exposure to be fully protected, to monitor for HIV seroconversion illness, and to avoid long-term nonsteroidal anti-inflammatory drug use (**Box 1**). A 1-month prescription for emtricitabine–tenofovir disoproxil fumarate is sent to the pharmacy (**Table 1**), and Thomas is asked to do repeat bloodwork 1 week before running out of his prescription (**Table 2**).

*The **PrEP infographic** and the **Preexposure prophylaxis (PrEP) for prevention of HIV: drug comparison chart** are available from **https://www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

Table 2. Suggested PrEP investigations at baseline and follow-up visits for MSM: *A hepatitis C serology test should be done every 12 mo (or more frequently if there is ongoing risk; eg, shared injection drug supplies).*

BASELINE INVESTIGATIONS	1-MO INVESTIGATIONS*	STANDING-ORDER INVESTIGATIONS, EVERY 3 MO*
• HIV serology test (and assess HIV signs and symptoms†)	• HIV serology test	• HIV serology test
• Hepatitis A serology test‡	• Serum creatinine level and eGFR tests	• Chlamydia and gonorrhea test using urine plus throat or rectal swabs if applicable
• Hepatitis B serology test‡	• Optional: — Chlamydia and gonorrhea test using urine plus throat or rectal swabs if applicable — Syphilis serology test — Urinalysis	• Syphilis serology test
• Hepatitis C serology test		• Serum creatinine level and eGFR tests
• Chlamydia and gonorrhea test using urine plus throat or rectal swabs if applicable		• Optional: — Urinalysis
• Syphilis serology test		
• Serum creatinine level and eGFR tests		
• Urinalysis		
• CBC		

CBC—complete blood count, eGFR—estimated glomerular filtration rate, MSM—men who have sex with men, PrEP—preexposure prophylaxis.
*Ensure investigations are done approximately 1-2 wk before patient appointment (either virtual or in-person appointment).
†Ensure HIV negative test result within past 7 d (5-14 d) and no new exposures.
‡Refer to public health organizations for vaccinations if nonimmune; if hepatitis B positive consider consultation with infectious disease services.

Box 1. Key counseling tips for continuous daily dosing method of PrEP for MSM

Administration
- PrEP medication must be taken 7 days in a row to have full protection before sexual activity
- When stopping PrEP treatment, continue to take PrEP medication for 2 days after last sexual encounter

Adherence
- Adherence is important. Work with the individual to develop strategies to improve fidelity to treatment plan (eg, telephone alarm, pill box, or pill keychain)
- PrEP is not nPEP—if the patient has missed doses, they should call their provider for management advice
- Monitor for sore throat, monolike illness, or rash—the patient should call their provider if symptoms last a few days as this may be associated with HIV seroconversion

Common side effects and management

Rates of the following usually lessen over time and can be managed symptomatically; see the PrEP infographic* for more details
- Loose bowel movements: take over-the-counter loperamide as needed
- Nausea: take over-the-counter dimenhydrinate as needed; take with food or take at bedtime
- Headache: take over-the-counter acetaminophen as needed; this is preferred over NSAIDs

Follow-up
- Do initial follow-up 1 month after starting PrEP, and then every 3 months thereafter
- Make sure investigations are completed approximately 1 week before each appointment so they are available for review
- Discuss other HIV risk reduction strategies, such as condom use

MSM—men who have sex with men, nPEP—nonoccupational post-exposure prophylaxis, NSAID—nonsteroidal anti-inflammatory drug, PrEP—preexposure prophylaxis.

*The **PrEP infographic** is available from **https://www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

Follow-up in office, 1 month later

Thomas had loose bowel movements after starting PrEP, but this resolved after 2 days. His 1-month bloodwork results were within normal limits, including kidney function, and he is confirmed HIV negative. He tells you he is less anxious about acquiring HIV during sexual encounters since starting PrEP. He has heard from some friends that they only take PrEP when they need to (or on demand) and is wondering if he could switch.

Bringing evidence to practice: continuous versus on demand

Both continuous daily and on-demand dosing methods are evidence-based options for MSM. On-demand dosing requires a loading dose (2 tablets of 200 mg–300 mg emtricitabine–tenofovir disoproxil fumarate given as 1 dose) 2 to 24 hours before sexual activity, followed by 1 tablet daily until 2 days after the last sexual activity (**Table 1** and **CFPlus***). In a randomized controlled trial, this dosing strategy reduced the incidence of HIV by 86% in high-risk MSM compared with placebo (event rate=1% vs 7%; hazard ratio=0.86; 95% CI 0.40 to 0.98).[12] Study drug was not detected in the participants who acquired HIV, and the trial was stopped early after 9.3 months for benefit.[12] More participants taking on-demand dosing experienced gastrointestinal adverse events compared with placebo (event rate=14% vs 5%; number needed to harm=12); this was thought to be related to the loading dose.[12] There was also more serum creatinine level elevation with emtricitabine–tenofovir disoproxil fumarate compared with placebo (18% vs 10%; *P*=.03), but none of these events led to drug discontinuation.[12] There was no difference in fractures between groups.[12]

Usually, the continuous daily dosing method is prescribed initially to determine an individual's tolerance of PrEP, and then the on-demand dosing method can be considered based on an individual's adherence, preference, and other factors. Continuous daily dosing of PrEP has a larger body of evidence supporting its on-label use in MSM and can be beneficial for those who prefer the habit of daily administration or who have regular sexual activity. Although it is an off-label use, on-demand dosing is endorsed by a Canadian guideline and can offer less pill burden with less drug exposure for those with predictable sexual activity.[2] However, some individuals experience more gastrointestinal symptoms from the on-demand loading dose. This method should be used with caution and in consultation with infectious disease specialists for hepatitis B–positive individuals as continuous daily dosing is often preferred. Investigation and monitoring (**Table 2**) remain the same for both continuous daily and on-demand dosing methods.

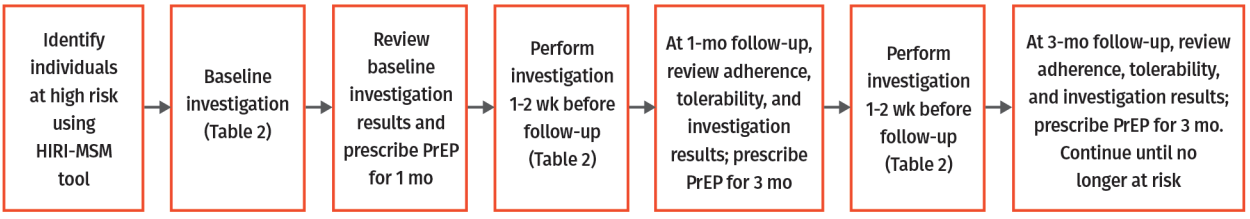
Case resolution

You and Thomas discuss both PrEP dosing methods.

Doctor: "The daily method is better for those who have a hard time remembering to take medications, since it would be a part of your routine. It also provides continuous protection if you have sex often or have sexual encounters that aren't planned. The on-demand method is when you take 2 tablets of PrEP 2 to 24 hours before sex, followed by 1 tablet daily until 48 hours after the last time you have sex. It is a bit more difficult to remember but may be a better option if you have sex infrequently and more predictably. Both methods work well."

Using shared decision making, Thomas decides to continue with once-daily dosing of PrEP as this will be easiest for him to remember. He also anticipates new partners in the future and unpredictable sexual encounters. A 3-month prescription is given to him with instructions to complete bloodwork and STI screening 1 to 2 weeks before his next follow-up appointment in 3 months. Review of these investigations is required before providing the next renewal of the 3-month prescription. If his sexual practices change, his risk of HIV acquisition can be re-assessed at his next follow-up visit. **Figure 1** summarizes the management of PrEP.

Figure 1. PrEP management timeline



HIRI-MSM—HIV Incidence Risk Index for men who have sex with men, PrEP—preexposure prophylaxis.

Conclusion

Preexposure prophylaxis is a safe, well-tolerated, evidence-based strategy to decrease the risk of HIV transmission; however, many MSM individuals at risk of acquiring HIV are not using this therapy. Family physicians can initiate PrEP by identifying individuals at high risk, conducting baseline investigations, providing patient education, prescribing PrEP, and conducting ongoing follow-up to ensure PrEP adherence, effectiveness, and safety.

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References

1. Public Health Agency of Canada. *Estimates of HIV incidence, prevalence and Canada's progress on meeting the 90-90-90 HIV targets*. Ottawa, ON: Government of Canada; 2020. Available from: **https://www.canada.ca/en/public-health/services/publications/diseases-conditions/summary-estimates-hiv-incidence-prevalence-canadas-progress-90-90-90.html#s7**. Accessed 2022 Feb 1.
2. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *CMAJ* 2017;189(47):E1448-58. Erratum in: *CMAJ* 2018;190(25):E782.
3. *Guidance for the use of pre-exposure prophylaxis (PrEP) for the prevention of HIV acquisition in British Columbia*. Vancouver, BC: British Columbia Centre for Excellence in HIV/AIDS; 2020. Available from: **http://bccfe.ca/sites/default/files/uploads/publications/centredocs/prep_guidelines_17-jun-2020.pdf**. Accessed 2022 Feb 1.
4. Cox J, Apelian H, Moodie EEM, Messier-Peet M, Hart TA, Grace D, et al. Use of HIV pre-exposure prophylaxis among urban Canadian gay, bisexual and other men who have sex with men: a cross-sectional analysis of the Engage cohort study. *CMAJ Open* 2021;9(2):E529-38.
5. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2012;60(4):421-7.
6. Lachowsky NJ, Cui Z, Sereda P, Stephenson K, Rich A, Brown J, et al. *HIV incidence rate and predictors among gay and other men who have sex with men (MSM) in Vancouver: additional benefit of an administrative health data linkage*. Presented at: 25th Canadian Conference on HIV/AIDS Research; 2016; Winnipeg, MB.
7. Hull M, Lachowsky N, Moore D, Harris M, Guillemi S, Zhang W, et al. *High incidence of subsequent HIV seroconversion amongst MSM accessing recurrent non-occupational post-exposure prophylaxis (NPEP) in Vancouver, BC*. Presented at: 25th Canadian Conference on HIV/AIDS Research; 2016; Winnipeg, MB.
8. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363(27):2587-99. Epub 2010 Nov 23.
9. Mayer KH, Molina JM, Thompson MA, Anderson PL, Mounzer KC, De Wet JJ, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet* 2020;396(10246):239-54.
10. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* 2016;387(10013):53-60. Epub 2015 Sep 9.
11. LeBras M. *Pre-exposure prophylaxis (PrEP) for prevention of HIV: drug comparison chart*. Saskatoon, SK: RxFiles; 2021. (Available from **CFPlus**.*)
12. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med* 2015;373(23):2237-46. Epub 2015 Dec 1.

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