Review CPD

Pre-exposure prophylaxis for HIV: effective and underused

Amanda Hempel MD, Mia J. Biondi PhD NP-PHC, Jean-Guy Baril MD, Darrell H.S. Tan MD PhD

■ Cite as: *CMAJ* 2022 September 6;194:E1164-70. doi: 10.1503/cmaj.220645

Incidence of HIV has been rising in Canada. The Public Health Agency of Canada estimated 2242 new HIV infections in 2018, which highlights the need for comprehensive prevention strategies.[1] Pre-exposure prophylaxis (PrEP) is an important means of preventing acquisition of HIV; however, it is underused.[2–4] Although generalists (e.g., family physicians, nurse practitioners and general internists) could play a vital role in implementing PrEP, a recent small survey of general practitioners in Nova Scotia found that most did not prescribe PrEP.[5] We describe PrEP for HIV and discuss current uptake and potential barriers to its use, as well as the approach to prescribing PrEP (Box 1).

Key points

- Pre-exposure prophylaxis (PrEP) is a highly effective modality for HIV prevention that can be prescribed by generalists.
- Pre-exposure prophylaxis should be offered to patients who are at high risk of HIV exposure, including gay, bisexual and other men who have sex with men (GBM), women reporting condomless intercourse with partners of confirmed or unknown transmissible HIV status and persons who inject drugs and share injection equipment.
- Once daily PrEP (tenofovir disoproxil fumarate/emtricitabine [TDF/FTC] or tenofovir alafenamide fumarate/emtricitabine tablets) is approved by Health Canada.
- On-demand TDF/FTC can be prescribed to gay, bisexual and other men who have sex with men and has similar efficacy.
- The Canadian guideline details protocolized monitoring for PrEP follow-up including HIV screening, screening for sexually transmitted infection and renal monitoring.

What is pre-exposure prophylaxis for HIV?

Pre-exposure prophylaxis for HIV is the use of antiretroviral agents by people who are HIV negative that begins before and continues after potential HIV exposures to prevent acquisition of HIV.[6,7] It can be taken daily or on demand before an anticipated exposure.[6,7] Pre-exposure prophylaxis is best used as part of a comprehensive HIV and sexual health strategy that includes harm-reduction education, screening for sexually transmitted infections (STIs), reproductive and mental health care, and attention to co-occurring conditions such as hepatitis B and depression.

How effective is pre-exposure prophylaxis for HIV?

High-quality evidence from randomized controlled trials (RCTs) and observational studies has shown that use of daily PrEP among gay, bisexual and other men who have sex with men (GBM) is associated with almost 100% prevention of HIV acquisition when adherence is high.[8–10] High-quality evidence has shown that efficacy of PrEP is as high as 95% for heterosexual exposure, depending on adherence.[11–13] A 2013 RCT involving people who inject drugs in Bangkok, Thailand, (the Bangkok Tenofovir Study) showed 48.9% efficacy of PrEP but had very low adherence among participants; efficacy increased to 74% among a subgroup of participants who had detectable antiviral levels.[14] Research in all populations has shown the importance of adherence for efficacy, and observational data have shown high effectiveness in real-world settings, with breakthrough infections being uncommon.[15] Uptake of PrEP has been clearly associated with a decline in HIV diagnoses at the population level.[16,17]

The Intervention Préventive de l'Exposition aux Risques avec et pour les Gays (IPERGAY) trial showed that on-demand PrEP is efficacious in GBM, with a reduction in risk of acquiring HIV of 86%; only 2 breakthrough infections occurred in 2 participants who were not adherent to the prophylaxis regimen.[6,18] Participants took a median of 15 pills per month and, although a post hoc analysis showed similar efficacy in participants using fewer than 15 pills per month, there remain modest data on effectiveness in those with more sporadic exposures.[18,19]

Box 1: Evidence used in this review

We conducted a PubMed search of original research and review articles published from January 2017 to January 2021, using the terms "HIV PrEP" or "HIV pre-exposure prophylaxis" and "Canada" or "Canadian." We used this time frame because the Canadian pre-exposure prophylaxis (PrEP) guideline was released in 2017. In addition, we reviewed the current Canadian and American guidelines on PrEP. We selected relevant studies and manually searched their references for additional articles.

Who should be offered pre-exposure prophylaxis for HIV?

The risk of HIV acquisition depends on the likelihood that the contact person has transmissible HIV infection and on the exposure type (Box 2). Several studies have shown that a person who is HIV positive, is receiving antiretroviral therapy and has a viral load of less than 200 copies/mL cannot transmit HIV to sexual partners.[20–22] The indication for PrEP is based on the likelihood of high-risk exposure to transmissible HIV.[6]

Guidelines have been published to assist with identifying patients who may benefit from PrEP (e.g., from the Centers for Disease Control and Prevention [CDC]; Figure 1); however, these recommendations should be considered in the context of the patient's individual risk factors and local epidemiology, and should be seen as a tool rather than rigid instructions. Shared decision-making with the patient is essential, and people should not be denied PrEP if they self-identify as being at risk for HIV outside of current guidance.[6,7]

Although Canadian and American guidelines on PrEP differ slightly, in general, PrEP is recommended for persons engaging in condomless anal or vaginal sex either with partners of unknown HIV status or with partners with known transmissible HIV (i.e., detectable or unknown viral load).[6,7,23] Additional risk factors such as previous use of HIV post-exposure prophylaxis and specific bacterial STIs (Figure 1) are also useful in identifying people at elevated risk of HIV exposure.[6,7,23] Tools for risk stratification (e.g., HIV Incidence Risk Index for men who have sex with men [HIRI-MSM]) are available to assist health care providers in identifying patients who are at elevated risk of HIV.[6]

On-demand PrEP can be considered as an effective alternative in GBM or transgender women who do not want to take daily pills or who have few potential exposures per month.[6] It is not currently recommended in other populations owing to a lack of evidence.

Canadian and American guidelines have recommended PrEP in patients who share injection equipment.[6,7] Risk stratification tools for people who inject drugs have been developed, such as the Assessing the Risk of Contracting HIV in Injection Drug Users (ARCH-IDU) screening tool.[24]

Box 2: Risk of HIV transmission by exposure[6]

Risk that a person has transmissible HIV infection

Substantial

- HIV positive with viral load > 40 copies/mL
- HIV status unknown but from a population with high HIV prevalence

Low but nonzero

- HIV positive with viral load < 40 copies/mL with concomitant sexually transmitted infection present at time of exposure

Negligible or none

- Confirmed HIV negative
- HIV positive with confirmed viral load < 40 copies/mL and no sexually transmitted infection at time of exposure
- HIV status unknown, general population

Risk of HIV transmission by exposure type from HIV-positive source

High

- Receptive anal intercourse
- Needle sharing

Moderate

- Insertive anal intercourse
- Receptive vaginal intercourse
- Insertive vaginal intercourse

Low

- Giving oral sex
- Receiving oral sex
- Oral–anal contact
- Sharing sex toys
- Blood on compromised skin

How is pre-exposure prophylaxis prescribed and monitored?

Currently available daily PrEP regimens (Table 1) include the once-daily combination tablets tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide fumarate/emtricitabine (TAF/FTC).[6,7,23,25] On-demand PrEP (also known as "2-1-1" PrEP) is 2 tablets taken 2–24 hours before unprotected sex, followed by 1 pill daily until 48 hours after the last sexual exposure.[6,7] Long-acting formulations of PrEP have also been developed, such as injectable cabotegravir, which is administered every 8 weeks. Although not yet approved for PrEP in Canada, it may in the future be considered for people who prefer injections over daily tablet regimens.[26]

Prescribers should complete an assessment when PrEP is started and every 3 months while the patient is taking prophylaxis (Table 2).[6,7] Assessments should include reviewing whether the patient has ongoing indications for PrEP and discussing strategies for adherence. Quarterly HIV testing is important because ongoing PrEP use in patients with undiagnosed HIV can lead to drug resistance.[27]

Pre-exposure prophylaxis should be part of comprehensive sexual health care and HIV prevention including education, STI screening and reproductive health, as well as harm reduction and mental health assessment and management.

Both formulations of PrEP can be associated with mild gastrointestinal adverse effects, but these symptoms rapidly subside and rarely cause patients to stop PrEP.[28] Tenofovir disoproxil fumarate is associated with a small risk of renal toxicity and a slight decrease in bone mineral density, both of which are usually reversible when the medication is stopped.[28,29] Tenofovir alafenamide fumarate has been associated with higher rates of triglyceride elevation and weight gain than TDF.[30] For most people at risk of HIV, the efficacy of HIV prevention outweighs the risks of these adverse effects.

Tenofovir disoproxil fumarate/emtricitabine can be prescribed for PrEP in people who are pregnant or breastfeeding.[6,7,23] This drug has been used widely for treatment of HIV in pregnancy with no evidence of adverse outcomes, and the 2021 guideline update from the CDC and a 2019 analysis of PrEP implementation among

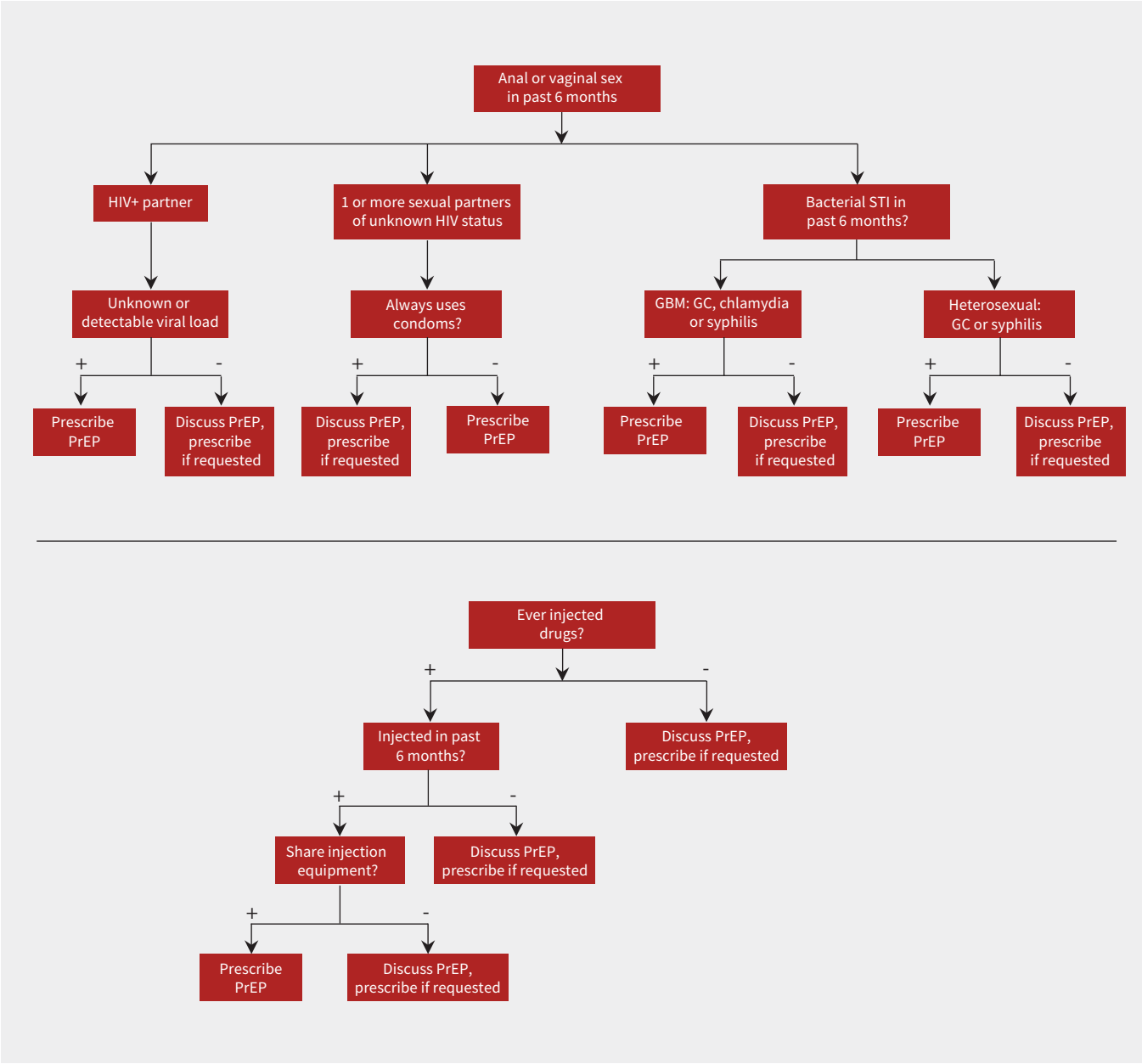

Figure 1: Pre-exposure prophylaxis (PrEP) algorithm, based on the CDC guideline.[6] Note: CDC = Centers for Disease Control and Prevention, GBM = gay, bisexual and men who have sex with men, GC = gonorrhea, STI = sexually transmitted infection.

pregnant and postpartum women in Western Kenya reported no difference in pregnancy outcomes in women receiving perinatal PrEP.[7,31]

Tenofovir disoproxil fumarate/emtricitabine and TAF/FTC also have activity against hepatitis B virus (HBV) and, if they are stopped, patients with HBV infection may have hepatitis flares.[6,7] This underscores the importance of baseline HBV testing, and vaccination for patients who are not immune to HBV. When HIV PrEP is started in patients with chronic HBV infection, it also functions as HBV treatment and requires guideline-driven monitoring in consultation with an experienced HBV provider if needed.[6,7]

Adolescents who weigh at least 35 kg can also safely take PrEP using TDF/FTC or TAF/FTC.[7]

What proportion of eligible patients in Canada are taking pre-exposure prophylaxis?

National surveillance of PrEP use in Canada is not undertaken, which makes patterns of use difficult to quantify. However, use is likely increasing. Pre-exposure prophylaxis was used off label until Health Canada approved daily TDF/FTC for PrEP in 2016, lower-cost generic versions became available in 2017 and the Canadian guideline was released in 2017.[2,6,32]

A study of prescription data in 8 provinces estimated that 9657 patients were receiving PrEP in 2018, about 98% of whom identified as male.[32] Between 2017 and 2019, eligibility for PrEP by Canadian guidelines for GBM in major urban centres ranged

Table 1: Pre-exposure prophylaxis regimens for HIV[6,7]

Regimen type	Available regimens	Population
Daily PrEP	Tenofovir disoproxil/emtricitabine (TDF/FTC) 1 tablet daily administered orally	All populations
	Tenofovir alafenamide/emtricitabine (TAF/FTC) 1 tablet daily administered orally	Sexual exposures excluding receptive vaginal intercourse
On-demand PrEP	Tenofovir disoproxil/emtricitabine (TDF/FTC) 2 tablets administered orally 2–24 h before first exposure and then once daily for 48 h after last exposure	GBM and transgender women

Note: GBM = gay, bisexual and other men who have sex with men, PrEP = pre-exposure prophylaxis.

Table 2: Recommended monitoring for patients receiving pre-exposure prophylaxis for HIV[6,7]

Laboratory analysis	Baseline	Q3 months	Q12 months
HIV serology	X	X	
Hepatitis A total antibody	X (vaccinate if not immune)		
Hepatitis B screen (surface antigen, surface antibody and core antibody)	X (vaccinate if not immune)		X (if not immune)
Hepatitis C antibody	X		X
Gonorrhea and chlamydia screen (urine, throat swab or rectal swab NAAT depending on type of sexual activity reported)	X	X	
Syphilis serology	X	X	
Serum creatinine	X	X	
Lipid panel (TAF/FTC only)	X		X
Urinalysis	X		
Pregnancy test (as appropriate)	X	X	

Note: NAAT = nucleic acid amplification test, TAF/FTC = tenofovir alafenamide fumarate/emtricitabine.

from 44.9% to 58.1%, yet only 14.5%–21.8% had used PrEP.[3] Even among GBM at elevated risk of HIV, only 24.6% were taking PrEP in 2017.[4]

In 2018, women made up 25% of new HIV diagnoses yet accounted for only 2% of PrEP users in Canada.[1,32] Minimal data on uptake in other populations are available.

What barriers exist for patients in accessing pre-exposure prophylaxis?

The basic prerequisite for PrEP uptake is recognition that a patient is at risk of acquiring HIV. However, HIV risk is often underappreciated by both patients and providers. Because most efforts to increase uptake of PrEP in Canada and elsewhere have focused on GBM, risk is particularly underappreciated in other groups, such as women and people who inject drugs, people for whom there are few validated tools for risk assessment.[33,34]

Even among patients who know that they are at elevated risk of acquiring HIV, low awareness about, and low acceptability of, PrEP pose additional challenges; systemic discrimination often exacerbates the problem. For instance, among GBM, being "less out" or not identifying as gay have been linked to lower PrEP awareness, knowledge and uptake owing to discomfort with disclosure, fear that PrEP will "out" them or having less access to PrEP awareness campaigns.[3,4,35] Identifying as Black, Indigenous or other racialized groups has also been associated with lower awareness and knowledge regarding PrEP.[4,36] A 2022 analysis based on interviews with Black GBM in Toronto reported that community outreach programs did not focus on PrEP and, even when advertised, PrEP was often inadequately explained or seemed to encourage condomless sex.[37] Many communities have expressed concerns around pervasive stigma that associates PrEP with "promiscuity."[37]

Potential users must find a provider with adequate knowledge, comfort in discussing sexual health and a willingness to prescribe

PrEP. Both lack of access to a primary provider and little experience with prescribing PrEP among many generalist physicians contribute to this problem; these challenges are exacerbated in rural or remote areas.[2–5] Provider biases regarding who they expect to adhere to PrEP can also lead to inequities in access. The frequency of visits and laboratory tests for monitoring are burdensome for both patients and providers.

Affordability is one of the primary barriers to using PrEP in all populations.[2,37] Although all provinces and territories provide some amount of coverage for PrEP, who qualifies and how much is covered varies (https://hivclinic.ca/wp-content/uploads/2022/02/2022-Jan_ARV-access-for-PrEP.pdf). Even perceptions of treatment unaffordability may prevent patients from seeking PrEP and learning if they are covered.[37]

What strategies can be used to increase appropriate use of pre-exposure prophylaxis?

Clinicians should start discussions about risk of acquiring HIV and PrEP as part of routine preventative health care to reduce reliance on patients self-identifying that they are at risk. In particular, discussion about PrEP should be considered standard care for those who present with bacterial STIs or undergo STI testing.[6,7,38,39] This requires creating a safe space to discuss HIV risk by explicitly combating homophobia and stigma related to sexual and substance use behaviours.[4] Providers can also increase acceptability of PrEP to patients by addressing misconceptions of PrEP as being an intervention solely for gay or highly sexualized people.[4,34,37]

As a relatively simple primary prevention intervention, PrEP can be delivered in routine primary care. However, prescribing PrEP requires provider knowledge, comfort with discussing sexual health and cultural competence in working with historically marginalized populations.[40] Guidelines such as those provided by the CDC can assist clinicians in prescribing PrEP, and easy-to-access Continuing Medical Education modules have been developed to train community-based primary care providers (e.g., https://hivprevention.talentlms.com/shared/start/key:LZGIDNHR).[5–7,35]

Systemic solutions are also needed for patients who do not get identified within primary care. For example, automated systems can identify and expedite referral to PrEP clinics for patients with risk factors that may otherwise be missed, such as through incorporating predictive models into inpatient electronic medical records or automated referrals when STIs are reported to public health.[4,41,42]

The pool of potential providers can also be expanded by harnessing the highly protocolized nature of PrEP to task shift from physicians to other professionals working under a medical directive. Successful examples include nurse-led community or sexual health clinics and pharmacist-led delivery and mobile drop-in clinics that offer low-barrier PrEP.[4,41,43]

Technology can also be used to improve access to PrEP in less-resourced settings or to increase convenience of appointments via telehealth or virtual care to connect with providers in more well-resourced areas.[43] Community-based peer-support programs can increase engagement based on trust and culturally informed perspectives for marginalized communities.[37,43] Public health leaders also have a responsibility to raise awareness about PrEP as a safe and effective preventive health strategy for many populations.

Among the most important interventions to increase PrEP uptake is reducing financial barriers. Clinicians should be aware of options for drug coverage that are available in their jurisdiction and advocate to extend public coverage where not universally available. On-demand PrEP may also reduce cost-related barriers.

Box 3: Unanswered questions

- What are evidence-based tools to help identify women and people who inject drugs who would most benefit from pre-exposure prophylaxis (PrEP) in a high income country such as Canada?
- How can uptake and awareness of PrEP be increased in communities that are already facing barriers to health care access?
- What are the optimal strategies to increase knowledge of and comfort in suggesting PrEP among health care providers?

Conclusion

Pre-exposure prophylaxis is an important modality for preventing acquisition of HIV that can approach 100% efficacy among people who adhere well to treatment. It should be employed as part of a comprehensive strategy for HIV prevention, and generalist physicians can play an important role in increasing access and uptake. Guidelines provide easy-to-follow protocols for identifying eligible patients, prescribing medications and ongoing monitoring. Barriers to PrEP include underestimation of HIV risk in some populations, lack of PrEP awareness, inadequate access to those who will prescribe PrEP and medication costs (Box 3). Pervasive stigma and structural inequities in access to knowledge and care exacerbate these gaps. Health care providers can help close these gaps by increasing their knowledge about PrEP, routinely starting PrEP discussions with patients and advocating for system changes such as medication coverage.

References

1. Estimates of HIV incidence, prevalence and Canada's progress on meeting the 90-90-90 HIV targets, 2020. Ottawa: Public Health Agency of Canada; modified 2022 July 25. Available: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/estimates-hiv-incidence-prevalence-canada-meeting-90-90-90-targets-2020.html (accessed 2022 July 28).
2. Tan DHS, Dashwood TM, Wilton J, et al. Trends in HIV pre-exposure prophylaxis uptake in Ontario, Canada, and impact of policy changes: a population-based analysis of projected pharmacy data (2015–2018). *Can J Public Health* 2021; 112:89-96.
3. Cox J, Apelian H, Moodie EEM, et al.; Engage Study Team. Use of HIV pre-exposure prophylaxis among urban Canadian gay, bisexual and other men who have sex with men: a cross-sectional analysis of the Engage cohort study. *CMAJ Open* 2021;9:E529-38.
4. Colyer S, Lachowsky NJ, Schmidt AJ, et al. Measures of HIV pre-exposure prophylaxis uptake among gay, bisexual, and other men who have sex with men in Canada and demographic disparities among those at elevated likelihood for HIV acquisition. *AIDS Behav* 2021;25:3638-50.

5. Sinno J, Doria N, Cochkanoff N, et al. Attitudes and practices of a sample of Nova Scotian physicians for the implementation of HIV pre-exposure prophylaxis. *HIV AIDS (Auckl)* 2021;13:157-70.
6. Tan DHS, Hull MW, Yoong D, et al.; Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *CMAJ* 2017;189:E1448-58.
7. Preexposure prophylaxis for the prevention of HIV in the United States: 2021 update — a clinical practice guideline. Atlanta: Centers for Disease Control and Prevention; 2021. Available: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf (accessed 2022 Jan. 16).
8. Grant RM, Lama JR, Anderson PL, et al.; iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363:2587-99.
9. Grant RM, Anderson PL, McMahan V, et al.; iPrEx study team. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014; 14:820-9.
10. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* 2016;387:53-60.
11. Baeten JM, Heffron R, Kidoguchi L, et al.; Partners Demonstration Project Team. Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-1-serodiscordant couples: a prospective implementation study in Kenya and Uganda. *PLoS Med* 2016;13:e1002099.
12. Baeten JM, Donnell D, Ndase P, et al.; Partners PrEP Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med* 2012;367:399-410.
13. Thigpen MC, Kebaabetswe PM, Paxton LA, et al.; TDF2 Study Group. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med* 2012;367:423-34.
14. Choopanya K, Martin M, Suntharasamai P, et al.; Bangkok Tenofovir Study Group. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2013;381:2083-90.
15. Grulich AE, Jin F, Bavinton BR, et al.; Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) research group. Long-term protection from HIV infection with oral HIV pre-exposure prophylaxis in gay and bisexual men: findings from the expanded and extended EPIC-NSW prospective implementation study. *Lancet HIV* 2021;8:e486-94.
16. Grulich AE, Guy R, Amin J, et al.; Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) research group. Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. *Lancet HIV* 2018;5:e629-37.
17. Estcourt C, Yeung A, Nandwani R, et al. Population-level effectiveness of a national HIV preexposure prophylaxis programme in MSM. *AIDS* 2021;35: 665-73.
18. Molina J-M, Capitant C, Spire B, et al.; ANRS IPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med* 2015;373:2237-46.
19. Antoni G, Tremblay C, Delaugerre C, et al.; ANRS IPERGAY study group. On-demand pre-exposure prophylaxis with tenofovir disoproxil fumarate plus emtricitabine among men who have sex with men with less frequent sexual intercourse: a post-hoc analysis of the ANRS IPERGAY trial. *Lancet HIV* 2020;7:e113-20.
20. Cohen MS, Chen YQ, McCauley M, et al.; HPTN 052 Study Team. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med* 2016;375:830-9.
21. Rodger AJ, Cambiano V, Bruun T, et al.; PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA* 2016;316:171-81.
22. Bavinton BR, Pinto AN, Phanuphak N, et al.; Opposites Attract Study Group. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet HIV* 2018;5: e438-47.
23. Product monograph: PrTruvada. Mississauga (ON): Gilead Sciences Canada, Inc.; revised 2018 July 5. Available: https://pdf.hres.ca/dpd_pm/00046237.PDF (accessed 2022 Jan. 11).
24. Smith DK, Pan Y, Rose CE, et al. A brief screening tool to assess the risk of contracting HIV infection among active injection drug users. *J Addict Med* 2015;9: 226-32.
25. Product monograph including patient medication information: PrDescovy. Mississauga (ON): Gilead Sciences Canada, Inc.; revised 2020 Nov. 27. Available: https://pdf.hres.ca/dpd_pm/00059007.PDF (accessed 2022 Feb. 10).
26. Highlights of prescribing information: Apretude. Silver Spring (MD): US Food and Drug Administration; 2021. Available: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf (accessed 2022 Mar. 6).
27. Powell VE, Gibas KM, DuBow J, et al. Update on HIV preexposure prophylaxis: effectiveness, drug resistance, and risk compensation. *Curr Infect Dis Rep* 2019; 21:28.
28. Pilkington V, Hill A, Hughes S, et al. How safe is TDF/FTC as PrEP? A systematic review and meta-analysis of the risk of adverse events in 13 randomised trials of PrEP. *J Virus Erad* 2018;4:215-24.
29. Yacoub R, Nadkarni GN, Weikum D, et al. Elevations in serum creatinine with tenofovir-based HIV pre-exposure prophylaxis: a meta-analysis of randomized placebo-controlled trials. *J Acquir Immune Defic Syndr* 2016;71:e115-8.
30. Mayer KH, Molina J-M, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (Drosoph Inf ServCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. *Lancet* 2020;396:239-54.
31. Dettinger JC, Kinuthia J, Pintye J, et al. Perinatal outcomes following maternal pre-exposure prophylaxis (PrEP) use during pregnancy: results from a large PrEP implementation program in Kenya. *J Int AIDS Soc* 2019;22:e25378.
32. Popovic N, Yang Q, Archibald C. Trends in HIV pre-exposure prophylaxis use in eight Canadian provinces, 2014–2018. *Can Commun Dis Rep* 2021;47:251-8.
33. Card KG, Fournier AB, Sorge JT, et al. Substance use patterns and awareness of biomedical HIV prevention strategies among sexual and gender minority men in Canada. *AIDS Care* 2020;32:1506-14.
34. Orser L, O'Byrne P. Examining patient characteristics and HIV-related risks among women with syphilis as indicators for pre-exposure prophylaxis in a nurse-led program (PrEP-RN). *Int J STD AIDS* 2021;32:45-51.
35. Charest M, Sharma M, Chris A, et al. Decentralizing PrEP delivery: implementation and dissemination strategies to increase PrEP uptake among MSM in Toronto, Canada. *PLoS One* 2021;16:e0248626.
36. Raifman J, Dean LT, Montgomery MC, et al. Racial and ethnic disparities in HIV pre-exposure prophylaxis awareness among men who have sex with men. *AIDS Behav* 2019;23:2706-9.
37. Lee-Foon NK, Logie CH, Siddiqi A, et al. Exploring young Black gay, bisexual and other men who have sex with men's PrEP knowledge in Toronto, Ontario, Canada. *Cult Health Sex* 2022;24:301-14.
38. Pathela P, Braunstein SL, Blank S, et al. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. *Clin Infect Dis* 2013;57:1203-9.
39. Pathela P, Braunstein SL, Blank S, et al. The high risk of an HIV diagnosis following a diagnosis of syphilis: a population-level analysis of New York City men. *Clin Infect Dis* 2015;61:281-7.
40. Calabrese SK, Krakower DS, Mayer KH. Integrating HIV preexposure prophylaxis (PrEP) into routine preventive health care to avoid exacerbating disparities. *Am J Public Health* 2017;107:1883-9.
41. O'Byrne P, Vandyk A, Orser L, et al. Nurse-led PrEP-RN clinic: a prospective cohort study exploring task-Shifting HIV prevention to public health nurses. *BMJ Open* 2021;11:e040817.
42. Marcus JL, Hurley LB, Krakower DS, et al. Use of electronic health record data and machine learning to identify candidates for HIV pre-exposure prophylaxis: a modelling study. *Lancet HIV* 2019;6:e688-95.
43. Rousseau E, Julies RF, Madubela N, et al. Novel platforms for biomedical HIV prevention delivery to key populations: community mobile clinics, peer-supported, pharmacy-led PrEP delivery, and the use of telemedicine. *Curr HIV/AIDS Rep* 2021;18:500-7.

Competing interests: Jean-Guy Baril has received consultant fees from ViiV Healthcare, Merck and Gilead, and honoraria for lectures from Merck and Gilead. He is also a member of the HIV and HCV advisory boards for the Ministère de la santé du Québec. Mia Biondi has received speaking fees from Gilead Canada and is an independent contractor with Omega Specialty Nurses. Darrell Tan holds a Tier 2 Canada Research Chair in HIV Prevention and STI Research. No other competing interests were declared.

This article was solicited and has been peer reviewed.

Affiliations: Department of Medicine (Hempel, Tan), University of Toronto; Toronto Centre for Liver Disease (Biondi), University Health Network; School of Nursing (Biondi), York University; Division of Infectious Disease (Tan), St. Michael's Hospital, Toronto, Ont.; Department of Family Medicine (Baril), Centre Hospitalier de l'Université de Montréal; Clinique de médecine urbaine du Quartier Latin (Baril), Montréal, Que.

Contributors: Darrell Tan conceived the review. Amanda Hempel performed the literature review and drafted the manuscript. All of the authors edited the manuscript, reviewed the manuscript critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Funding: Jean-Guy Baril has received grants from GSK, Merck and Gilead (paid to his institution). Darrell Tan has received grants from AbbVie (in-kind support to his institution for investigator-initiated research), Gilead (support to his insitution for investigator-initiated research) and GSK (support to his institution for conducting industry-sponsored clinical trials).

Acknowledgement: The authors acknowledge that they live and work on the traditional territory of many Indigenous people, including the Abenaki, Anishnaabe, Attawandaron, Chippewa, Haudenosaunee, Huron/Wendat, Kanien'kehà:ka, Lūnaapéewak and Mississaugas of the Credit.

Correspondence to: Amanda Hempel,
amanda.hempel@mail.utoronto.ca