Guideline CPD

Canadian guideline on HIV pre- and postexposure prophylaxis: 2025 update

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Abstract

Background: New HIV infections occur annually in Canada, highlighting the need for pre- and postexposure prophylaxis (PrEP and PEP). Through the Canadian Institutes of Health Research (CIHR) Pan-Canadian Network for HIV/AIDS and STBBI (sexually transmitted and bloodborne infections) Clinical Trials Research, we have updated the 2017 guideline on clinical indications and drug regimens for PrEP and PEP in Canada.

Methods: Drawing on meetings with community-based organizations representing key populations affected by HIV in Canada, along with evidence from 3 systematic reviews on PrEP, PEP, and HIV risk assessment tools (searches to June 2024), our diverse panel of 19 experts formulated recommendations on PrEP and PEP. We used a formal evidence-to-decision-making framework and the Grading of Recommendations, Assessment, Development, and Evaluation system. We followed the Guidelines International Network principles for managing competing interests. Our guideline development and reporting adhere with Appraisal of Guidelines for Research and Evaluation II.

Recommendations: This guideline contains 31 recommendations and 10 good practice statements. Although it is appropriate to prescribe PrEP to adults and adolescents who request it, clinicians are also encouraged to assess HIV risk during routine health visits to identify people who would benefit from PrEP. Clinicians should elicit information about patients' anatomy and sexual partners in a culturally sensitive and affirming manner to determine which PrEP regimens — daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), on-demand TDF/FTC, daily oral tenofovir alafenamide/emtricitabine, or long-acting injectable cabotegravir — are suitable options. When assessing whether PEP is needed, clinicians should consider the likelihood that the source person has transmissible HIV, as well as the biological risk of HIV transmission based on exposure type. Preferred PEP regimens are dolutegravir plus TDF/FTC, or bictegravir/tenofovir alafenamide/emtricitabine.

Interpretation: Multiple safe, effective PrEP and PEP regimens are now available in Canada, making it increasingly possible to find suitable options for all who could benefit. Implementation of this guideline should expand access to biomedical HIV prevention interventions for those at risk and decrease the incidence of HIV in Canada.

New HIV infections occur frequently in Canada, highlighting the need to scale up pre-exposure prophylaxis (PrEP) and postexposure prophylaxis (PEP). Pre-exposure prophylaxis involves use of certain antiretroviral medications (ARVs) by HIV-negative people at ongoing risk of HIV acquisition, beginning before and continuing after potential HIV exposures. Postexposure prophylaxis involves 28 days of ARVs immediately after a potential HIV exposure.

HIV infections in Canada remain disproportionately concentrated in key populations (Appendix 1, Table A3, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content), with 38.4% of incident infections occurring in gay, bisexual, and other men who have sex with men (GBM); 24.5% in people who inject drugs (PWID); and 3.7% in GBM-PWID in 2022.[1] One-third (35.5%) of infections occur in females.[1] Although 2022 incidence estimates among Indigenous people are not available, the rate in 2020 was markedly higher than for the overall Canadian population, at 15.2 per 100 000.[2] Geographic variation also exists, with substantially higher HIV incidence in Saskatchewan and Manitoba (24 and 19 per 100 000 population, respectively) compared with the national average (4.7 per 100 000) in 2022.[1]

This heterogeneity by population and geography means that clinicians should be familiar with local HIV epidemiology, in addition to nationwide trends, to contextualize HIV risk during

clinical assessments. Population-level data on transgender, gender-diverse, and racialized people are lacking — an important gap because uptake of biomedical prevention technologies has been inequitable. Pre-exposure prophylaxis use in cisgender women, for instance, is far lower than in GBM.[3] Importantly, epidemiologic risk constructs may inadvertently contribute to stigma and discrimination, and caution is needed when applying them to individuals.

This guideline was developed through the Canadian Institutes of Health Research (CIHR) Pan-Canadian Network for HIV and STBBI (sexually transmitted and blood-borne infections) Clinical Trials Research (CTN+) and updates the previous guideline from 2017.[4] Our aim is to guide diverse interested parties on expanding use of these safe and effective tools for preventing HIV, in pursuit of Canada's goal to eliminate HIV as a public health threat by 2030.[5] An array of PrEP and PEP options is now available in Canada, making it possible to find prevention strategies suitable for all. In this article, we provide a synopsis of the full guideline, which is available in Appendix 1.

Scope

Our primary purpose is to support clinical decision-making in primary care, infectious diseases, emergency medicine, sexual health, nursing, pharmacy, and related disciplines, and to support community workers, who play an important role in promoting PrEP and PEP. Policy-makers and public health groups may also use this guideline for informing policy and improving access.

We focus on adults and adolescents, using the Canadian Paediatric Society's definition of adolescence as the period between the onset of physiologically normal puberty and ending when an adult identity and behaviour are accepted, roughly corresponding to the ages of 10 to 19 years.[6] For guidance on potential application of our PEP recommendations in pediatrics and appropriate dose adjustments, clinicians should consult an experienced pediatrician or pharmacist.

Recommendations

We provide 31 recommendations and 10 good practice statements regarding clinical indications and recommended drug regimens for PrEP and PEP in adults and adolescents, as well as several implementation considerations (Table 1). Strength and certainty of evidence are graded according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE; Box 1) system.[7]

In this synopsis of the full guideline, we review selected recommendations and good practice statements for PrEP and PEP (complete list in Table 1). The full guideline is available in Appendix 1, which also includes a review of the underlying evidence; extensive practical advice for providing PrEP and PEP; considerations for use in specific populations; and a more thorough discussion of HIV epidemiology, transmission, and testing. A visual summary of the guideline is available in Figure 1.

Pre-exposure prophylaxis

Counselling

All sexually active adolescents and adults, and those who inject drugs, should be counselled regarding PrEP and PEP as part of a comprehensive approach to preventing HIV and other STBBIs. They should be made aware of the excellent safety and efficacy profile of PrEP and PEP, and how they can be accessed. This information should be framed in a positive light to counteract the stigma and apprehension that sometimes surround PrEP and PEP (good practice statement).

Awareness of PrEP and PEP is critical for people to access them. Clinicians have an important role in providing evidence-based information to people who could benefit and are encouraged to use information in this guideline to counsel potential users on their safety and efficacy.

Indications

It is appropriate to prescribe PrEP to adults and adolescents who request it (good practice statement).

The impetus for PrEP initiation may come from individuals themselves, or from health care professionals. If individuals actively seek out PrEP based on self-assessed HIV risk, it is appropriate to prescribe PrEP. There are many reasons people may not disclose HIV risk behaviours to health care providers, including shame, medical mistrust, and structural barriers linked to homophobia, transphobia, racism, colonial practices, HIV stigma, and other forms of discrimination.[8,9] Providing PrEP to those who request it decreases such barriers. Providers should make this safe and effective intervention available to the widest possible array of users, rather than "gatekeeping" access.

Clinicians are encouraged to assess HIV risk (e.g., using HIV risk-assessment tools) during routine health visits to identify people at increased risk of HIV who would benefit from PrEP, but who do not request it themselves, and to recommend PrEP to them (good practice statement).

In addition to offering PrEP to people who request it, clinicians should also actively offer PrEP to individuals in their care when risk for HIV is identified. Many individuals underestimate their HIV risk, and may not be aware of PrEP.[10,11] Many types of health care encounters provide opportunities to offer PrEP, including visits for sexual health (e.g., sexually transmitted infection [STI] testing or treatment), PEP visits, reproductive health (e.g., contraception, pregnancy-related care, cervical cancer screening), harm reduction services, mental health and addictions services, and primary care.

Although there is no gold-standard strategy for identifying HIV risk, validated assessment tools exist to aid clinicians. We conducted a systematic review of HIV risk assessment tools in adults and adolescents[12] and identified 27 studies published between 1998 and May 2024, which described 11 tools that may be useful to practitioners in Canada, including 9 tools for GBM, 1 for PWID, and 1 for use in a general adult population (Appendix 2, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content). Overall, the tools

performed well (area under the receiver operating characteristic curve 0.65 to 0.8) at predicting incident HIV infection. Although another 6 tools were identified for use in cisgender heterosexual women, they were derived and validated among cohorts of women in Africa. Because the dynamics of the HIV epidemic vary by region, the applicability of these tools to Canada is very limited, even among newcomers from Africa.

Given the multitude of similarly performing tools available for GBM, and the relative lack of tools for other populations, the panel did not recommend specific tools for use. Clinicians may choose to adopt 1 of the available validated tools to help identify PrEP candidates, based on the population they serve or programmatic considerations (e.g., feasibility of implementation within an electronic medical record system). Variables

Table 1 (part 1 of 2): Recommendations regarding the use of pre-exposure prophylaxis and postexposure prophylaxis in Canada

Recommendations	Strength of recommendation and certainty of evidence
Counselling	
• All sexually active adolescents and adults, and those who inject drugs, should be counselled regarding PrEP and PEP as part of a comprehensive approach to preventing HIV and other sexually transmitted and blood-borne infections. They should be made aware of the excellent safety and efficacy profile of PrEP and PEP, and how they can be accessed. This information should be framed in a positive light to counteract the stigma and apprehension that sometimes surround PrEP and PEP.	Good practice statement
Pre-exposure prophylaxis	
Indications	
• It is appropriate to prescribe PrEP to adults and adolescents who request it. • Clinicians are encouraged to assess HIV risk (e.g., using HIV risk-assessment tools) during routine health visits to identify people at increased risk of HIV who would benefit from PrEP, but who do not request it themselves, and to recommend PrEP to them. • For people suitable for PrEP for the prevention of sexually acquired HIV, whose sex assigned at birth and gender identity (or that of their partners) are not specifically named in the recommendations below, clinicians should follow recommendations that align with the person's anatomy and sexual partners.	Good practice statements
Regimens	
For all HIV-negative individuals suitable for PrEP:	
• We recommend daily oral TDF/FTC 300 mg/200 mg as a PrEP option	Strong recommendation, high-certainty evidence
For HIV-negative cisgender men and transgender women in whom risk of HIV acquisition is related to sex with cisgender men:	
• We recommend on-demand (2-1-1) oral TDF/FTC 300 mg/200 mg as a PrEP option	Strong recommendation, moderate-certainty evidence
• Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option	Weak recommendation, high-certainty evidence
• We recommend CAB-LA 600 mg as a PrEP option	Strong recommendation, high-certainty evidence
For HIV-negative cisgender men in whom risk of HIV acquisition is related to heterosexual activity:	
• On-demand (2-1-1) oral TDF/FTC 300 mg/200 mg may be considered as a PrEP option	Weak recommendation, moderate-certainty evidence
• Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option	Weak recommendation, moderate-certainty evidence
• CAB-LA 600 mg may be considered as a PrEP option	Weak recommendation, moderate-certainty evidence
For HIV-negative cisgender women in whom risk of HIV acquisition is related to heterosexual activity:	
• We recommend against using on-demand oral TDF/FTC as PrEP	Strong recommendation, low-certainty evidence
• Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option	Weak recommendation, low-certainty evidence
• We recommend CAB-LA 600 mg as a PrEP option	Strong recommendation, high-certainty evidence
For HIV-negative people in whom risk of HIV acquisition is related to injection drug use:	
• On-demand oral TDF/FTC as PrEP is not recommended	Strong recommendation, very low-certainty evidence
• Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option	Weak recommendation, very low-certainty evidence
• CAB-LA 600 mg may be considered as a PrEP option	Weak recommendation, very low-certainty evidence
For people using CAB-LA PrEP:	
• We suggest not routinely using HIV RNA testing to screen for incident HIV infection among people using CAB-LA PrEP	Weak recommendation, moderate-certainty evidence

common to validated tools that may prove useful in identifying HIV risk include condomless vaginal or front hole, or anal sex outside a closed relationship; previous bacterial STIs (e.g., gonorrhea, chlamydia, syphilis); higher numbers of partners; use of methamphetamines or inhaled nitrates in association with sex; and sharing injection drug use equipment.

Table 1 (part 2 of 2): Recommendations regarding the use of pre-exposure prophylaxis and postexposure prophylaxis in Canada

Recommendations	Strength of recommendation and certainty of evidence
Postexposure prophylaxis	
Indications	
• PEP is clinically appropriate if the source person has a substantial risk of having transmissible HIV infection, and the exposure type was of higher or moderate risk. • The exposed person should undergo baseline HIV testing (fourth-generation antigen–antibody assay or point-of-care third-generation assay, or both) when starting PEP, but PEP initiation should not be delayed while awaiting the result. • PEP should not be initiated when the source person is confirmed to be HIV negative, when the source person is of unknown HIV status but from the general population, or in the setting of sexual exposures to people living with HIV with an undetectable viral load. • Decisions regarding PEP in other contexts warrant case-by-case evaluation and shared decision-making between the clinician and patient. Consultation with a specialist experienced in this area may be helpful but should not delay initiation of PEP if potentially indicated.	Good practice statements
Regimens	
Duration and timing	
• PEP should be initiated as soon as possible after an exposure, up to a maximum of 72 hours afterward. • PEP should be given for a total of 28 days.	Good practice statements
We recommend the following regimens for use as PEP:	
• Bictegravir 50 mg/TAF 25 mg/FTC 200 mg once daily	Strong recommendation, low-certainty evidence
• Dolutegravir 50 mg once daily + TDF 300 mg/FTC 200 mg once daily	Strong recommendation, low-certainty evidence
The following regimens may be considered for use as PEP:	
• Darunavir 800 mg/cobicistat 150 mg once daily + TAF 10 mg/FTC 200 mg once daily	Weak recommendation, low-certainty evidence
• Darunavir 800 mg/cobicistat 150 mg once daily + TDF 300 mg/FTC 200 mg once daily	Weak recommendation, low-certainty evidence
• Darunavir 800 mg once daily + ritonavir 100 mg once daily + TAF 10 mg/FTC 200 mg once daily	Weak recommendation, low-certainty evidence
• Darunavir 800 mg once daily + ritonavir 100 mg once daily + TDF 300 mg/FTC 200 mg once daily	Weak recommendation, moderate-certainty evidence
• Dolutegravir 50 mg once daily + TAF 25 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Doravirine 100 mg/TDF 300 mg/lamivudine 300 mg once daily	Weak recommendation, low-certainty evidence
• Doravirine 100 mg + TAF 25 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Raltegravir 400 mg twice daily + TDF 300 mg/FTC 200 mg once daily	Weak recommendation, low-certainty evidence
We suggest not using the following regimens as PEP:	
• Elvitegravir 150 mg/cobicistat 150 mg/TAF 10 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Elvitegravir 150 mg/cobicistat 150 mg/TDF 300 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Raltegravir 400 mg twice daily + TAF 25 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Rilpivirine 25 mg/TAF 25 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
• Rilpivirine 25 mg/TDF 300 mg/FTC 200 mg once daily	Weak recommendation, very low-certainty evidence
Delivery strategies	
• We suggest starter kits be available for HIV-negative individuals in whom PEP is being initiated.	Weak recommendation, very low-certainty evidence
• We suggest PEP-in-pocket be considered for HIV-negative individuals with infrequent moderate- to high-risk exposures.	Weak recommendation, low-certainty evidence

Note: CAB-LA = long-acting cabotegravir, FTC = emtricitabine, PEP = postexposure prophylaxis, PrEP = pre-exposure prophylaxis, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate.

Box 1: Grading of Recommendations, Assessment, Development, and Evaluation system for recommendations and definitions[7]

This guideline was developed using the GRADE system, which specifies 2 categories of strength of recommendations, and 4 categories of certainty of the evidence on which recommendations are based.

Strength of recommendations

- Strong recommendations are those for which the guideline panel is confident that the desirable effects of an intervention outweigh undesirable effects (or vice versa), across the range of patients for whom the recommendation is intended. Strong recommendations for an intervention are generally worded as follows: "the panel recommends that the intervention be done." Strong recommendations against an intervention are either worded as "the panel recommends that the intervention not be done," if there are compelling reasons not to pursue it, or "the intervention is not recommended," if a major reason for the negative recommendation is a lack of evidence.
- Weak or conditional recommendations are actions that could be considered, for which the panel is less confident of the balance between desirable and undesirable consequences. Although most individuals in this situation would want the suggested course of action, many would not, and clinicians must recognize that different choices will be appropriate for different individuals. Weak recommendations for an intervention generally state that it "may be considered," whereas weak recommendations against an intervention state that "the panel suggests not using" it.

Certainty of evidence

- High (starting point for randomized controlled trials): the panel is very confident that the true effect lies close to that of the estimate of the effect.
- Moderate: there is moderate confidence in the effect estimate. The true effect is likely close to the estimate, but there is a possibility that it is substantially different.
- Low (starting point for observational studies): the panel has limited confidence in the effect estimate. The true effect may be substantially different from the estimate.
- Very low: there is very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate.

Good practice statements

- According to the GRADE framework, good practice statements provide clear and actionable guidance in situations where there is high certainty that the desirable effects of an intervention clearly outweigh the undesirable effects, but for which the body of supportive evidence is indirect and the collection and summary of the evidence is considered a poor use of a guideline panel's time and resources.

Note: GRADE = Grading of Recommendations, Assessment, Development, and Evaluation.

Regimens

For people suitable for PrEP for the prevention of sexually acquired HIV, whose sex assigned at birth and gender identity (or that of their partners) are not specifically named in the recommendations in Table 1, clinicians should follow recommendations that align with the person's anatomy and sexual partners (good practice statement).

Most HIV infections in Canada are related to sex between cisgender men, heterosexual activity, and injection drug use.[1] Most of our recommendations on PrEP regimens therefore address these modes of transmission and populations, which have been studied in large trials.[13] However, people of all sexes and genders may benefit from PrEP and should be actively included in programs and policies. Clinicians should elicit information about patients' anatomy and sexual partners (e.g., partners' anatomy, partners' gender identities, relationship type, frequency of encounters) in a culturally sensitive and affirming manner to determine which recommendations apply.

Multiple safe and effective PrEP regimens — including daily pills, event-based or "on-demand" pills, and long-acting injectable medications — are now available in Canada (Appendix 3, Evidence Summaries, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content). The diversity of choices renders it increasingly possible to find suitable options for all who could benefit.

Daily oral tenofovir disoproxil fumarate/emtricitabine

For all HIV-negative individuals suitable for PrEP:

- *We recommend daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) 300 mg/200 mg as a PrEP option (strong recommendation, high-certainty evidence).*

Daily oral TDF/FTC is the most widely evaluated PrEP regimen,[13] with high-quality studies documenting excellent safety, efficacy, and acceptability in multiple populations, and nearly 100% efficacy at decreasing HIV acquisition risk if used consistently.[14–19] It is the only approved PrEP product currently available in generic formulations in Canada, rendering it the most affordable. A meta-analysis of 10 placebo-controlled trials showed that the frequency of adverse events is similar to that with placebo (odds ratio [OR] 1.01, 95% confidence interval [CI] 0.99 to 1.03),[20] although extended use can have negative effects on kidney and bone health (Appendix 1, Sections 6.1.5–6.1.6).

On-demand or "2-1-1" oral tenofovir disoproxil fumarate/emtricitabine

For HIV-negative cisgender men and transgender women in whom risk of HIV acquisition is related to sex with cisgender men:

- *We recommend on-demand (2-1-1) oral TDF/FTC 300 mg/200 mg as a PrEP option (strong recommendation, moderate-certainty evidence).*

For HIV-negative cisgender men in whom risk of HIV acquisition is related to heterosexual activity:

- *On-demand (2-1-1) oral TDF/FTC 300 mg/200 mg may be considered as a PrEP option (weak recommendation, moderate-certainty evidence).*

For HIV-negative cisgender women in whom risk of HIV acquisition is related to heterosexual activity:

- *We recommend against using on-demand oral TDF/FTC as PrEP (strong recommendation, low-certainty evidence).*

HIV PrEP and PEP: 2025 guideline update

COUNSELLING

Who

- All sexually active teens and adults
- People who inject drugs

When

- Routine health visits

What

- **Discuss** role of PrEP and PEP in preventing HIV
- **Describe** how to access
- **Frame** information positively

PRE-EXPOSURE PROPHYLAXIS

Indications

- **Prescribe** PrEP for all adults and teens who want it
- **Assess** HIV risk and recommend PrEP to people who would benefit

Recommended regimens*

- Multiple safe and effective options are available for all HIV-negative individuals suitable for PrEP
- Preferred regimens differ by population

Note: PEP = postexposure prophylaxis, PrEP = pre-exposure prophylaxis

* See guideline and appendices for specific recommendations, strength of recommendations and certainty of evidence, and decision-making and implementation resources (www.cmaj.ca/-lookup/doi/10.1503/cmaj.250511L)

POSTEXPOSURE PROPHYLAXIS

Indications

- **Prescribe** PEP to exposed patient with:
  - Moderate or high-risk exposure, *and*
  - Source person with substantial risk of having transmissible HIV infection
- **Do not prescribe** PEP if:
  - Source person is HIV negative
  - Source person has unknown HIV status and not from a high-prevalence population
  - Patient had a sexual exposure to partners living with HIV with undetectable viral load

Duration and timing

- Initiate PEP as soon as possible, within 72 hours after exposure
- Order baseline HIV testing for exposed patient but do not delay PEP
- Give PEP for 28 days

Recommended regimens*

- Coformulated bictegravir / tenofovir alafenamide / emtricitabine, *or*
- Dolutegravir plus tenofovir disoproxil fumarate / emtricitabine
- Multiple alternative options available

Figure 1: Summary of the guideline recommendations. See Related Content tab for accessible version.

For HIV-negative people in whom risk of HIV acquisition is related to injection drug use:

- *On-demand oral TDF/FTC as PrEP is not recommended (strong recommendation, very low-certainty evidence).*

For cisgender men and transgender women in whom HIV risk is related to sex with cisgender men, "on-demand" oral TDF/FTC — in which the medication is used only around the time of anticipated sexual exposures — is another strongly recommended PrEP option, based on high-quality clinical trials[21,22] and real-world effectiveness studies.[23–26] This regimen is also nicknamed "2-1-1" PrEP because it involves a loading dose (2 tablets) of TDF/FTC taken 2 to 24 hours before sex, followed by 1 tablet daily for 48 hours after the last pre-sex dose (i.e., 1 tablet 24 hours after the loading dose, and a final tablet 24 hours later). If another sexual exposure occurs during those 48 hours, the user should continue taking 1 tablet every 24 hours until 2 doses after the last exposure. If sexual activity resumes within a week, then the pre-exposure loading dose can be reduced to only 1 tablet rather than 2.

On-demand TDF/FTC should not be used in people with active hepatitis B because of the risk of hepatitis flares during treatment interruption, or among those who may have difficulty adhering to the dosing regimen (Appendix 1, Section 6.2.2). Because there are no clinical data to support its use for preventing injection-related and vaginal HIV acquisition, we also do not recommend on-demand TDF/FTC in other populations, except in cisgender men who have insertive sex with cisgender women, for whom data can be extrapolated from GBM because of the shared risk of penile HIV acquisition (Appendix 1, Section 5.2.2). Transgender women using feminizing hormones who consider this regimen should be counselled about drug–drug interactions (Appendix 1, Section 6.2.5). Considerations that may be helpful in choosing between daily and on-demand oral TDF/FTC PrEP are provided in Appendix 1, Table A6.

Daily oral tenofovir alafenamide/emtricitabine

For HIV-negative cisgender men and transgender women in whom risk of HIV acquisition is related to sex with cisgender men:

- *Daily oral tenofovir alafenamide/emtricitabine (TAF/FTC) 25 mg/200 mg may be considered as a PrEP option (weak recommendation, high-certainty evidence).*

For HIV-negative cisgender men in whom risk of HIV acquisition is related to heterosexual activity:

- *Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option (weak recommendation, moderate-certainty evidence).*

For HIV-negative cisgender women in whom risk of HIV acquisition is related to heterosexual activity:

- *Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option (weak recommendation, low-certainty evidence).*

For HIV-negative people in whom risk of HIV acquisition is related to injection drug use:

- *Daily oral TAF/FTC 25 mg/200 mg may be considered as a PrEP option (weak recommendation, very low-certainty evidence).*

In the DISCOVER trial, daily oral TAF/FTC PrEP had noninferior efficacy at preventing HIV acquisition compared with daily oral TDF/FTC among GBM and transgender women who have sex with men (incidence rate ratio [IRR] 0.47, 95% CI 0.19 to 1.15).[27,28] Tenofovir alafenamide/emtricitabine was associated with fewer adverse effects on bone mineral density and renal biomarkers, but greater weight gain (+1.7 kg v. +0.5 kg at 96 wk, $p < 0.0001$) compared with TDF/FTC, possibly linked to the weight-suppressive effect of TDF. Tenofovir alafenamide/emtricitabine may thus be preferred in people with kidney problems or osteoporosis. However, lack of a generic version means it is more costly, and not currently publicly reimbursed in most jurisdictions.

Efficacy data on daily oral TAF/FTC in heterosexual cisgender women from the PURPOSE-1 trial were disappointing (IRR 0.84, 95% CI 0.55 to 1.28 compared with background HIV incidence).[29] However, because these findings were driven by low adherence (odds of HIV were much lower in women with medium and high versus low adherence; OR 0.11, 95% CI 0.01 to 0.49), because daily oral TDF/FTC is highly effective in this population, and because the pharmacokinetics of TAF in the female genital tract are favourable for protection,[30] TAF/FTC can be considered as PrEP in this group after risks and benefits have been discussed. Similarly, despite the lack of trial data, TAF/FTC may be considered in PWID after risks and benefits have been discussed, based on clinical trial evidence showing efficacy of daily oral TDF alone in this setting[31] and favourable pharmacokinetic and pharmacodynamic modelling.[32] On-demand TAF/FTC as PrEP is not currently recommended for any other populations because of the lack of published data.

Long-acting injectable cabotegravir

For HIV-negative cisgender men and transgender women in whom risk of HIV acquisition is related to sex with cisgender men:

- *We recommend long-acting injectable cabotegravir (CAB-LA) 600 mg as a PrEP option (strong recommendation, high-certainty evidence).*

For HIV-negative cisgender men in whom risk of HIV acquisition is related to heterosexual activity:

- *Long-acting CAB 600 mg may be considered as a PrEP option (weak recommendation, moderate-certainty evidence).*

For HIV-negative cisgender women in whom risk of HIV acquisition is related to heterosexual activity:

- *We recommend CAB-LA 600 mg as a PrEP option (strong recommendation, high-certainty evidence).*

For HIV-negative people in whom risk of HIV acquisition is related to injection drug use:

- *Long-acting CAB 600 mg may be considered as a PrEP option (weak recommendation, very low-certainty evidence).*

Long-acting CAB is an injectable integrase strand transfer inhibitor (INSTI) approved by Health Canada in 2024 as PrEP. Administration involves a 600 mg injection in the ventrogluteal muscle, followed by a second 600 mg dose injected 1 month later, then a

600 mg dose injected every 2 months. An optional 28-day lead-in of daily oral CAB 30 mg can be used to ensure tolerability but is not required, because clinical trials have not shown advantages of this strategy (Appendix 1, Section 5.2.4.1).

Long-acting CAB had superior HIV prevention efficacy over daily oral TDF/FTC among GBM and transgender women in the HIV Prevention Trials Network (HPTN) 083 trial (hazard ratio [HR] 0.34, 95% CI 0.18 to 0.62),[33] and among cisgender women in Africa in HPTN 084 (HR 0.12, 95% CI 0.05 to 0.31).[34] These results are largely explained by the ability of CAB-LA to overcome the suboptimal adherence observed in the TDF/FTC arm. Long-acting CAB has a favourable adverse event profile compared with TDF/FTC. Injection-site reactions are the most common adverse effect, but are mostly mild, decline substantially over time, and rarely lead to product discontinuation (0% to 2.4% in HPTN 083 and 084).

Because it also has high acceptability and could be useful for marginalized populations in whom adherence to pills is challenging, CAB-LA PrEP is another strongly recommended PrEP option for preventing sexually acquired HIV. Although clinical data are lacking, CAB-LA can be considered for use in preventing HIV related to injection drug use if careful monitoring and follow-up can be assured (based on extrapolation from the HPTN 083 and 084 trials),[33,34] because there is no definitive reason to believe it would not be efficacious in this setting. People who inject drugs may also be at risk for sexually acquired HIV and may be appropriate candidates for CAB-LA on that basis.

Medication costs and logistical considerations related to injection administration (e.g., training personnel, scheduling injections) must be considered before use. All users should be counselled about the small risk of clinical failure despite on-time injections and the need to use another HIV prevention modality (e.g., oral PrEP) for 1 year after discontinuation, starting 2 months after the last injection, if at continued HIV risk, because subtherapeutic drug levels may persist for a year or more, potentially resulting in drug resistance if the person acquires HIV during that time (Appendix 1, Section 5.2.4.2).

Documentation of HIV seronegativity

Documentation of HIV seronegativity using the most sensitive locally available assay is essential shortly before PrEP initiation and should be repeated every 3 months for people on oral PrEP, and with every injection (every 2 months) for those on CAB-LA. In Canada, the most sensitive locally available assays are usually a fourth-generation HIV antigen–antibody test, although in some remote regions, a point-of-care third-generation assay could be used while waiting for results of laboratory-based testing. A detailed discussion of HIV testing modalities appears in Appendix 1, Section 3.3.

We suggest not routinely using HIV RNA testing to screen for incident HIV infection among people using CAB-LA PrEP (weak recommendation, moderate-certainty evidence).

Although PrEP is extremely effective, breakthrough infections do occur, albeit rarely. In addition, any form of PrEP can delay the timing and detection of HIV seroconversion when standard HIV serology is used. This phenomenon is more pronounced with CAB-LA, and can lead to clinically relevant resistance mutations, prompting the United States Centers for Disease Control and Prevention guideline to propose that regular HIV testing on PrEP be done using HIV RNA testing.[35] However, emerging data suggest that routine HIV RNA testing has low positive predictive value, with false-positive results sometimes prompting delays in PrEP administration.[36,37] The panel thus thought that the potential benefits of HIV RNA screening in the context of CAB-LA PrEP do not outweigh the potential disadvantages, and that cost, acceptability, and feasibility do not support routine use.

Clinical considerations

The panel's suggested clinical evaluations and practical advice for providing PrEP are summarized in Table 2[38–40] and Box 2.[38,41–43] Appendix 1 contains additional detail regarding use of PrEP in specific contexts (i.e., transitioning to PrEP from PEP; chronic hepatitis B; renal, bone, and metabolic disease; pregnancy and breastfeeding or chestfeeding; and gender-affirming hormone use).

As part of a comprehensive STBBI prevention package, vaccination for hepatitis A, hepatitis B, human papillomavirus, and mpox should be offered in accordance with national guidelines.[38,42,43] Regular screening for bacterial STIs is indicated at follow-up according to the types of sexual activity reported, although the ideal frequency of screening for gonorrhea and chlamydia in GBM is debated.[44] Regular screening for hepatitis C, renal function, and pregnancy (as appropriate) are also advised.

Postexposure prophylaxis

Indications

Postexposure prophylaxis is clinically appropriate if the source person has a substantial risk of having transmissible HIV infection, and the exposure type was of higher or moderate risk (good practice statement).

The exposed person should undergo baseline HIV testing (fourth-generation antigen–antibody assay or point-of-care third-generation assay, or both) when starting PEP, but PEP initiation should not be delayed while awaiting the result (good practice statement).

Postexposure prophylaxis should not be initiated when the source person is confirmed to be HIV negative, when the source person is of unknown HIV status but from the general population, or in the setting of sexual exposures to people living with HIV with an undetectable viral load (good practice statement).

Decisions regarding PEP in other contexts warrant case-by-case evaluation and shared decision-making between the clinician and patient. Consultation with a specialist experienced in this area may be helpful but should not delay initiation of PEP if potentially indicated (good practice statement).

Table 2: Suggested clinical evaluation of people initiating and continuing pre-exposure prophylaxis

Evaluation	Baseline	30 days	Every 2–3 months	Every 3–4 months	Every 12 months
Laboratory evaluation					
HIV testing*	X	X	X†		
Hepatitis A immunity (hepatitis A IgG)†	X				
Hepatitis B screen (surface antigen, surface antibody, core antibody)†‡	X				X
Hepatitis C screen (HCV antibody or HCV RNA)§	X				X
Screening for gonorrhea and chlamydia¶ (urine nucleic acid amplification test, throat and rectal swabs for culture or nucleic acid amplification; test anatomic sites depending on type of sexual activity reported)	X			X	
Syphilis serology¶	X			X	
Creatinine	X			X**	
Pregnancy test (as appropriate)	X			X	
Clinical evaluation					
Symptoms of HIV seroconversion	X	X	X		
PrEP adherence		X		X	
Indication for PrEP	X	X		X	
Use of other HIV and STI prevention strategies (e.g., vaccines, condoms)	X	X		X	
Screening for coexisting mental health conditions and refer if needed	X	X		X	

Note: CAB-LA = long-acting injectable cabotegravir, FTC = emtricitabine, HCV = hepatitis C virus, IgG = immunoglobulin G, PrEP = pre-exposure prophylaxis, STI = sexually transmitted infection, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate.
*Preferred HIV test is a fourth-generation antibody–antigen combo assay, but rapid third-generation point-of-care assays may be used while waiting for results of laboratory-based testing. People with signs or symptoms of acute HIV should also undergo HIV RNA or pooled nucleic acid amplification test. Testing should be done every 2 months in people using CAB-LA, and every 3 months in those on oral PrEP.
†Hepatitis A and B testing is suggested in people of unknown status because vaccine should be initiated in unvaccinated individuals at increased risk[38] (Appendix 1, Section 6.1.9, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content). Those who remain nonimmune to hepatitis B virus should be considered for annual rescreening.
‡Hepatitis B testing is suggested in people of unknown status because individuals with chronic active hepatitis B should be managed in consultation with an expert on hepatitis B virus, according to a Canadian guideline.[39]
§People with no history of HCV infection should undergo HCV antibody testing; those with previous resolved (cured) infection should be screened with HCV RNA testing.
¶People with diagnosed STIs should be offered standard therapy and follow-up as per local guidelines.[40] See further comments on gonorrhea and chlamydia screening frequency in Appendix 1, Section 6.1.9.
**Creatinine monitoring recommendations depend on PrEP regimen and renal function. For TDF/FTC-based PrEP, people at low risk of renal dysfunction should be tested every 6 months (definitions in Appendix 1, Section 6.1.5) and every 3 months otherwise; for TAF/FTC, testing should be done every 6–12 months.

Risk of HIV acquisition depends on the likelihood the source has transmissible HIV infection, and the biological risk of HIV transmission based on exposure type. Clinicians should combine these considerations, using the framework in Table 3, to decide whether PEP is needed. Baseline HIV testing of the exposed person is important to confirm HIV seronegativity, and because individuals seeking PEP often belong to populations with high rates of pre-existing undiagnosed HIV.[45]

Assessment of whether the source has transmissible HIV must draw on local and national epidemiology (Appendix 1, Table A3) if individual-level details are unknown. Exposures to people living with HIV with undetectable viral load (serum HIV RNA < 200 copies/mL) confer no risk of sexually transmissible HIV (the "undetectable equals untransmittable" [U = U] principle).[46–49] If the source person is known, laboratory testing or review of medical records may be helpful but should be undertaken only with that person's consent.

The biological risk of transmission varies by exposure type. The panel agrees with international scientific consensus that the per-act risk of HIV transmission through sexual contact with a person who has transmissible HIV is low, in absolute terms, at less than 2%.[50] The absolute risk through blood-borne exposures is also low (with the exception of a blood transfusion containing HIV, which would not be expected in Canada). However, when determining whether an exposed person should use PEP, it is helpful to differentiate between categories of risk for different exposure types, which the panel has labelled as "higher," "moderate," or "low" in Appendix 1, Table A7. These terms are intended for clinical decision-making only, and the panel condemns efforts to apply this framework to the unjust criminalization of people living with HIV.

Box 2: Practical advice for providing pre-exposure prophylaxis

Sexual history-taking

- A detailed sexual history should be collected in a nonjudgmental, sex-positive way, covering partners, practices, and protection strategies

HIV testing at baseline and follow-up

- A fourth-generation HIV antigen–antibody combination test is generally preferred
- Point-of-care tests may also be considered as they provide immediate results, but only when serology can also be performed for confirmation
- Clinical assessment for signs and symptoms of acute HIV infection should be performed at each visit
- HIV RNA testing may be considered in people who are not yet taking PrEP, owing to its enhanced sensitivity
- Testing is indicated every 3 months on oral PrEP and with each injection (every 2 months) on CAB-LA

Managing suspected HIV seroconversion in PrEP users

- PrEP failure can occur rarely, owing to poor adherence, circulating drug resistance, and other factors
- Suspected seroconversion should be managed urgently in consultation with an HIV specialist

Renal monitoring

- Daily TDF/FTC is not advised when eGFR is < 60 mL/min; TAF/FTC is not advised when eGFR is < 15–30 mL/min
- People on TDF/FTC PrEP at low renal risk (i.e., eGFR > 90 mL/min; age < 50 years; no diabetes, hypertension, or renal disease) should undergo serum creatinine monitoring every 6 months
- People on TDF/FTC with renal risk factors should undergo creatinine monitoring every 3 months
- People on TAF/FTC may undergo serum creatinine monitoring every 6–12 months

Bone health

- Bone densitometry is not routinely advised unless indicated as per Osteoporosis Canada guideline[41]
- TDF/FTC PrEP may be considered in people with low bone mass or osteoporosis after risks and benefits have been discussed; non–TDF-based regimens should be prioritized in this setting when possible
- People on TDF/FTC should be counselled on calcium and vitamin D intake and weight-bearing exercise

Metabolic health

- PrEP users should be counselled about the possibility of weight gain, particularly on TAF/FTC and CAB-LA
- People on TAF-based regimens should be considered for annual lipid monitoring

Injection-site reactions

- Most CAB-LA recipients experience mild or moderate ISRs, including pain and tenderness lasting a median of 3 days; management involves reassurance and supportive care. Injection-site reaction decrease over time

Sexually transmitted infections and viral hepatitis

- Laboratory screening for syphilis, gonorrhea, and chlamydia is suggested at baseline and every 3–4 months, from all exposed body sites, with appropriate therapy for any identified infections
- Hepatitis A, B, and C serologies should be performed at baseline, with vaccination for hepatitis A and B for nonimmune individuals and annual repeat screening for hepatitis B and C for those who remain susceptible[38]
- Vaccination for human papillomavirus and mpox should be provided as per national guidelines[42,43]

Frequency of follow-up

- We suggest initial follow-up at 1 month to repeat HIV testing, assess tolerability, and reinforce counselling messages, with clinical follow-up every 3–4 months thereafter

Reproductive health considerations

- Routine testing for pregnancy is warranted as applicable

Counselling

- PrEP clinical encounters should include assessments and counselling regarding other STBBI prevention strategies, syndemic mental health conditions, harm reduction strategies, potential drug toxicities, and adherence

PrEP use in specific populations

People with chronic HBV

- People with chronic active hepatitis B should be offered TDF- or TAF-containing PrEP if therapy for HBV is also required
- Regular HBV DNA monitoring (every 3–6 mo) while on PrEP is suggested
- People discontinuing PrEP who did not initially meet HBV treatment indications should undergo ongoing monitoring of HBV DNA and ALT to determine when HBV therapy is indicated

People with previous PEP use

- People receiving PEP for sexual and needle-sharing exposures should be offered routine transition to PrEP
- HIV serologic testing can be undertaken before PEP completion with immediate transition to PrEP after completion of the PEP course. Subsequent HIV serologic testing at 4 weeks and then every 2–3 months (depending on PrEP regimen) is suggested

People using gender-affirming hormones

- Standard PrEP regimens may be used without concern for impact on feminizing hormones
- People using feminizing hormones should be counselled about potential impact on on-demand PrEP levels (i.e., lowering them)
- People using masculinizing hormones should be offered standard PrEP regimens, although data on drug interactions are limited, particularly for CAB-LA

People who are pregnant or breast- or chestfeeding

- Standard TDF PrEP can be offered.
- Use of TAF or CAB-LA PrEP should be undertaken only after counselling and through shared decision-making, given the very limited data for use in this setting

Adolescents

- Adherence support interventions may be of particular value among adolescents.
- Non-TDF/FTC PrEP regimens may be preferred, to minimize adverse impacts of TDF on bone mineral density during this period of peak bone development

Note: ALT = alanine aminotransferase, CAB-LA = long-acting injectable cabotegravir, eGFR = estimated glomerular filtration rate, FTC = emtricitabine, HBV = hepatitis B virus, ISR = injection-site reaction, PEP = postexposure prophylaxis, PrEP = pre-exposure prophylaxis, STBBI = sexually transmitted and blood-borne infection, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate.

Table 3: Summary of indications for HIV postexposure prophylaxis*

Status of source person	Exposure type				
	Percutaneous†	Blood or body fluid on compromised skin or mucosa, bites	Insertive or receptive anal or vaginal sex‡	Performing oral sex‡	Receiving oral sex‡
HIV-positive and viral load > 200 copies/mL *or* HIV status unknown but from high-prevalence population (see Appendix 1, Table A3)	Initiate PEP	Case-by-case decision (see full guideline in Appendix 1)	Initiate PEP	Case-by-case decision (see full guideline in Appendix 1)	Do not initiate PEP
HIV-positive with viral load < 200 copies/mL	Case-by-case decision (see full guideline in Appendix 1)	Case-by-case decision (see full guideline in Appendix 1)	Do not initiate PEP	Do not initiate PEP	Do not initiate PEP
HIV status unknown and from general population	Do not initiate PEP	Do not initiate PEP§	Do not initiate PEP§	Do not initiate PEP§	Do not initiate PEP§
Confirmed HIV negative	Do not initiate PEP	Do not initiate PEP	Do not initiate PEP	Do not initiate PEP	Do not initiate PEP

Note: PEP = postexposure prophylaxis.
*Appendix 1 is available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content.
†Percutaneous exposures refer to injuries where there is meaningful exposure to blood; trivial or superficial exposures and exposures to other body fluids are not included here.
‡"Sex" refers to sexual exposures where barrier precautions (e.g., condoms) fail or are not used.
§When assessing a survivor of sexual assault, it is reasonable to offer PEP except in cases where the perpetrator is unlikely to have transmissible HIV.

Regimens

Duration and timing

Postexposure prophylaxis should be initiated as soon as possible after an exposure, up to a maximum of 72 hours afterward (good practice statement).

Postexposure prophylaxis should be given for a total of 28 days (good practice statement).

Although there are no data on adult humans regarding the maximum time threshold after which PEP no longer offers protective benefit, animal models show a gradient of prevention benefit, with no transmission events among animals treated within 24 hours of exposure, only partial protection among those treated at 72 hours, and no benefit if initiation was delayed beyond 72 hours.[51–53] Animal models have further demonstrated a decreased risk of seroconversion when PEP was administered for 28 compared with 10 days or 3 days.[54] These findings form the basis for the global standard of care that PEP be initiated as soon as possible within 72 hours after exposure and last for 28 days, and are supported by pharmacokinetic modelling data.[55]

Strongly recommended regimens

We recommend the following regimens for use as PEP:

- *Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg once daily (strong recommendation, low-certainty evidence).*
- *Dolutegravir 50 mg once daily plus tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg once daily (strong recommendation, low–certainty evidence).*

While noting that all PEP use is off label in Canada, the panel recommends dolutegravir or bictegravir (both INSTI agents), in combination with tenofovir-based backbones, as PEP. Dolutegravir with TDF/FTC (or with TDF/lamivudine, a coformulation not available in Canada) PEP has been evaluated among more than 1000 people across 5 observational studies.[56–60] Bictegravir/TAF/FTC PEP has been evaluated in 259 people across 4 observational studies.[56,57,61,62] Whereas the completeness of outcome reporting varied across studies, for both regimens, no HIV seroconversions were reported; adherence to all 28 days of PEP was high (86.2% to 90% in the dolutegravir studies and 90.4% to 99% in the bictegravir studies); discontinuation owing to tolerability concerns was rare at about 1%; and moderate and severe adverse events appeared to be rare. Compared with alternatives, both regimens cause few drug–drug interactions and have a high genetic barrier to resistance, suppressing HIV even in the presence of common resistance mutations such as M184V/I (which compromises FTC and may arise in people in whom PrEP was ineffective). Both regimens can be used in pregnancy (Appendix 1, Section 8.2.7).[63]

Choosing between dolutegravir- and bictegravir-based regimens can be based on preferences and pragmatic considerations related to drug availability, cost, pill burden, and pharmacologic considerations (Appendix 1, Table A9). Although drug interactions with these regimens are few, slight differences may dictate which to prescribe. Administration of INSTI-based PEP should be separated from oral medications containing polyvalent cations (e.g., cation-containing antacids, iron, calcium) to avoid chelation and reduced absorption of the INSTI.

Other regimens

Many other PEP regimens may be considered, providing flexibility (e.g., allowing regimen switches as needed) when

clinicians are limited by drug availability, costs, drug interactions, idiosyncratic drug intolerances, or other factors (Table 1). Appendix 1 contains details on these regimens (Section 7.6.3), regimens that are not recommended (Section 7.6.4), and antiretroviral agents that are not recommended as part of a PEP regimen (e.g., abacavir, nevirapine, efavirenz; Section 7.6.5).

Delivery strategies

We suggest starter kits be available for HIV-negative individuals in whom PEP is being initiated (weak recommendation, very low-certainty evidence).

We suggest PEP-in-pocket be considered for HIV-negative individuals with infrequent moderate- to high-risk exposures (weak recommendation, low-certainty evidence).

A common practice when dispensing PEP medications is to initially provide a partial supply or "starter pack or kit," enabling prescribers to reassess the need for PEP when baseline laboratory results become available, modify therapy in cases of drug intolerance or resistance and, ultimately, limit drug costs and toxicities by preventing unnecessary use. The medication costs for starter kits must be borne by the delivering institution (e.g., emergency department). Providing access to a full 28-day supply at initial presentation is associated with fewer PEP refusals and superior PEP completion rates than with providing a starter kit,[64] so the former is appropriate when the indication for PEP is clearly established and medication access is not a concern. However, starter kits may improve PEP access by facilitating timely PEP initiation by nonexperts (e.g., emergency, primary care, prison and community pharmacy settings) and before insurance coverage is in place; hence, the panel advises that institutions make them available and consider coupling them with a prescription to avoid missed doses if follow-up is delayed.

A variation on PEP implementation is the proactive provision of a 28-day PEP prescription to be used in the event of a potential HIV exposure (e.g., condomless anal or vaginal sex with a partner of unknown HIV status, needlestick injury during work abroad); the individual can then self-initiate the medications if and when needed.[65] Variously known as PEP-in-pocket (PIP), PEP on-demand, or self-start PEP,[65–67] this modality is best suited to people who decline PrEP and have infrequent, unanticipated, high-risk HIV exposures. Such individuals should be thoroughly counselled on how to assess HIV risk (Table 3) and instructed to initiate PEP as soon as possible, but no later than 72 hours, after exposures. This strategy appears safe, effective, and acceptable to users in studies using a variety of drug regimens.[56,58,66,67] People considering PIP should be counselled on the range of available PrEP strategies, for which the volume and quality of data are considerably greater.

Clinical considerations

The panel's suggested clinical evaluations and practical advice for providing PEP are summarized in Table 4[38–40] and Box 3. Appendix 1 contains additional detail regarding specific populations (adolescents, people using gender-affirming hormones, those with chronic kidney disease, people with suspected acute HIV infection, PrEP users, people with hepatitis B, people who are pregnant or breast- or chestfeeding, and sexual assault survivors).

Methods

This guideline is an initiative of CIHR Pan-Canadian Network for HIV and STBBI CTN+. This project was supported by CIHR and in-kind support from the CTN+, along with unrestricted educational grants from Gilead Science and ViiV Healthcare for publication costs. We followed the GRADE system of recommendation development,[68] and our methodology and reporting adheres with Appraisal of Guidelines for Research and Evaluation II (AGREE II).[69]

Composition of participating groups

We assembled a panel of 18 experts on HIV PrEP or PEP from across Canada, seeking geographic, demographic, and disciplinary diversity (co-chairs D.H.S.T. and M.W.H.). The panel comprised expertise in infectious diseases (4 panellists), primary care (2), emergency medicine (1), internal medicine (1), adolescent medicine (1), pharmacy (3), nursing (1), public health (2), knowledge translation (1), and implementation science (1), along with a community representative (1). Indigenous, Black, and other racialized and sexual minority perspectives were meaningfully represented within both the lived experiences and professional expertise of panel members.

To solicit additional community input, we conducted online consultation meetings with 7 national or regional organizations representing key populations affected by the HIV epidemic in Canada, and 2 professional societies representing Canadian HIV pharmacists and nurses, in mid 2023 (Appendix 1, Table A1). We requested general input on the guideline scope and processes, along with community perspectives on important health outcomes relevant to PrEP and PEP.[70]

Selection of priority topics

Drawing on the feedback from our consultations, the panel jointly developed the guideline PICO (Population, Intervention, Comparator, Outcome) questions (Appendix 1, Box A1) and determined which health outcomes to prioritize through voting (Appendix 1, Section 2.1).

Literature review and quality assessment

To compile evidence, we conducted a systematic review of published clinical trials and cohort studies about HIV PrEP and another about HIV PEP. Key PrEP outcomes considered were HIV incidence, adherence, toxicity, and drug resistance; key PEP outcomes were HIV seroconversion, PEP regimen completion, moderate or severe adverse events, and discontinuations because of adverse events. A health science librarian assisted with these searches using MEDLINE, Embase, and CINAHL, from July 2017 (when the search that informed the previous iteration of our guideline ended) to June 2024. We conducted a

Table 4: Suggested baseline and follow-up evaluations for postexposure prophylaxis

Test	Baseline	Week 4–6	Week 12
HIV testing*	X	X††	X‡‡
Hepatitis A immunity (hepatitis A IgG)†	X		
Hepatitis B screen†,‡ (surface antigen, surface antibody, core antibody)	X		X§§
Hepatitis C screen (HCV antibody)§	X		X§
Screening for gonorrhea and chlamydia¶ (urine NAAT, throat and rectal swabs for culture or NAAT; anatomic sites should be tested depending on type of sexual activity reported)	X		X¶¶
Syphilis serology¶	X	X¶¶	X¶¶
ALT**	X		
Serum creatinine**	X		
Pregnancy testing (if appropriate)	X		

Note: ALT = alanine aminotransferase, HBC = hepatitis B virus, HCV = hepatitis C virus, IgG = immunoglobulin G, NAAT = nucleic acid amplification, PEP = postexposure prophylaxis, PrEP = pre-exposure prophylaxis, STI = sexually transmitted infection.
*Preferred HIV test is a fourth-generation antigen–antibody assay, but rapid third-generation point-of-care assays may be used while waiting for results of laboratory-based testing. Those with signs or symptoms of acute HIV should also undergo HIV RNA or pooled NAAT test.
†Hepatitis A and B testing is recommended in people of unknown status because vaccine should be initiated in unvaccinated individuals at increased risk[38] (see Appendix 1, Section 8.1.3, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content).
‡People with chronic active HBV should be referred for HBV care as per local guidelines.[39]
§People with no history of HCV infection should undergo HCV antibody testing, and the final time point for testing should be 6 months after exposure; consideration can be given to HCV RNA screening at 3–6 weeks after exposure as well. Those with previous resolved infection should be screened with HCV RNA testing and the final time point for testing can be 3–12 weeks after exposure.
¶People diagnosed with concurrent STI during PEP should be offered standard therapy and follow-up as per local guidelines.[40]
**ALT may be helpful but may not be essential in choosing a PEP regimen. After baseline evaluation of liver and renal function, ongoing monitoring is needed only if abnormalities are identified and in people who develop signs or symptoms of organ dysfunction or medication-related adverse effects.
††Immediate transition to PrEP should be considered for people at ongoing risk of HIV acquisition.
‡‡Repeating HIV serology at 6 months after exposure should be considered if HCV infection was acquired from the exposure.
§§Hepatitis B testing may be indicated if non-immune at baseline, as recommended by Canadian immunization guidelines.
¶¶Repeat STI testing should be considered at follow-up as clinically indicated; note that syphilis testing may be particularly important at 4–6 weeks as it requires 2–4 weeks for an antibody response to develop.
**ALT may be helpful but may not be essential in choosing a PEP regimen. After baseline evaluation of liver and renal function, ongoing monitoring is needed only if abnormalities are identified and in people who develop signs or symptoms of organ dysfunction or medication-related adverse effects.

third systematic review of the same databases from January 1980 to May 2024 to identify HIV risk assessment tools in adults and adolescents, in order to guide clinicians in identifying candidates for PrEP.[12]

Two research staff independently screened abstracts, screened publications, and extracted data, with disagreements resolved through consensus. Two panel members (D.H.S.T. and D.Y.) reviewed extracted data. We evaluated the quality of studies using the Cochrane Collaboration's Risk of Bias 2 (RoB 2) instrument for randomized controlled trials,[71,72] and the Newcastle–Ottawa Scale for observational studies.[73]

We also invited a guest speaker to present to the panel findings from a scoping review on values and preferences related to HIV PEP.[74]

Development of recommendations and good practice statements

We convened 13 online meetings between January and August 2024 (cumulative total of 26 hours) to review evidence and formulate recommendations using a formal evidence-to-decision-making framework that considered 10 domains, including desirable and undesirable effects, certainty of evidence, resource use, feasibility, acceptability, and equity (Appendix 1, Figure A1) for each PICO question. We aimed to achieve consensus, but used voting in rare instances when necessary, with a two-thirds majority required to finalize decisions. Based on these judgments, the panel then formulated a strong or weak (or conditional) recommendation, either for or against the specific intervention (Box 1); details of the evidence-to-decision-making process are outlined in Appendix 4 (available at www.cmaj.ca/lookup/doi/10.1503/cmaj.250511/tab-related-content). Good practice statements were originally drafted by the co-chairs, based on their existing knowledge of the literature, and then discussed and finalized during panel meetings. Panellists were also divided into 16 writing groups of 2 to 4 members to compose guideline text; the co-chairs further refined the text.

External review

To solicit feedback from the HIV community in Canada, we partnered with the Canadian AIDS Treatment Information Exchange (CATIE) to conduct an English- and a French-language webinar for the Canadian HIV community in September 2024. We shared a draft of the full guideline online via the CATIE website and via email dissemination to our professional networks, with an accompanying feedback survey from December 2024 to January 2025. We further solicited feedback from endorsing professional organizations, including

Box 3: Practical advice for providing postexposure prophylaxis

Screening for sexual assault

- Providers undertaking initial assessment for PEP should distinguish between consensual and nonconsensual exposures and refer to sexual assault services accordingly

Baseline HIV testing

- When considering or initiating PEP, baseline HIV status should be determined using a fourth-generation antigen–antibody combination test
- Where available, an HIV point-of-care test can also be included, but should not replace the standard serology test

Additional laboratory testing

- Evaluation should include evaluation for relevant STBBIs (syphilis, gonorrhea, chlamydia, and hepatitis A, B, and C for those with sexual exposures; hepatitis B and C for those with parenteral exposures), with appropriate subsequent management
- Baseline renal and hepatic testing, as well as a complete blood count and differential, may help to identify signs of acute HIV infection, viral hepatitis, or renal dysfunction that might affect regimen choice
- Ongoing laboratory monitoring of complete blood count and biochemistry during PEP is advised only for people with baseline laboratory abnormalities, or in those who develop signs or symptoms of organ dysfunction or medication-related adverse effects during therapy

Counselling

- Baseline counselling should address how to take PEP, missed-dose management, potential drug toxicities, medication adherence, and strategies to reduce forward transmission (e.g., barrier precautions for sexual activity with regular partners, avoiding blood and body fluid donation)
- Follow-up counselling should address other STBBI prevention strategies, syndemic mental health conditions, and harm reduction strategies

Adherence support

- Interventions to support PEP adherence may include patient counselling, education, medication reminders, behavioural feedback and reinforcement, peer support, follow-up telephone calls or text messages, and minimization of out-of-pocket expenses

Follow-up HIV testing

- Follow-up HIV testing should be performed using a fourth-generation assay at 4–6 weeks after exposure (shortly after completion of PEP), in conjunction with testing for other STBBIs and a potential transition onto PrEP (Appendix 1, Section 8.1.6)
- Final testing should be done 12 weeks after exposure (8 wk after completion of PEP)
- People who are exposed but do not take PEP should also undergo follow-up testing, 8 weeks after exposure

Stopping PEP early

- PEP can be stopped early if the source tests HIV negative using a fourth-generation assay
- PEP can be stopped early if the source is living with HIV and found to have an undetectable viral load (< 200 copies/mL) in the setting of sexual exposures; for nonsexual exposures, discontinuation can be considered based on shared decision-making
- If ≥ 72 consecutive hours of PEP have been missed, discontinuation of PEP can be considered

Transitioning from PEP to PrEP

- After completion of PEP, transition onto PrEP should be suggested to PEP users at ongoing risk for HIV
- Repeat HIV testing at 4–6 weeks after exposure can facilitate timely transition

PEP use in specific populations

People with chronic HBV

- People with chronic active hepatitis B should be monitored with liver enzymes at baseline and then at PEP completion (4–6 wk) after exposure to ensure there is no hepatitis flare with discontinuation of TDF- or TAF-containing PEP
- People discontinuing PEP who did not initially meet HBV treatment indications should undergo ongoing monitoring of HBV DNA and ALT to determine when HBV therapy is indicated, with an appropriate care provider, particularly if they are not transitioned to TDF- or TAF-based PrEP

People with chronic kidney disease

- People with CKD can receive TDF- (eGFR > 60 mL/min), or TAF-based PEP (eGFR > 15 mL/min). For people with eGFR < 15 mL/min who are not on dialysis, regimen selection should be based on expert advice

People using gender-affirming hormones

- Standard PEP regimens may be used without concern for impact on feminizing hormones

People who are pregnant or breast- or chestfeeding

- Standard TDF/FTC and TAF/FTC-based PEP regimens can be offered

People who are on PrEP

- People who experience an exposure meeting criteria for PEP during a period of PrEP interruption (no use of daily PrEP for at least 3 consecutive days, or no use of on-demand PrEP for exposure in question) should be offered 1 of the standard recommended PEP regimens

Note: ALT = alanine aminotransferase, CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, HBV = hepatitis B virus, PEP = postexposure prophylaxis, PrEP = pre-exposure prophylaxis, STBBI = sexually transmitted and blood-borne infection, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate.

the Canadian Association of Emergency Physicians, the Canadian Association of Nurses in HIV/AIDS Care, the Canadian HIV and Viral Hepatitis Pharmacists Network, and the Canadian Public Health Association. Feedback was considered by the panel, and multiple suggestions (primarily related to inclusion of additional explanatory information and use of inclusive language) were incorporated into the draft guideline, based on panel consensus. All panel members critically reviewed and approved the final document.

Management of competing interests

To manage potential competing interests, we followed the Guidelines International Network principles,[75] including using standardized forms to document conflicts of interest from all panel members at the beginning (January 2024), midpoint (July 2024), and end (March 2025) of the guideline development process. Panel members with direct financial competing interests did not participate in final discussions about the direction and strength of recommendations. The co-chairs

(D.H.S.T. and M.W.H.) and project coordinator (S.O.O.) jointly oversaw this process.

Funders had no influence on the guideline process or development of recommendations. In particular, funding for publication costs was sought after the draft recommendations were developed.

Implementation

Medication costs have been a barrier to PrEP and PEP implementation, as public funding varies widely by jurisdiction. Limited data exist for the cost-effectiveness of PEP, but multiple studies from industrialized-world settings show that PrEP is cost effective when used in populations with high HIV incidence, although definitions of "high risk," model assumptions, and time horizons vary among studies.[76] In some studies, cost-effectiveness was dependent on generic drug pricing, good adherence, or the absence of risk compensation.[76] Until there is universal access for all in Canada, with no out-of-pocket costs, information about PrEP and PEP medication coverage will be compiled and updated periodically by the Canadian HIV and Viral Hepatitis Pharmacists Network at https://hivclinic.ca/drug-information/drug-reimbursement-information/.

Both PrEP and PEP should be part of a combination prevention strategy that includes behavioural interventions (e.g., condoms, sterile injecting equipment, risk reduction counselling), biomedical interventions (e.g., treatment of people living with HIV; testing, treatment and prevention of STIs) and attention to syndemic conditions that contribute to HIV risk (e.g., depression, substance use, housing instability) as appropriate. Because lack of PrEP and PEP awareness among key populations and clinicians is a common barrier to implementation, public health officials, professional societies, and other trusted authorities should play leadership roles in promoting these strategies in collaboration with community organizations and tracking uptake in conjunction with HIV surveillance data.

Health systems should strive to engage a broad number and range of clinical providers in PrEP and PEP delivery, including family physicians and other specialists, nurses, nurse practitioners, and pharmacists, where provincial scope of practice allows, or under appropriate delegation of responsibility. Nonprescribing health care and service providers should be encouraged to have a role in PrEP and PEP delivery, including clinical monitoring, screening and management of STIs, counselling on risk reduction, and adherence support.

Updates to this guideline are planned when a new PrEP or PEP product obtains Health Canada regulatory approval, and will be posted together with implementation and auditing tools (as they are developed) at www.ctnplus.ca/guidelines.

Other guidelines

An important difference from the previous 2017 Canadian guideline[4] is our explicit inclusion of self-identified HIV risk as an indication for PrEP initiation. Our recommendations on PrEP regimens emphasize the diversity of PrEP choices now available, incorporating newer regimens and expanding recommendations on some regimens beyond what has been demonstrated in clinical trials, based on panel deliberations. We have also abandoned previous distinctions between occupational and nonoccupational PEP (for which the core principles of intervention are similar), because the previous distinction overlooked sex work as a form of occupational sexual exposure and invited stigma for sexual- and drug-related exposures occurring in the context of voluntary practices.

Our recommendations are broadly consistent with current guidelines from other industrialized-world settings, including the United States,[13,77] United Kingdom,[78,79] Europe,[80] and Australia,[81,82] regarding both PrEP and PEP. Notably, the Australian guideline uniquely recommends only 2-drug PEP for lower-risk exposures;[82] we adopted the majority global position that 3-drug PEP regimens simplify prescribing, maximize efficacy, and increase the likelihood that rare individuals with undiagnosed baseline HIV infection receive a fully active regimen. Other modest differences among guidelines are discussed in Appendix 1, Section 10.

Gaps in knowledge

Our PrEP recommendations were constrained by the lack of clinical data for on-demand PrEP and TAF/FTC in populations other than GBM and transgender women, and on CAB-LA for PWID. Safety and efficacy data on PrEP for transgender men and other gender-diverse individuals are also relatively lacking. There are also few data describing use of approved regimens in Indigenous people, racialized groups, and PWID. Data gaps also include the optimal HIV screening strategy during PrEP (particularly for CAB-LA), management of the CAB-LA PrEP pharmacokinetic tail, optimal timing of PEP initiation, potential for shorter durations of PEP, and strategies for transitioning PEP users to PrEP. Implementation research is needed on raising population awareness in a stigma-free fashion, and engaging more health care providers to maximize access, acceptability, feasibility, and efficiency.

Limitations

Although diverse in many ways, our panel did not have representatives from all regions of Canada. We also lacked representation from such specialties as obstetrics and gynecology, and mental health and addictions medicine. We plan to integrate expertise from such disciplines into future guideline updates. We focused on adults and adolescents, to the exclusion of pediatrics, for whom some clinical issues may differ. The timing of our work meant that recent developments related to lenacapavir PrEP are not directly addressed, although future updates will include this literature.

Conclusion

A range of safe and effective PrEP and PEP options are now available in Canada. People at risk of HIV acquisition, as well as diverse clinical, social service, and community-based providers, should be supported in advancing the broader uptake of these tools, which are integral to Canada's efforts to eliminate HIV as a public health threat.

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