Canadian guideline on HIV preexposure prophylaxis and nonoccupational postexposure prophylaxis for pharmacists

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Introduction

Despite advances in human immunodeficiency virus (HIV) treatment and prevention approaches over the past decade, a significant number of new HIV infections occur each year. At the end of 2016, estimates suggest that 63,000 people were living with HIV in Canada, of whom 14% were unaware of their HIV infection.¹ Approximately 2200 people were newly diagnosed in 2016, and more than half (52%) of new HIV infections occurred in gay, bisexual and other men who have sex with men (MSM). Other populations in Canada where there is a higher rate of new HIV diagnoses include Indigenous people, people from HIV-endemic countries and people who inject drugs.¹

HIV is transmitted through sexual or blood-borne exposure to the virus, as well as from mother to child during pregnancy, childbirth or breastfeeding. The risk of acquiring HIV is dependent on the type of exposure as well as the likelihood the source has transmissible HIV (Table 1).² Prevention of new infections is critical to controlling the HIV epidemic. Two notable pharmacologic HIV prevention strategies are preexposure prophylaxis (PrEP), the regular use of specific antiretroviral drugs by HIV-uninfected persons at high and ongoing risk of HIV acquisition, and postexposure prophylaxis (PEP), the use of antiretroviral agents beginning immediately after an HIV exposure and continuing for 28 days. The term *nonoccupational* PEP (nPEP) refers to PEP used after sexual or

injection drug use exposures, while PEP prescribed after a potential HIV exposure in the work environment (e.g., needlestick injury) is termed *occupational* PEP (oPEP).

Whereas PEP has been used to manage HIV exposures for almost 2 decades, the use of PrEP in Canada has been gaining momentum since 2016, following Health Canada's approval of tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) for this indication. To provide frontline health care practitioners with evidence-based guidance using these important HIV prevention strategies, Canadian guidelines were recently developed by the Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network (CTN) and are available at www.hivnet.ubc.ca/publications/canadian-guideline-hiv-pre-exposure-prophylaxis-nonoccupational-postexposure-prophylaxis.² In this article, we provide an overview of these guidelines and highlight the role pharmacists can have in HIV prevention (Box 1).

Preexposure prophylaxis (PrEP)

Who should receive PrEP?

Clinical trials have demonstrated that the use of PrEP significantly reduced the risk of acquiring HIV in MSM and men and women in heterosexual serodiscordant relationships (i.e., one partner is infected with HIV and the other is not). In these studies, the efficacy of PrEP was dependent on medication adherence. Increases

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DOI:10.1177/1715163519826171

TABLE 1 Likelihood source has transmissible HIV²

Risk	Examples
Substantial	HIV positive and viremic (i.e., viral load >40 copies/mL) HIV status unknown but from a population with high HIV prevalence compared to the general population (e.g., MSM, people who inject drugs)
Low but non-negligible	HIV positive and believed to have a viral load <40 copies/mL and presence of sexually transmitted infection at time of exposure
Negligible / none	Confirmed HIV negative HIV positive and confirmed viral load <40 copies/mL and no known concurrent sexually transmitted infection at time of exposure HIV status unknown, general population

HIV, human immunodeficiency virus; MSM, men who have sex with men.

BOX 1 Summary of pharmacists' role in PrEP and nPEP

- Refer or direct at-risk individuals to providers
 - Urgent care (e.g., emergency department) after potential HIV exposure for assessment, including indication for PEP
 - PrEP providers if screened to be at high risk for HIV acquisition
- Maintain stock of PEP drugs to minimize delays (or know where to refer individuals)
- Assess and manage drug-drug interactions (especially for PEP)
- Provide drug counselling about PrEP/PEP use and counsel on risk reduction
- Educate and reinforce need for medical attention if the person has any signs of acute HIV infection (e.g., fever, fatigue, myalgia, rash, cervical lymphadenopathy, night sweats)
- Support medication adherence through medication counselling, adverse effect management and assistance with dose scheduling times
- Assist with medication procurement and coverage

in PrEP adherence were associated with much lower risk of acquiring HIV—approaching 100% reduction in some observational studies in MSM.³⁻⁵ Tenofovir-based PrEP has also been shown to be effective in reducing the risk of HIV infection in people who inject drugs, although data are more limited.² While PrEP should be considered in any person at continual high risk of HIV infection, specific recommendations for individuals where PrEP is recommended are outlined in Table 2.²

What drugs are used?

Coformulated TDF/FTC is currently the only Health Canada-approved regimen for PrEP. The approved dosing is 1 tablet (TDF 300 mg/FTC 200 mg) once daily, beginning before and continued after potential HIV exposures. Pharmacokinetic studies suggest that it can take several days for drug concentrations in genital tissues to

be at levels consistent with protection (4-7 days for rectal tissue among MSM and up to 7 days for cervicovaginal exposures)^{6,7}; thus, patients should be counselled to start daily therapy in advance of potential exposures. Alternatively, some clinicians may suggest an off-label “on-demand” schedule (2 pills of TDF/FTC taken together 2 to 24 hours before first sexual exposure, followed by 1 pill daily until 48 hours after the last sexual activity), which has been shown in 1 randomized controlled trial to reduce HIV risk in MSM having frequent sexual activity.^{2,8}

TDF and FTC are favourable agents to use for PrEP based on their long intracellular half-lives, concentrations in genital secretions and overall excellent tolerability profile.⁹ It is important to note that TDF and FTC are nucleoside reverse transcriptase inhibitors (NRTIs) that are also used in the treatment of established HIV infection, although when used as treatment, they

TABLE 2 Recommendations for preexposure prophylaxis (PrEP)²**Men who have sex with men (MSM)**

- PrEP is recommended for MSM and transgender women who report condomless anal sex within the past 6 months and any of the following:
 - Infectious syphilis or rectal bacterial sexually transmitted infection (STI), particularly if diagnosed in the preceding 12 months
 - Recurrent use of nonoccupational postexposure prophylaxis (nPEP)
 - Ongoing sexual relationship with human immunodeficiency virus (HIV)–positive partner with *substantial* risk of transmissible HIV
 - High-incidence risk index (HIRI)–MSM risk score ≥ 11 (see Supplementary Table 2 in full guidelines*)
- PrEP is not recommended in a stable closed relationship with a single partner with no or *negligible* risk of having transmissible HIV.

Heterosexual exposure

- PrEP is recommended for the HIV-negative partner in heterosexual serodiscordant relationships reporting condomless vaginal or anal sex where the HIV-positive partner has a *substantial* risk of having transmissible HIV.
- PrEP may be considered for the HIV-negative partner in heterosexual serodiscordant relationships reporting condomless vaginal or anal sex, where the HIV-positive partner has a *low* risk of having transmissible HIV.

People who inject drugs

- PrEP may be considered for people who inject drugs if they share injection drug use paraphernalia with a person with a *nonnegligible* risk of HIV infection.

*www.hivnet.ubc.ca/publications/canadian-guideline-hiv-pre-exposure-prophylaxis-nonoccupational-postexposure-prophylaxis/

must be administered in combination with at least 1 other agent from a different class of anti-retrovirals (e.g., nonnucleoside reverse transcriptase inhibitors, protease inhibitors or integrase strand transfer inhibitors). They also have activity against hepatitis B virus. Because of these distinct but potentially overlapping clinical indications, it is critical that pharmacists confirm the indication(s) for prescribing TDF/FTC to help ensure their appropriate use. Tenofovir alafenamide (TAF) is a newer prodrug of tenofovir that has a lower risk of systemic side effects compared to TDF¹⁰; however, until human data are published on using this prodrug for PrEP, TAF/FTC is not currently recommended for this indication.

How should individuals be assessed and monitored?

HIV testing prior to starting PrEP (including individuals restarting PrEP) and before each follow-up prescription is critical. While a fourth-generation antigen/antibody test is recommended to confirm an HIV-negative status, evaluation for symptoms of an acute infection should also occur to rule out an infection during

the approximate 4-week “window period” before this test can confirm the presence of the virus.² Cases of drug resistance to TDF or FTC have occurred when PrEP was initiated in individuals with undiagnosed HIV infection, as TDF/FTC alone is insufficient to suppress viral replication in HIV-infected individuals. TDF is associated with a small increased risk of nephrotoxicity, and therefore serum creatinine should be routinely monitored; TDF/FTC for PrEP should not be started or continued in individuals with an estimated glomerular filtration rate (eGFR) less than 60 mL/min. TDF can also cause a small decrease in bone mineral density, although specific bone health monitoring is not routinely required.² Suggestions for pharmacists’ follow-up monitoring are outlined in Table 3. While TDF/FTC is not typically associated with significant pharmacokinetic drug-drug interactions, the risk of TDF-associated nephrotoxicity in HIV-infected individuals is higher with concomitant use of other nephrotoxic drugs, including nonsteroidal anti-inflammatory drugs (NSAIDs). Thus, regular use of NSAIDs or other nephrotoxic agents while taking TDF/FTC should be avoided.¹¹

TABLE 3 Pharmacist checklist for preexposure prophylaxis (PrEP)

INITIAL ASSESSMENT
<p>Screened <i>indication</i> for PrEP and referral provided to PrEP provider if needed</p> <ul style="list-style-type: none"> ☐ Individual is human immunodeficiency virus (HIV) negative and is at high risk for acquiring HIV infection (see Table 2 for indication) ☐ Discussed need for daily medication adherence and routine follow-up and testing
<p>Reviewed the prescription and medication schedule for efficacy</p> <ul style="list-style-type: none"> ☐ Prescription written for the correct drug, dose and frequency: Daily schedule: tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine 200 mg 1 tablet orally daily On-demand schedule: (see text under “What drugs are used” for details) ☐ First prescription written for 30 days with no automatic refills ☐ Discussed dosing time required to achieve desired drug concentrations (up to 7 days after initiating PrEP)
<p>Evaluated for any safety concerns</p> <ul style="list-style-type: none"> ☐ Verified short interval between date of the prescription and the request to fill the prescription ☐ Recent testing completed to confirm HIV-negative status, hepatitis B and C and pregnancy status (if applicable) ☐ No symptoms of acute HIV infection within the past 12 weeks* ☐ Profile reviewed for evidence of renal dysfunction or osteoporosis (i.e., creatinine clearance CrCl <60 mL/min, renal/bone medications) ☐ Reviewed if patient taking any drugs that may increase the risk of TDF renal toxicity (e.g., nonsteroidal anti-inflammatory drugs, aminoglycosides)
<p>Provided counselling to support adherence</p> <ul style="list-style-type: none"> ☐ Discussed effectiveness of PrEP and reinforced its role as part of a combination HIV prevention strategy, including correct condom use, sterile needles and other HIV risk reduction methods ☐ Reviewed medication dosage and schedule, including missed dose management ☐ Provided recommended discontinuation schedule if PrEP is stopped (i.e., 2-28 days after the last risk exposure). Follow-up HIV testing at 8 weeks should be completed. If the person has hepatitis B and no other medication is continued for hepatitis B, additional monitoring is advised. ☐ Reviewed importance of medication adherence and strategies to avoid missed doses (e.g., reminders on smartphones, incorporating medication into daily routines with work or social schedules) ☐ Counselling on common side effects and management, including over-the-counter medications that can be used ☐ Reinforced importance of routine follow-up testing, including sexually transmitted infection screening and the need for urgent HIV testing/evaluation if there are any symptoms of acute HIV. Reviewed the symptoms of acute HIV infection.* ☐ Determined if any out-of-pocket costs may be a barrier to adherence and explored options to reduce cost
FOLLOW-UP ASSESSMENT (at least every 3 months)
<p>Screened for continued indication/eligibility</p> <ul style="list-style-type: none"> ☐ Established individual remains HIV-negative but continues to be at high risk of HIV infection (see Table 2) ☐ Ascertained the individual is adhering to the medication and the testing schedule
<p>Reviewed the prescription and medication schedule for efficacy</p> <ul style="list-style-type: none"> ☐ Prescription written for the correct drug, an appropriate dose and frequency (see above) ☐ Prescription written for no more than 3 months, with no automatic refills unless requested by the prescriber ☐ Prescription not extended without prior discussion with the prescriber
<p>Evaluated for any safety concerns</p> <ul style="list-style-type: none"> ☐ As above (see Initial Assessment)
<p>Provided counselling to support continued education/adherence (see counselling above and review as needed)</p> <ul style="list-style-type: none"> ☐ Reinforced importance of adherence in terms of efficacy and reducing the risk of drug resistance ☐ Probed if there were any barriers to adherence (e.g., side effects, drug costs, stigma issues, substance use) and discussed management and supports available (e.g., taking with food, insurance plans, blister pack, support groups)

*Symptoms of acute HIV infection include fever, fatigue, myalgia, rash, headache, pharyngitis, arthralgia, cervical adenopathy, night sweats and diarrhea.

What are other considerations for PrEP use?

An important consideration when using PrEP is that it should be offered as part of a combination prevention strategy. This might include counselling on regular use of condoms, effective antiretroviral therapy for HIV-positive partners, use of needle and syringe programs and opiate substitution therapy. Health care providers should also screen candidates considering PrEP for co-occurring or “syndemic” conditions such as mental health and addiction issues and provide appropriate referrals as needed.² These coexisting conditions are often more prevalent among PrEP users and can predispose individuals to higher risk-taking behaviours.

In individuals in whom it is decided PrEP is no longer indicated, the guidelines recommend stopping PrEP up to 28 days after the last potential HIV exposure; however, a shortened follow-up dosing schedule of just 2 days postexposure could be considered in individuals who have been using PrEP for an extended period.⁸ HIV testing should be repeated 8 weeks after stopping PrEP.²

As both TDF and FTC have antiviral hepatitis B activity, there have been concerns of hepatitis B-related liver flares after TDF/FTC discontinuation in patients chronically infected with hepatitis B. Close monitoring of liver enzymes is recommended upon discontinuation of PrEP in such individuals.²

Is PrEP safe to use in people who are pregnant or breastfeeding?

The use of TDF/FTC PrEP in pregnancy and breastfeeding may be considered after discussing the benefits and risks with the individual. In HIV-infected people, TDF/FTC has not been shown to increase the likelihood of birth defects.¹² TDF/FTC was also not associated with increased risk of pregnancy loss, preterm birth, congenital malformations, infant mortality or infant growth outcomes in a large PrEP study in heterosexual couples.¹³ Although TDF and FTC are detected in plasma samples of breastfed infants, the amount of drug ingested was estimated to be a very small fraction of what therapeutic pediatric doses would be.¹⁴

Nonoccupational postexposure prophylaxis (nPEP)

Who should receive nPEP?

The indication to start nPEP is based on 3 important considerations: the risk for HIV

transmission associated with the exposure type, the likelihood the source has transmissible HIV and the timing of nPEP initiation.

nPEP is recommended in individuals following an exposure that is categorized as moderate risk (e.g., receptive or insertive vaginal intercourse) or high risk (e.g., receptive anal intercourse, needle sharing), where the source has a substantial risk of having transmissible HIV (Table 4). Oral sex and sharing sex toys would be considered low-risk exposures, and therefore chemoprophylaxis is not required regardless of the source status.² Blood or other potentially infectious body fluids that come into contact with compromised skin is considered a low-risk exposure.² However, nPEP may be considered on a case-by-case basis depending on whether the source has transmissible HIV (either substantial or low risk).

Whenever possible, efforts should be made to determine the HIV status of the source. Persons known to be HIV positive with detectable plasma viral loads have a higher likelihood of transmitting HIV.¹⁵ The presence of sexually transmitted infections (STIs) also increases the risk of infectivity.¹⁶ Conversely, if the source is confirmed to have an undetectable level of virus (commonly defined as <40 copies/mL in most Canadian centres) with no known STIs, current studies have failed to report linked HIV transmissions. The risk of transmission under these circumstances is virtually zero¹⁷ (Table 1). If indicated, nPEP should be started promptly after an exposure and no later than 72 hours.² Data from animal models have shown that delaying PEP beyond 72 hours did not prevent infection, highlighting the need for rapid initiation of PEP.¹⁸

What drugs are used?

Preferred antiretrovirals for nPEP include TDF 300 mg/FTC 200 mg daily in combination with a third drug: darunavir 800 mg plus ritonavir 100 mg once daily, dolutegravir 50 mg once daily or raltegravir 400 mg twice daily (Table 5).² These regimens were selected based on greater tolerability data and completion rates over other regimens in randomized trials and observational cohorts.² For a list of alternate agents, please see Appendix 1 in the full guidelines (www.hivnet.ubc.ca/publications/canadian-guideline-hiv-pre-exposure-prophylaxis-nonoccupational-postexposure-prophylaxis/).

TABLE 4 Indication for nonoccupational postexposure prophylaxis (nPEP)²

Likelihood that source has transmissible HIV (see Table 1)	Risk from exposure type		
	High -Anal sex (receptive) -Needle sharing	Moderate -Anal sex (insertive) -Vaginal sex (receptive, insertive)	Low -Oral sex (giving, receiving) -Oral-anal contact -Sharing sex toys -Blood on compromised skin*
Substantial	Initiate nPEP	Initiate nPEP	nPEP not required
Low but nonzero	Consider nPEP	Consider nPEP	nPEP not required
Negligible or none	nPEP not required	nPEP not required	nPEP not required

*When blood comes in contact with compromised skin, nPEP may be considered on a case-by-case basis if the likelihood that the source person has transmissible HIV is *substantial* or *low*.

TABLE 5 Recommended nonoccupational postexposure prophylaxis regimens²

Preferred agents	Advantages	Disadvantages
Tenofovir disoproxil fumarate/emtricitabine 300/200 mg daily	-No food requirement -Well tolerated	-Renal toxicity -Dose adjustment in mild to moderate renal impairment -Contraindicated in severe renal impairment
PLUS EITHER		
Raltegravir 400 mg twice daily	-No food requirement -Lower risk of drug interactions -Preferred integrase inhibitor-based regimen in pregnancy	-Twice-daily dosing -Dose adjustment required with UGT inducers; separate administration from polyvalent cations -Myopathy, elevated CK and rhabdomyolysis rarely reported
OR		
Dolutegravir 50 mg daily*	-Once-daily dosing -Low pill burden	-Dose adjustment required with UGT and potent CYP3A4 inducers; separate administration from polyvalent cations -Drug interaction with metformin; caution when using in patients on >1000 mg metformin/day
OR		
Darunavir 800 mg daily + ritonavir 100 mg daily	-Once-daily dosing -Preferred protease inhibitor-based regimen in pregnancy -No dosage adjustment required in renal/mild to moderate liver dysfunction	-Gastrointestinal side effects -Rash -Many drug interactions involving CYP450 enzyme system

CK, creatine kinase; UGT, uridine diphosphate-glucuronosyltransferase.

*Avoid dolutegravir in sexually active women of childbearing potential who are not using effective birth control methods as well as in the first trimester of pregnancy.

Drug interactions are more common with some antiretroviral drugs and thus this may guide selection of nPEP agents. Protease inhibitors (e.g., darunavir) and pharmacokinetic boosters such as ritonavir and cobicistat inhibit CYP3A4 while modulating other isoenzymes or elimination pathways.¹⁹ Integrase inhibitors such as dolutegravir and raltegravir do not inhibit or induce CYP450 metabolism and are ideal candidates in patients with complex pharmacotherapy. However, all integrase inhibitors are susceptible to chelation with simultaneous coadministration of polyvalent cations (e.g., such as iron, calcium and magnesium).²⁰⁻²² It is recommended to consult antiretroviral product monographs, specific pharmacological HIV literature or drug interaction websites (e.g., app. hivclinic.ca, www.hiv-druginteractions.org) as guidance for management of drug interactions.

nPEP treatment should be continued for 28 days, stopping early only if the source is confirmed HIV negative and acute HIV infection is not suspected or if the source is HIV positive, has an undetectable viral load for at least 6 months and has no known concurrent STIs.²

How should individuals be monitored?

In general, recommended nPEP regimens are well tolerated and do not require additional laboratory monitoring for safety. Initial assessment should include baseline fourth-generation HIV antibody/antigen test (with consideration of additional HIV RNA testing in the form of RNA nucleic acid amplification [NAT] in individuals with signs or symptoms of acute HIV infection); hepatitis A, B and C serology; and STI screening (e.g., syphilis, gonorrhea and chlamydia), including sampling at all relevant mucosal sites (e.g., pharynx, rectum in addition to genital sampling/urine). In addition, alanine aminotransferase, a complete blood count and serum creatinine should be checked to rule out preexisting liver or renal conditions, although this should not delay the start of antiretrovirals. Individuals with normal baseline laboratory values would not require subsequent repeat monitoring unless symptoms suggestive of an adverse reaction occur during nPEP use. However, additional evaluation may be necessary in patients with abnormal baseline laboratories or if adverse effects emerge. For example, close monitoring would be prudent in persons who have underlying renal impairment and are prescribed TDF/

FTC, as TDF may further exacerbate renal disease and dosage adjustment of TDF/FTC may be required to limit toxicity.²³

Modification of the initial nPEP regimen or adjunctive treatment for adverse effects management may be required for some individuals. The protease inhibitors, darunavir and ritonavir, can cause gastrointestinal adverse effects such as nausea or diarrhea in up to 50% of individuals, which can add a significant amount of distress for patients.²⁴ In general, studies have found completion rates for currently recommended nPEP regimens average 90%,²⁴⁻²⁶ which is well above completion rates with older nPEP regimens (40%-60%).²⁷⁻²⁹ As noncompletion of nPEP regimens has been implicated as a primary reason for nPEP failures, efforts should be made to address factors known to improve adherence and interventions tailored to individual patients.³⁰ These interventions may include medication counselling, adverse effect management, follow-up phone calls or text messages and minimization of drug expenses.

Final evaluation should occur 12 weeks after exposure with repeat HIV and viral hepatitis serology. If acute HIV infection is suspected before the completion of therapy, nPEP should be continued and the patient referred to an HIV specialist.²

Special situations

In persons taking PrEP as prescribed, there are no benefits to initiating nPEP. If suboptimal PrEP adherence is suspected, however, management is less clear. Such cases should be referred to expert HIV clinicians.

In individuals chronically infected with hepatitis B virus, close monitoring of liver enzymes is recommended upon discontinuation of nPEP regimens containing TDF/FTC.³¹

Pregnancy

Raltegravir and darunavir with ritonavir are categorized as preferred agents in the setting of HIV and pregnancy, based on the quality of evidence on safety and efficacy.¹² While twice-daily darunavir administration is recommended in HIV-infected pregnant women,¹² the panel considered that the achieved darunavir concentrations from once-daily dosing would be adequate in the setting of PEP where there is a reduced viral burden.² Although dolutegravir is listed as an alternative in pregnancy in

the Canadian guidelines, preliminary analysis from an observational study conducted in Botswana has subsequently been released and found that dolutegravir use at the time of conception in HIV-infected people was associated with an increased risk of neural tube defects in the infant.³² However, this safety signal was not seen in people who initiated dolutegravir-based regimens during pregnancy. Until additional information is available, the use of dolutegravir for PEP should be avoided in women of child-bearing potential who are not using effective birth control and who are sexually active or have been sexually assaulted, as well as early in pregnancy.³³ Current guidelines for the management of HIV during pregnancy recommend switching elvitegravir to another effective antiretroviral regimen due to unfavourable pharmacokinetics and potential viral replication.¹² TDF and FTC are secreted in low amounts into breast milk.¹² Passage of darunavir and raltegravir into breast milk is unknown. Due to the potential for HIV transmission through breast milk, potential drug toxicity to the neonate and the availability of alternate feeding options (e.g., formula), breastfeeding is not recommended during nPEP.^{2,12}

Pharmacist's role in PrEP and nPEP

Primary care pharmacists (especially those in community practice) can play an important role in HIV prevention efforts (Box 1). Pharmacists are the most accessible health care providers and can provide needed education as well as condoms and sterile needles to reduce the risk of HIV transmission.

In terms of PrEP delivery, pharmacists may be involved in screening candidates for PrEP; providing information about PrEP and risk reduction counselling, including use of posters or pamphlets; referral to PrEP prescribers; collaborating on initiation and follow-up of individuals started on PrEP; assisting with medication procurement and coverage; and supporting PrEP adherence. Adherence interventions may include education about the importance of medication adherence, ensuring accurate knowledge about medication risk and benefits, preparing for and managing adverse effects, screening for depression and substance use, promoting use of dosettes or phone apps as reminders and having automated telephone or text medication refill reminders.² An issue that many candidates for PrEP face is medication coverage. At the

time of writing, TDF/FTC for PrEP is covered by provincial programs in Ontario, Quebec, Saskatchewan, New Brunswick, Alberta and British Columbia for individuals who meet criteria in each of those provinces; the nature of coverage varies in each province (see coverage information available at https://hivclinic.ca/wp-content/uploads/2018/04/ARV-Coverage_PEP-and-PrEP.pdf). It is also covered by some private insurance providers on a province-to-province basis. The recent availability of generic TDF/FTC in Canada has significantly reduced the monthly cost of PrEP, which may make it more affordable for those paying out of pocket. Depending on provincial scope of practice and competencies, pharmacists may also be able to prescribe PrEP. A model of a pharmacist-run HIV PrEP clinic in the United States using collaborative drug therapy agreements demonstrated very good patient acceptability and feasibility.³⁴ Table 3 outlines a suggested checklist for pharmacists providing PrEP.

For PEP, pharmacists can help to identify and direct appropriate individuals to urgent care after a potential HIV exposure. Each jurisdiction may differ in the delivery of nPEP, and pharmacists should be aware of the various providers and hours of nPEP assessment. For example, 6 sites in Vancouver manage and provide nPEP, while in most other regions, PEP is generally initiated in the emergency department. Having posters or pamphlets in the pharmacy detailing what individuals should do if they have a potential exposure to HIV may also be helpful. Once an individual is determined to require PEP, pharmacists can assist in assessing therapeutic options incorporating details regarding potential drug resistance, regimen complexity and drug interactions. They may help in determining more favourable regimens depending on the characteristics of both the regimen and the patient. Pharmacies that frequently see PEP patients should maintain a stock of drugs used for PEP to minimize delays. Similarly, pharmacies that do not have a supply on hand may need to direct patients to a pharmacy that can fill the prescription without delay. Cost and access of the antiretrovirals may also be a determining factor in which regimen is selected. In many jurisdictions in Canada, there is no public coverage for these drugs for this use; thus, pharmacists, familiar with the cost of drugs and various support programs, can be instrumental

TABLE 6 Pharmacist checklist for nonoccupational postexposure prophylaxis (nPEP)

INITIAL ASSESSMENT
<p>Screened whether nPEP is indicated and referred to provider as necessary</p> <ul style="list-style-type: none"> ☐ Determined the individual may have had a moderate- to high-risk exposure to a person that has a low to substantial likelihood of having transmissible HIV (see Table 4) within the last 72 hours ☐ Referred individual to an urgent care provider or the emergency department for assessment
<p>Reviewed the prescription and medication schedule for efficacy</p> <ul style="list-style-type: none"> ☐ Reviewed any known antiretroviral history, drug resistance data, or HIV viral load results of the source with the prescriber to help guide treatment decisions ☐ Prescription was written for a recommended regimen at the correct dose and frequency (see Table 5). If a nonrecommended drug chosen, discussed decision and therapeutic options with prescriber. ☐ Verified the prescription is being filled or has been started within 72 hours of the exposure ☐ Provided the full PEP regimen (to complete 28 days), ensuring there is no gap or treatment interruption because of access
<p>Evaluated for any safety concerns</p> <ul style="list-style-type: none"> ☐ Determined baseline testing of the exposed individual completed to confirm HIV-negative status (e.g., fourth-generation antibody/antigen test)* ☐ Established baseline testing completed for hepatitis B and C infection, STI screening, complete blood count, hepatic and renal function and pregnancy status (if applicable) ☐ eGFR is ≥ 60 mL/min if TDF 300 mg/FTC 200 mg orally daily prescribed as part of the regimen. If renal function is reduced, dose adjustment is required or an alternate regimen should be considered. ☐ Reviewed profile for any drug-drug interactions that may require an alternate PEP regimen or dosage adjustment ☐ Discussed importance of reducing the risk for secondary HIV transmission during the 12-week follow-up period. Counselling on use of condoms, avoidance of pregnancy and breastfeeding, needle sharing or donating blood
<p>Provided counselling to support adherence</p> <ul style="list-style-type: none"> ☐ Discussed effectiveness of PEP and the importance of medication adherence ☐ Reviewed strategies to avoid missed doses and tailor approaches to the individual (e.g., reminders on smartphones, incorporating medication into daily routines until completion) ☐ Counselling on medication dosage and schedule, including missed dose management ☐ Counselling on common adverse effects and management ☐ Provided contact number if adverse effects develop or are unmanageable (e.g., rash, severe abdominal pain) ☐ Reinforced the schedule and importance of follow-up testing, including STI screening and the need for urgent HIV testing/evaluation if there are any symptoms of acute HIV. Reviewed the symptoms of acute HIV infection.[†] ☐ Determined if any out-of-pocket costs may be a barrier to adherence and explored options to reduce cost
FOLLOW-UP ASSESSMENT
<p>Evaluated for any safety concerns</p> <ul style="list-style-type: none"> ☐ Monitored biochemistry and hematology parameters after 2 weeks if abnormal at baseline or if symptoms of organ dysfunction or medication-related adverse effects develop ☐ Evaluated new or persisting side effects and developed plan for management ☐ Confirmed HIV testing at week 12 after exposure (up to 6 months if hepatitis C infection was acquired) ☐ Inquired about any symptoms of acute HIV infection within the past 12 weeks[†]
<p>Provided counselling as needed to support continued adherence (see above in initial assessment)</p> <ul style="list-style-type: none"> ☐ Probed if there were any barriers to adherence (e.g., scheduling, side effects, drug costs, stigma issues, substance use) and discussed management tailored to the individual
<p>Discussed strategies to avoid future HIV exposures and infection</p> <ul style="list-style-type: none"> ☐ Reviewed or provided information on all HIV prevention strategies, including treatment as prevention, correct condom use, behavioural counselling and PrEP, and linked individual to appropriate provider/services

eGFR, estimated glomerular filtration rate; FTC, emtricitabine; HIV, human immunodeficiency virus; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection; TDF, tenofovir disoproxil fumarate.

*In individuals with symptoms of acute HIV infection, testing should also include HIV RNA if available.

[†]Symptoms of acute HIV infection include fever, fatigue, myalgia, rash, headache, pharyngitis, arthralgia, cervical adenopathy, night sweats and diarrhea.

in suggesting and facilitating access to an affordable yet effective and safe regimen (see https://hivclinic.ca/wp-content/uploads/2018/04/ARV-Coverage_PEP-and-PrEP.pdf). As adherence to the regimen as prescribed is an essential component to the success of PEP, pharmacists must implement and tailor strategies to support adherence—namely, providing education on the benefits and the relationship of medication adherence and success, counselling and managing side effects and incorporating dosing with the individual's daily routine. Finally, many PEP users may be at continuous risk for HIV, and pharmacists can increase awareness for transition from nPEP to PrEP.^{35,36} A checklist of the potential initial assessment and follow-up

activities a pharmacist can complete is provided in Table 6.

Conclusions

New HIV infections continue to occur each year in Canada and are associated with significant economic as well as societal impact. PrEP and nPEP are important strategies that can be used to help prevent new HIV infections. As front-line health care professionals, pharmacists are well positioned to play an important role in the provision and monitoring of PrEP and nPEP. It is important for pharmacists to be aware of evidence-based guidelines to improve quality of care and reduce inappropriate discrepancies in practice. ■

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Author Contributions: All authors approved the final version of the article. All authors contributed to conception and design of the manuscript; Yoong, Giguere and Hughes contributed to drafting sections of the manuscript; Hughes compiled the manuscript drafts; all authors critically revised and gave final approval of the article.

Declaration of Conflicting Interests: Christine Hughes reports personal fees from ViiV Healthcare, Merck and Gilead Sciences outside the submitted work. Deborah Yoong reports receiving honoraria for advisory board representation from Merck and Gilead Sciences. Pierre Giguère reports grants and personal fees from Gilead Sciences, ViiV Healthcare and Merck outside the submitted work. Mark Hull reports receiving honoraria for advisory board representation and speaking engagements regarding HIV and HCV from BMS, Gilead, Merck and ViiV Healthcare, paid to his institution. Darrell Tan reports personal fees from Gilead and ViiV Healthcare outside the submitted work, and his institution has received fees from GSK outside the submitted work.

Funding: The authors received no financial support for the research, authorship and/or publication of this article.

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