BRITISH COLUMBIA
CENTRE *for* EXCELLENCE
*in* HIV/AIDS

# GUIDANCE FOR THE USE OF PRE-EXPOSURE PROPHYLAXIS (PrEP) FOR THE PREVENTION OF HIV ACQUISITION IN BRITISH COLUMBIA

**UPDATED: OCTOBER 2025**

Providence Health Care
How you want to be treated.

VERSION: OCTOBER 9, 2025

# TABLE OF CONTENTS

# I BACKGROUND

Pre-exposure prophylaxis (PrEP) refers to the use of antiretroviral medication by people without HIV, prior to and after potential exposure to HIV to reduce the risk of acquiring HIV infection. PrEP differs from post-exposure prophylaxis (PEP) where a 28-day course of a standard three-drug antiretroviral regimen is used following a high-risk exposure event. Since 2010, six randomized controlled trials involving men who have sex with men (MSM), heterosexual HIV-serodiscordant couples, and people who inject drugs (PWID) have been published showing that tenofovir disoproxil fumarate (TDF)-based PrEP (in combination with emtricitabine (FTC), or in two studies as TDF alone) is effective as part of an HIV prevention package in individuals with high levels of adherence to medication (1-6). FTC/TDF (Truvada®) was approved by the US Food and Drug Administration (7) in July 2012, and by Health Canada in February 2016 (8), for daily oral use to prevent HIV infection. Since then, two additional products have received Health Canada approval for use as HIV PrEP: emtricitabine-tenofovir alafenamide (FTC/TAF; Descovy®) in 2020, and injectable cabotegravir (Apretude®) in 2024.

# II PrEP PROGRAM FUNDING IN BC

Since January 2018, generic FTC/TDF-based PrEP has been publicly funded in BC for individuals who meet the eligibility criteria outlined in this document. These updated clinical practice guidelines reflect a detailed assessment of the epidemiology of new HIV infections and diagnoses within BC, existing evidence for PrEP effectiveness, and where PrEP may have maximal impact at reducing HIV transmission. These guidelines are largely consistent with the 2017 Canadian guideline on HIV PrEP (9), with some exceptions based on more recent information or more precise BC-specific data. Note that for each recommendation, a level of evidence is noted based on the GRADE criteria (10).

## Grading of Recommendations Assessment, Development and Evaluation (GRADE)

| Code | Quality of Evidence | Definition |
|---|---|---|
| A | High | Further research is very unlikely to change our confidence in the estimate of effect.<br>• Several high-quality studies with consistent results<br>• In special cases: one large, high-quality multi-centre trial |
| B | Moderate | Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.<br>• One high-quality study<br>• Several studies with some limitations |
| C | Low | Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.<br>• One or more studies with severe limitations |
| D | Very Low | Any estimate of effect is very uncertain.<br>• Expert opinion<br>• No direct research evidence<br>• One or more studies with very severe limitations |

# III GUIDANCE ON THE USE OF EMTRICITABINE/TENOFOVIR DF (FTC/TDF) FOR PrEP: RECOMMENDATIONS BY KEY POPULATIONS

## 1) Recommendations for FTC/TDF in Cisgender and Transgender Men Who Have Sex with Men (MSM), Other Transmasculine People Who Have Sex with Men, and Transfeminine People Who Have Sex with Men:

**Daily oral FTC/TDF is recommended for cis- and transgender MSM, other transmasculine people and transfeminine people who have sex with men at high risk of acquiring HIV infection (GRADE A recommendation for cisgender MSM; GRADE D recommendation for transgender MSM and transmasculine people who have sex with men; GRADE C recommendation for transfeminine people)**

**High risk** is defined as reporting condomless anal sex **and** having **any** of the following:

a) Infectious syphilis or rectal bacterial sexually transmitted infection (STI), particularly if diagnosed in the preceding 12 months
b) Use of post-exposure prophylaxis (PEP) following a sexual exposure on more than one occasion
c) Ongoing sexual relationship with a partner living with HIV who is not consistently taking antiretroviral therapy (ART) and/or does not have an HIV viral load consistently <200 copies/mL or unable to verify partner's ART adherence/ viral load.
d) HIV Incidence Risk Index for men who have sex with men (HIRI-MSM) score ≥10 (See **Table 1**)

**An alternative FTC/TDF on-demand dosing schedule may also be considered for cis-gender MSM (GRADE B recommendation). This schedule consists of two tablets of FTC/TDF, two to 24 hours prior to anal sex, followed by one tablet daily until 48 hours after the last episode of anal sex**

On-demand dosing may be considered for cis-gender MSM who are able to effectively plan their FTC/TDF dosing around planned sexual activity, who are

able to understand the need for a double (i.e. "loading") dose prior to having sex, who are having sex less frequently than once per week, and who do not have hepatitis B. For other individuals daily dosing is recommended.

**PrEP should be part of a combination prevention strategy that includes behavioural interventions such as condoms and risk reduction counselling.** All HIV-negative cis- and transgender MSM, transmasculine people and transfeminine people reporting condomless anal sex within the last 6 months should be counselled about PrEP.

**Rationale for use of PrEP in cis- and transgender MSM, transmasculine people and transfeminine people who have sex with men in BC:**

MSM constitute the largest at-risk population in BC, comprising over 52% of all new HIV diagnoses in the province (11).

1. The overall HIV incidence for MSM attending STI clinics in BC from 2003 – 2013 was 1.0 per 100 person-years (12). Similarly, among MSM in the Momentum Study in Vancouver from 2012-2017, HIV incidence was 1.25 per 100 person-years (13). In the BC STI clinic analysis, the risk of HIV following a diagnosis of syphilis was 3.6 per 100 person-years, and following rectal gonorrhea was 4.5 per 100 person-years. Following a dual diagnosis of rectal gonorrhea and syphilis, the HIV risk was 17.0 per 100 person-years (12). In the Momentum Study, a history of any previous STI diagnosis was associated with an HIV incidence rate of 4.8 per 100 person-years (14). HIV incidence in the Momentum 2 Study (2017 – 2023) among MSM in Vancouver was estimated to be 0.28 per 100 person-years, reflecting a 62% decrease from the Momentum 1 Study, likely as a result of improved virologic suppression among MSM living with HIV as well as HIV PrEP uptake among MSM without HIV. (15)
2. Post-exposure prophylaxis (PEP) has been used to prevent HIV following high risk sexual and needle-sharing encounters. Individuals who access PEP for such exposures more than once have been found to have a high risk of HIV infection,

with individuals who repeatedly initiate PEP for receptive condomless anal sex in Vancouver demonstrating an HIV incidence of 7.1 per 100 person-years (16).

3. The PARTNER2 cohort study followed 782 HIV-serodiscordant MSM couples and reported 76,088 episodes of condomless sex during which the partner living with HIV had an HIV viral load <200 copies/mL on ART (17). In a median of 1.0 years of follow-up, no genetically linked HIV transmissions were documented. Hence, PrEP is unlikely to provide any additional benefit to individuals who have sexual partners living with HIV who are receiving effective HIV treatment.
4. Use of validated clinical assessment tools, such as the HIRI-MSM (**Table 1**), is a clinically useful strategy that can identify MSM at higher risk of HIV seroconversion. A HIRI-MSM score ≥10 has high sensitivity to detect incident HIV infection (18). Use of HIRI-MSM has been validated in the Momentum Study in Vancouver where risk of HIV infection among individuals with a HIRI-MSM score of ≥10 was approximately 2.0 per 100 person-years of follow-up (14). For those with score >25, the risk was 7.0 per 100 person-years, in comparison to an overall HIV incidence rate of 1.25 per 100 person-years among all MSM in the study (14). Among those with HIRI-MSM score of <10, there were no incident HIV cases in a median of 2.23 years of follow-up (14).
5. Only one randomized trial of FTC/TDF PrEP, iPrex, included transgender women (TGW), and in this study 14% of participants were TGW (1, 19). In a sub-analysis of only TGW participants (n=339), which included follow-up in the open label extension, the overall efficacy of FTC/TDF was not significantly different from placebo (hazard ratio 1.1, 95% confidence interval [CI] 0·5–2·7) (19). However, none of the TGW who seroconverted had detectable levels of FTC/TDF in their blood at their seroconversion visit, and no TGW with blood levels consistent with taking at least 4 tablets per week of FTC/TDF developed a new HIV infection (9). The authors concluded that the lack of PrEP efficacy in TGW was primarily related to poor adherence among those who seroconverted. The evidence for effectiveness of PrEP is less certain for TGW who have sex with men than for cis-gender MSM.

6. None of the randomized trials of FTC/TDF PrEP included transgender MSM; therefore, the recommendation for transgender MSM is based on the opinion of committee members.
7. On-demand dosing of FTC/TDF PrEP has been studied in one randomized controlled trial among cis-gender MSM (5). The IPERGAY study showed an 86% relative risk reduction of HIV seroconversion among 199 MSM randomized to on-demand FTC/TDF in comparison to 201 MSM randomized to on-demand placebo. The on-demand dosing schedule was two pills of FTC/ TDF, taken two to 24 hours before sex, followed by a third pill 24 hours after the first drug intake and a fourth pill 24 hours later. In an open-label extension of this study, the use of on-demand PrEP was associated with a 97% risk reduction compared to placebo (20). Furthermore, among IPERGAY participants who used fewer than 15 pills per month and had a median number of 5 intercourse events per month, there were no seroconversions observed over 68.9 person-years of follow-up (21). In an observational study in Paris, France of 1043 MSM who were offered either on-demand or daily FTC/TDF as PrEP, more than 75% opted for the on-demand regimen (22). In 486 person-years of follow-up, 4 individuals acquired HIV, 2 in each of the on-demand and daily PrEP arms, suggesting that the on-demand regimen is as effective as daily PrEP (22). However, other studies have found reduced overall coverage in FTC/TDF-protected sex acts in some settings with non-daily prescribed dosing (23). FTC/TDF is not licensed in Canada for PrEP as on-demand dosing; therefore, prescribing it to be used in this manner is considered “off-label.” Furthermore, on-demand dosing would not be appropriate for individuals infected with hepatitis B virus, where continuous daily treatment is required.

## 2) Recommendations for PrEP in Cisgender Heterosexual Men and Women

**Daily oral FTC/TDF is recommended for cisgender heterosexual men and women at high risk of acquiring HIV infection (GRADE B recommendation)**

**High risk** is defined as reporting condomless vaginal or anal sex **and** meeting the following additional criteria:

a. Ongoing sexual relationship with a partner living with HIV who is not consistently taking ART **and/or** partner living with HIV does not have an HIV viral load consistently <200 copies/mL **or** unable to verify partner's ART adherence/viral load

**On-demand dosing of FTC/TDF is NOT recommended for heterosexual men or women, as there have been no clinical studies which have examined such dosing within these populations.**

**Rationale for use of PrEP in heterosexual men and women in BC:**

1. Among cisgender heterosexual men and women in BC, new HIV diagnoses are rare (29 cases in 2018 and 27 in 2020) relative to the size of the adult heterosexual population of over three million (11). Among individuals newly diagnosed with HIV in the province from 2008-2015 who reported only heterosexual exposures, 48% reported that they had a sexual partner who was known to be living with HIV (24).
2. The PARTNER cohort study evaluated HIV transmission in 548 HIV serodiscordant heterosexual couples reporting 36,000 episodes of condomless sex, during which the partner with HIV had an HIV viral load <200 copies/mL on ART (25). In a median of 1.9 years of follow-up, no genetically linked transmissions were documented. Hence, FTC/TDF as PrEP is unlikely to provide any additional benefit to individuals who have sexual partners living with HIV who are receiving effective HIV treatment.
3. Among individuals newly diagnosed with HIV from 2008-2015 in BC who reported only heterosexual exposures, only 5% reported participating in sex work (however

this statistic may be subject to underreporting). Sex work is more commonly reported (11%) among individuals newly diagnosed with HIV who report injecting drugs as a potential route of HIV exposure (24). A 2016 analysis from the VIDUS study also found that sex work itself was not associated with HIV incidence when adjusting for other risk factors among individuals who inject drugs (26). Therefore, sex work does not appear to substantially increase risk for acquiring HIV in BC, and therefore does not warrant a separate indication for PrEP to prevent heterosexual transmission.

4. Heterosexual exposure to partners who have other risk factors for HIV are reported relatively rarely. Of individuals newly diagnosed with HIV from 2008-2015 whose only exposure was through heterosexual sex, 6% reported having a sexual partner who was MSM, another 6% reported that their partner had a history of injecting drugs, and 13% were from countries with high HIV prevalence (24). As such, having a sexual partner with additional risk factors or who is from a country where HIV is endemic is not sufficient to warrant specific consideration for PrEP unless the above criteria are met.
5. No randomized clinical trials or observational studies examining the effectiveness of on-demand PrEP have been conducted among individuals at risk of acquiring HIV through heterosexual transmission. Pharmacokinetic data demonstrate that TDF levels do not concentrate in vaginal tissue as rapidly as they do in rectal tissue (27, 28), suggesting on-demand PrEP would be less effective for vaginal or frontal sex than daily PrEP.

## 3) Recommendations for PrEP in Persons Who Inject Drugs (PWID)

**Daily oral FTC/TDF is recommended for PWID who are at high risk of acquiring HIV infection (GRADE B recommendation)**

**High risk** is defined as reporting sharing of injection equipment **and** meeting the following additional criteria:

a. Having an injecting partner who is a person living with HIV and is not consistently taking ART **and/or** does not have an HIV viral load consistently <200 copies/mL, or unable to verify partner's ART adherence/ viral load.

**On-demand dosing of FTC/TDF is NOT recommended for PWID as there have been no studies examining such dosing within this population.**

All PWID who report the above-mentioned risk behaviours should be actively referred to harm reduction services**.**

**Rationale for use of PrEP in PWID in BC**

1. BC has seen a dramatic decrease in new HIV diagnoses among PWID, such that only 19 new diagnoses were made among PWID in 2018 and 25 in 2020. Furthermore, in the VIDUS and ARYS cohorts of PWID in Vancouver, the incidence of HIV infection from 2008 to 2015 was 0.28 per 100 person-years (11,29). While risk factors for HIV transmission among PWID have been identified through VIDUS (26), none of them would impart an expected risk of HIV acquisition of >1 per 100 person-years.
2. Among PWID newly diagnosed with HIV from 2008-2015, 43% reported have an injecting partner who is a person living with HIV and 48% reported sharing injection equipment (24).
3. While the effectiveness of HIV treatment in reducing transmission risk among PWID has not been well studied, it is assumed to be similar in magnitude to the effectiveness of treatment in reducing HIV transmission through vaginal or anal intercourse. An observational study of PWID in Vancouver from 1996-2007 found

large decreases in HIV incidence from a peak of 12 per 100 person-years to a low of <1 per 100 person-years, which paralleled decreases in the median viral load due to expanded use of ART among PWID living with HIV during the same period (30). Hence, FTC/TDF as PrEP is unlikely to provide any additional benefit to individuals whose injecting partners living with HIV are receiving effective HIV treatment.

4. TDF-based PrEP (without FTC) has been demonstrated to be 49% effective in preventing HIV acquisition in one randomized controlled trial of PWID in Bangkok, Thailand (4). The incidence of HIV infection even among participants in the placebo arm was quite low (0.68 per 100 person-years), likely due to the effectiveness of harm reduction equipment provided to all study participants.
5. No randomized controlled trials or observational studies examining the effectiveness of on-demand PrEP have been conducted among individuals at risk of acquiring HIV through injecting drugs.

## 4) Recommendations for Other Individuals Not Included in Key Populations in Recommendations 1-3.

PrEP may be considered for other individuals not included in populations discussed above, based on clinically assessed elevated risk of HIV. Sexual networks and routes of exposure should be taken into account when selecting a suitable PrEP option for these individuals.

## Alternative Requests:

PrEP medication requests outside the specified guidelines, may be submitted to the BC-CfE Drug Treatment Program for extended therapy review, with supporting clinical information: Fax **604-806-9044**.

**Guidance on the use of HIV PrEP: Assessment, Prescribing, Follow-Up and Discontinuation**

The following guidance applies to all PrEP medications in this document, unless otherwise specified.

For additional PrEP guidance for alternative PrEP medications see the **Alternatives to FTC/TDF for HIV PrEP** section.

# IV ASSESSMENT FOR PrEP

1. Confirm negative HIV antigen/antibody (Ag/Ab) test within 15 days before starting PrEP medication, using a 4th generation HIV Ag/Ab enzyme immunoassay (EIA) with consideration of the window period of this assay (median 18 days, interquartile range 16-24 days) in relation to last risk exposure.
    - If symptoms suggestive of acute HIV infection, and/or history of high-risk condomless sex are present in the previous 2 weeks, a nucleic acid amplification test (NAAT) for HIV RNA is recommended. This test can be arranged by contacting the medical microbiologist on call at the BC Centre for Disease Control (BCCDC; 604-707-5600). Defer PrEP initiation until acute HIV infection is ruled out.
2. For people who are able to become pregnant, determine if there are immediate plans to become pregnant, or if the person is currently pregnant or breastfeeding/chest-feeding. Both TDF and FTC are safe in pregnancy. Expert guidance on PrEP in pregnancy and breastfeeding/chest-feeding is available through the Oak Tree Clinic, BC Women's Hospital and Health Centre (604-875-2212;1-888-711-3030)[b].
3. Confirm adequate renal function for FTC/TDF: calculated creatinine clearance or estimated glomerular filtration rate (eGFR) ≥60 mL/minute, and absence of proteinuria on urinalysis and/or quantitative test (urine albumin to creatinine ratio [UACR]).[a]

4. Screen for hepatitis B and C virus **(see Table 3)** and vaccinate against hepatitis B if non-immune. **If FTC and tenofovir (TDF or TAF)-based PrEP is to be prescribed for a person with chronic hepatitis B virus (HBV) infection, appropriate HBV monitoring should be performed in accordance with Canadian HBV treatment guidelines (31), and referral to a qualified practitioner with HBV treatment experience is recommended.**
5. Evaluate for recommended immunizations for pathogens that may be transmitted through sexual exposure and/or injection drug use, as well as for other routine immunizations. People seeking HIV PrEP who have not received the human papillomavirus (HPV) vaccine and who are eligible for this vaccine should receive immunization with the 9-valent HPV vaccine. Hepatitis A and mpox immunizations are recommended for select populations that may overlap with individuals prescribed HIV PrEP. See the BC Immunization manual HERE for recommendations and availability of publicly funded vaccines.
6. Screen for and treat other STIs (gonorrhea, chlamydia, syphilis) following Canadian Guidelines (32) and consider doxycycline for bacterial STI prophylaxis, if appropriate. See the BC-CfE guidance HERE for details.
7. Review current medications for drug interactions with FTC/TDF.[c] Since FTC and TDF are primarily renally eliminated, there is a potential for increased nephrotoxicity with other agents that can affect renal function or compete for active tubular secretion, e.g. acyclovir, valacyclovir, and non-steroidal anti-inflammatory drugs (NSAIDS) (8).
8. As TDF has been associated with decreases in bone mineral density in both HIV treatment and PrEP settings (12, 27, 33-35), alternatives should be considered in persons with a diagnosis of osteoporosis or osteomalacia, fragility fractures, or significant risk factors or secondary causes (e.g. long-term glucocorticoid therapy, androgen deprivation therapy for prostate cancer, hypogonadism, primary hyperparathyroidism, and intestinal disorders for osteoporosis). At present, no specific bone mineral density screening is recommended before or during PrEP use. [a]

9. Counsel regarding PrEP medication adherence, HIV risk reduction, PEP access in the case of missed PrEP doses, and need to seek immediate medical attention if symptoms of acute HIV develop.

[a] Individuals with impaired renal function or bone density concerns may qualify for an alternative to FTC/TDF. See Alternatives section below.
[b] For HIV sero-discordant couples planning to become pregnant, or for individuals who are already pregnant or breastfeeding/chest-feeding, pre-assessment counselling regarding the use of PrEP should include information on maximal risk reduction. Clinicians should contact a qualified specialist or The Oak Tree Clinic at BC Women's Hospital and Health Centre (604-875-2212; 1-888-711-3030) for more detailed information.
[c] University of Liverpool and Toronto General Hospital immunodeficiency clinic websites have interactive drug interaction checkers specifically tailored to antiretroviral medications.

# V PRESCRIBING PrEP MEDICATION

- FTC/TDF PrEP should be prescribed as one tablet of emtricitabine (FTC) 200 mg/tenofovir disoproxil fumarate (TDF) 300 mg to be taken once per day at the same time each day with or without food.
- For MSM without HBV infection for whom on-demand PrEP is appropriate, the prescribed dose is two tablets of FTC-TDF 200-300mg it should be prescribed as two tablets of FTC/TDF, 2 to 24 hours prior to anal sex, followed by one tablet daily until 48 hours after the last episode of anal sex. The amount prescribed should be appropriate for the anticipated amount to be used over a one- (for initial prescriptions) or three-month (for refill prescriptions) period, in 30, 60, or 90 pill quantities.
- The time from initiation of daily oral doses of FTC/TDF to maximal protection against HIV infection is unknown. However, pharmacokinetic data from HIV-infected individuals suggest that steady-state level in the rectal mucosa is reached after 7 days (27, 28). More recent studies suggest that cervical-vaginal mucosa levels may also reach a steady state level within 7 days of starting FTC/TDF (36). Individuals should be counselled to continue safer sex practices during this period.

- Prescribe a 30-44 days supply initially, then reassess for adherence and tolerability. Prescriptions should be renewed only after repeat HIV testing confirms that the patient remains HIV-negative and eligibility criteria persist. Continuation prescriptions should be provided and reassessment performed at intervals not longer than 90 days.
- For people able to become pregnant, ensure that pregnancy test is negative or, if pregnant, that the patient has been informed about the potential risks and benefits of PrEP during pregnancy and breastfeeding/chest-feeding. Both TDF and FTC are safe in pregnancy. Expert guidance on PrEP in pregnancy and breastfeeding/chest-feeding is available through the Oak Tree Clinic, BC Women's Hospital and Health Centre (604-875-2212;1-888-711-3030).
- Regularly review ongoing HIV risk exposures and need for ongoing PrEP.
- Review additional HIV risk reduction counselling and PrEP medication-adherence counselling.
    - Adherence counselling should emphasize that efficacy of PrEP was greatly reduced amongst individuals who did not take the medication as prescribed.

# VI FOLLOW-UP WHILE PrEP IS BEING PRESCRIBED

**After first month, then at minimum every 3 months thereafter:**

- Monitor HIV antibody status using the 4th generation HIV Ag/Ab EIA and document negative status. **This is critical to ensure that seroconversion has not occurred and patients are not being inadequately treated with a suboptimal antiretroviral therapy.**
- Assess for symptoms of acute HIV infection since last visit (37). If symptoms are present, consider requesting a HIV RNA NAAT by consulting the medical microbiologist on call at the BCCDC Public Health Laboratory (604-661-7033) and consult with a prescriber with expertise in acute HIV infection regarding ongoing PrEP use while awaiting test results.

- Check serum creatinine and urinalysis and/or urine albumin to creatinine ratio (UACR). If renal dysfunction develops such that the eGFR falls to <60 mL/min on two measurements, at least two to four weeks apart, then FTC/TDF should be discontinued, and alternative HIV prevention strategies explored. If there is persistent significant proteinuria (urine samples positive for protein [i.e. more than trace]) on at least 2 occasions or severely increased albuminuria (UACR >30 mg/mmol), FTC/TDF should be discontinued regardless of eGFR, and alternative HIV prevention strategies should be explored.
- At each follow-up visit, perform full STI testing for syphilis, gonorrhea, and chlamydia from all appropriate body sites. Quarterly monitoring was performed in most PrEP studies, and a recent analysis in the US found that 20-40% of STIs would have been missed if screening was conducted only twice yearly in MSM (38).
- At each follow-up visit for people who are able to become pregnant, conduct a pregnancy test and document results; if pregnant, discuss continued use of PrEP with patient and prenatal care provider. Expert guidance on PrEP in pregnancy and breastfeeding/chest-feeding is available through the Oak Tree Clinic, BC Women's Hospital and Health Centre (604-875-2212;1-888-711-3030).
- Evaluate and support PrEP medication adherence at each follow-up visit, and more often if inconsistent adherence is identified.
- Assess risk behaviours and need for ongoing PrEP; provide risk-reduction counselling and condoms.
- Assess for mental health issues and addictions which might be contributing to HIV risk and refer to appropriate management services.

**At minimum every 6-12 months:**

- Test for hepatitis C antibody (unless already known to be hepatitis C antibody-positive), particularly in PWID and in MSM (39).

# VII STOPPING PrEP

- Individuals may stop PrEP for multiple reasons, including a change in HIV risk status, or personal choice.
- If FTC/TDF PrEP is to be halted, the optimal duration of PrEP continuation after a recent sexual exposure is unclear. FTC/TDF should be continued for at least 48 hours after a high risk exposure (based on data derived from the IPERGAY trial (5)); however, continued use for as long as 28 days after a high risk exposure is recommended by some groups (40).
- There are currently no data to support stopping strategies for individuals with only heterosexual exposures and/or PWID. Individuals with these exposures should follow the same recommendations as for MSM.
- Order HIV Ag/Ab tests as above to document current HIV status.
    - If diagnosed with HIV, order and document results of HIV resistance testing, and establish immediate linkage to HIV care.
    - If HIV-negative, establish linkage to risk reduction support services as indicated.
- If PrEP is to be resumed in the future, baseline assessment for HIV Ag/Ab status should be performed before resuming (see Assessment for PrEP).
- If patient has active hepatitis B (HBV) infection, ensure appropriate specialist referral prior to stopping FTC and tenofovir-based PrEP. If patient was receiving treatment for HBV prior to PrEP, these medications will need to be re-initiated for HBV management following withdrawal of FTC and tenofovir. Individuals with HBV should be monitored for liver enzyme flare following withdrawal of PrEP if no other HBV therapies are initiated.
- If pregnant, inform prenatal care provider of FTC/TDF use in early pregnancy and coordinate care to maintain HIV prevention during pregnancy and breastfeeding/chest-feeding. Perform HIV testing in each trimester and prior to delivery to ensure seroconversion during pregnancy has not occurred. Expert

guidance on PrEP in pregnancy and breastfeeding/chest-feeding is available through the Oak Tree Clinic, BC Women's Hospital and Health Centre (604-875-2212;1-888-711-3030).

### Requests for PrEP through the BC-CfE Drug Treatment Program (DTP)

- FTC/TDF (generic equivalent of Truvada®) is the standard formulary option in the BC-CfE PrEP Program. Requests are made by submitting an HIV PrEP Enrolment and Prescription Request Form to the BC-CfE DTP at 604-806-9044 (fax). Requests are assessed according to BC PrEP Guidelines and eligible individuals will obtain, at no cost, medication available through the Program.

- A request for a restricted, or non-BC-CfE formulary medication, may be submitted with clinical documentation supporting the request, for extended therapy review.

## VIII ALTERNATIVES TO FTC/TDF FOR HIV PrEP

Generic FTC/TDF is the standard formulary option available for individuals receiving PrEP through the BC-CfE PrEP program.

If a person at ongoing risk for acquiring HIV infection is unable to take FTC/TDF, the following alternatives with Health Canada approval for PrEP may be considered (see details below):

1. Daily oral emtricitabine/tenofovir alafenamide (200/25mg) (FTC/TAF) – available through the BC-CfE based on clinical need.
2. Long-acting injectable cabotegravir (CAB-LA) – **currently BC-CfE non-formulary for PrEP**

## Recommendations for use of FTC/TAF (Descovy®) for PrEP

**Persons at risk of sexually acquired HIV-1 unable to take FTC/TDF for PrEP due to contraindications or significant adverse reactions may be eligible for FTC/TAF for HIV PrEP through the BC-CfE. (GRADE A recommendation for cisgender MSM; GRADE C recommendation for transfeminine people who have sex with men, GRADE D recommendation for transmasculine people who have sex with men and who engage in anal sex only).**

**Availability through the BC-CfE:**

**Documentation of at least one of the following conditions:**

- Persistent* estimated glomerular filtration rate (eGFR) or CrCl ≥30 mL/min and <60 mL/min
    - *based on at least 2 separate measurements at least 2 to 4 weeks apart
    - N.B. safety and efficacy of FTC-TAF have not been established in severe renal impairment (CrCl <30 mL/min).
- Persistent significant proteinuria or albuminuria (uACR >30mg/mmol)
- Persistent moderate to severe hypophosphatemia (serum phosphate <0.64 mmoL/L)
- Documented osteoporosis: T-score < -2.5 at the hip or spine on DXA scan; or if <50 years of age, a Z-score ≤ -2.0
- High (>10%) 10-year risk of major osteoporotic fracture as determined by FRAX score (https://www.sheffield.ac.uk/FRAX/tool.aspx?country=19)
- History of fragility fracture (fracture resulting from minimal or no trauma)
- Documented osteomalacia (laboratory and/or imaging)
- Other clinically significant adverse reaction to FTC-TDF

FTC/TAF is ***not indicated*** for use as HIV PrEP in the following populations:

- persons at risk of HIV acquisition through *receptive vaginal or frontal sex*
- persons at risk of HIV acquisition exclusively through sharing *injecting equipment*

**Populations evaluated, efficacy and safety:**

The pivotal DISCOVER trial demonstrated non-inferior efficacy of FTC/TAF (n=2694) once daily vs FTC/TDF (n=2693) once daily for the prevention of sexually acquired HIV-1 in cisgender MSM and TGW at elevated risk of HIV, aged ≥ 18 years, weighing ≥ 35 kg. FTC/TAF daily was found to be non-inferior to FTC/TDF daily for HIV PrEP with a total of 23 incident HIV cases by week 96: 8 cases in the FTC/TAF group and 15 in the FTC/TDF group (IRR=0.544 [95% CI 0.23-1.26]; non-inferiority margin of 1.62) (41,42)

In the DISCOVER trial, FTC/TAF had more favourable renal and bone biomarkers compared to FTC/TDF, the clinical significance of which is uncertain. The number of renal adverse events that led to study discontinuation was low in both study arms: 2/2694 (0.07%) in the FTC/TAF arm and 6/2693 (0.2%) in the FTC/TDF arm (41,42).

With respect to clinical bone outcomes, the FTC/TAF and FTC/TDF groups each had a total of 53 fractures at week 48, and 60 fractures at week 96. Of these fracture events, only 1 in the FTC/TAF group and 2 in the FTC/TDF group were classified as nontraumatic (41) (42).

**Drug administration:**

FTC/TAF should only be taken daily for HIV PrEP. On-demand or intermittent use has not been evaluated, is not approved by Health Canada, and is NOT recommended.

**Drug Interactions:**

FTC/TAF should not be co-administered with P-glycoprotein inducers (e.g. carbamazepine, phenobarbital, phenytoin, rifampin, rifabutin, St. John's wort) as they may decrease TAF concentrations and result in loss of therapeutic effect. See product information for a complete list of drug interactions. (43)

# Recommendations for use of Long-acting Cabotegravir (CAB-LA) for HIV-1 PrEP

## Availability through the BC-CfE:

At the current time, **CAB-LA is BC-CfE non-formulary for PrEP**.

CAB-LA PrEP may be a suitable alternative for HIV-negative persons who are at ongoing elevated risk of acquiring sexually transmitted HIV infection (as discussed at the beginning of this document) where FTC/TDF or FTC/TAF are contraindicated, not tolerated, or infeasible due to one or more of the following: **(GRADE A evidence cisgender MSM and cisgender women; GRADE C recommendation for transfeminine people, GRADE D recommendation for transmasculine people)**

- Allergic reactions or other treatment-limiting toxicity to oral PrEP options that contain tenofovir and/or emtricitabine
- Chronic renal impairment (mild to severe)*. Cabotegravir has minimal renal excretion; however, CAB-LA has not been formally evaluated in people with CrCl<60mL/min or in people on dialysis.
- Unable to swallow or absorb oral medication

*severe = CrCL <30 mL/min and not on dialysis

With ongoing healthcare supports, and full understanding of the treatment and testing requirements and the risks of suboptimal adherence (including the potential risk of integrase inhibitor resistance), CAB-LA may be an acceptable PrEP alternative for individuals at ongoing elevated risk of HIV acquisition who have tried to take oral FTC/TDF and/ or FTC/TAF as PrEP, but have been unable to adhere to or continue with this therapy. CAB-LA has not been formally evaluated in persons who are non-adherent to oral PrEP.

**Exclusions:**

CAB-LA is not indicated for use as HIV PrEP in persons at risk of HIV acquisition through injecting drugs, due to absence of efficacy data in this population. (44)

**Populations evaluated in clinical trials:**

The pivotal trials (HIV Prevention Trials Network [HPTN] 083 and 084) demonstrated safety and superior efficacy of intramuscular CAB-LA injections every 8 weeks vs FTC/TDF orally once daily for the prevention of sexually acquired HIV-1 in in MSM and TGW (HPTN083) and in cisgender women (HPTN084) at elevated risk of HIV, aged ≥ 18 years, weighing ≥ 35 kg. (45,46,47)

HPTN083 included 4566 participants (2282 in the CAB-LA arm, 2284 in the FTC/TDF arm) in the United States, Latin America, Asia and Africa. HPTN084 included 3224 participants (1614 in the CAB-LA arm, 1610 in the FTC/TDF arm) in seven countries in sub-Saharan Africa.

Incidence of HIV in the CAB-LA arms in HPTN 083 and HPTN 084 was 0.41 and 0.20 per 100 person-years, respectively. For local context, the incidence of new HIV infections in the BC HIV PrEP program (using oral FTC/TDF) was less than 0.2 per 100 person-years over more than 39,000 person-years of follow-up amongst more than 12,000 persons at elevated risk of HIV. (45-48)

**Drug Administration and Dosing and Counselling**

- CAB-LA is administered as a 3mL (600mg) gluteal intramuscular (IM) injection (via the Z-track method)* once every 4 weeks for 2 consecutive IM injections, and every 8 weeks thereafter (+/- 7 days administration window). HIV testing is recommended every 8 weeks alongside scheduled injections. There is an optional oral lead-in of cabotegravir 30 mg daily for one month (minimum 28 days) before the first injection to assess drug tolerability. (44)

- The time from commencing CAB-LA injections to onset of HIV protection is unknown, but is thought to be approximately 7 days. (44,49)
- Rare cases of breakthrough HIV infection have occurred despite on-time injections of CAB-LA. (45)
- Patients should receive ongoing counselling on the importance of adhering to the recommended dosing schedule in order to maintain therapeutic drug levels and reduce the risk of acquiring HIV and developing integrase inhibitor (INSTI) resistance.

*Details of Z-track injection method can be found in the Apretude® Instructions for Use. Refer to the Instructions for Use for complete administration instructions with illustrations. (50)

**HIV testing recommendations**

- Before initiating CAB-LA for PrEP, HIV negative status should be confirmed via 4th generation Ag/Ab screening within 15 days of starting CAB-LA.
- There is a risk of delayed HIV detection associated with use of CAB-LA for PrEP. Long-acting Early Viral Inhibition (LEVI) syndrome is characterized by long periods of delayed HIV antibody production with viral suppression. This can delay HIV diagnosis, leading to CAB-LA administration after established HIV infection and potentially to INSTI resistance. (51)
  - Follow-up HIV Ag/Ab testing **and** qualitative NAAT testing is recommended 4 weeks after CAB-LA initiation and every 8 weeks thereafter, at the same time as CAB-LA injections are being administered. (44,52)
    - Due to challenges with delayed HIV diagnosis in the setting of CAB-LA failure, the addition of a qualitative NAAT is required during CAB-LA follow-up period.
  - There have been instances during clinical trials where discrepancies between tests resulted in unnecessary CAB-LA interruptions. (53) In the case that discrepancies between HIV Ag/Ab and NAAT test results arise, call the HIV Speciality Clinic ASAP at 604-806-8315 for expert guidance. A follow-up HIV

NAAT should be ordered as soon as possible, and if the next CAB-LA dose is due, it should not be delayed and should be administered as scheduled while awaiting the follow-up test result to inform next steps.

**Management of CAB-LA discontinuation**

- Due to the long half-life of CAB-LA, cabotegravir can persist in the body at a subtherapeutic level for 12 months or longer after discontinuation. (44,54)
- HIV infection occurring during the subtherapeutic CAB-LA tail phase may result in acquired resistance to integrase inhibitors. Patients must be made aware that, should they acquire HIV infection and develop resistance to integrase inhibitors while using CAB-LA, it is unlikely that they will respond to first-line integrase inhibitor-based HIV treatment in the future (e.g. dolutegravir or bictegravir). (44)
- To cover the subtherapeutic tail phase after discontinuing CAB-LA, alternative forms of PrEP should be used if the individual is at ongoing risk of HIV infection.
- Prior to starting CAB-LA, patients should be thoroughly counselled on the implications of the tail phase, in case of drug discontinuation/interruption for intolerance, preference, or non-adherence.

**Cautions / Side effects / Drug Interactions**

- CAB-LA is not recommended for people who cannot receive IM injections (e.g. on anticoagulation medication, bleeding disorder, needle-phobic).
- There is insufficient efficacy or safety data to recommend CAB-LA in people who are pregnant or breastfeeding/chest-feeding.
- Side effects
    - Injection site reactions (ISRs) are common and decrease over time. 81.5% of participants in the CAB-LA arm in HPTN083 and 38% of participants in the CAB-LA arm in HPTN084 reported at least one ISR. Pain and tenderness were the most commonly reported ISRs. (45,48)

- Other reported adverse drug reactions (≤5%) include diarrhea, headache, fatigue, nausea and dizziness. (45,48)
- In CAB-LA clinical trials, both study arms experienced an increase in body weight, with the CAB-LA group experiencing a greater increase in weight than the FTC/TDF group. In HPTN 083, the CAB-LA group saw an increase in body weight of 1.23 kg per year (95% CI 1.05 to 1.42) versus an increase of 0.37 kg (95% CI 0.18 to 0.55) in the FTC/TDF group. (45) In HPTN 084, there was a mean weight increase across both study arms: CAB-LA (2·4 kg per year [95% CI 1.9 to 3.0]), FTC/TDF (2·1 kg per year [95% CI 1.9 to 2.4]); p=0.041. (47)
- Decreased calculated creatinine clearance (CrCl) was observed in CAB-LA trial participants (in both CAB-LA and FTC/TDF groups); most changes were moderate (i.e., CrCl < 90 to 60 mL/min or 10 to <30% decrease from baseline). (45,48)

- Drug Interactions
  - Oral cabotegravir should not be administered at the same time as oral antacids or other products that contain polyvalent cations (aluminium, calcium, magnesium, iron, or zinc). Such products must be administered at least 2 hours before or 4 hours after oral cabotegravir. (44)
  - The co-administration of both oral and injectable cabotegravir is contraindicated with UGT1A1 and UGT1A9 inducers such as the anticonvulsants, carbamazepine, oxcarbazepine, phenobarbital and phenytoin, and the antimicrobials, rifampin and rifapentine.
  - Rifabutin may be co-administered with CAB-LA; however, the CAB-LA dosing schedule must be adjusted to maintain therapeutic levels of cabotegravir. See product monograph for details. (44)

- Hepatic Considerations
  - CAB-LA does not cover Hepatitis B (HBV) infection and PrEP alternatives containing tenofovir and FTC may be more suitable for people with HBV.
  - If using CAB-LA for PrEP in persons with HBV, appropriate HBV treatment should also be used.

- No clinically important pharmacokinetic differences between participants with moderate hepatic impairment and matching healthy participants were observed in pharmacokinetic studies (55). No CAB-LA dosage adjustment is necessary for individuals with mild to moderate hepatic impairment (Child-Pugh Score A or B).
- The effect of severe hepatic impairment (Child-Pugh Score C) on the pharmacokinetics of cabotegravir has not been studied. (44)

# TABLE 1: HIV INCIDENCE RISK INDEX FOR MEN WHO HAVE SEX WITH MEN (HIRI-MSM)

| MSM Risk Index | | |
|---|---|---|
| 1. How old are you today? | If <18 years, score 0<br>If 18-28 years, score 8<br>If 29-40 years, score 5<br>If 41-48 years, score 2<br>If 49 years or more, score 0 | _____ |
| 2. In the last 6 months, how many men have you had sex with? | If >10 male partners, score 7<br>If 6-10 male partners, score 4<br>If 0-5 male partners, score 0 | _____ |
| 3. In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom? | If 1 or more times, score 10<br>If 0 times, score 0 | _____ |
| 4. In the last 6 months, how many of your male sex partners were HIV-positive? | If >1 positive partner, score 8<br>If 1 positive partner, score 4<br>If 0 positive partner, score 0 | _____ |
| 5. In the last 6 months, how many times did you have insertive anal sex (you were the top) without a condom with a man who was HIV-positive? | If 5 or more times, score 6<br>If <5 times, score 0 | _____ |
| 6. In the last 6 months, have you used methamphetamines such as crystal or speed? | If yes, score 6<br>If no, score 0 | _____ |
| | Add entries in right column to calculate total score | _____<br>Total Score* |
| * If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.<br>If score is below 10, provide indicated standard HIV prevention services. | | |

# TABLE 2: SUMMARY OF GUIDANCE FOR PrEP USE IN BC

[Adapted from US Food and Drug Administration (7)]

| | Cisgender men, transmasculine people and transfeminine people who have sex with men | Cis-gender heterosexual men and women | People who use injection drugs |
|---|---|---|---|
| Detecting substantial risk of acquiring HIV infection | Reports condomless sex **and** at least one of:<br>• Diagnosis of syphilis or rectal gonorrhea or chlamydia within last 12 month; **or**<br>• Ongoing sexual relationship with an HIV-positive partner who is not receiving stable ART **and/or** does not have a viral load consistently <200 copies/mL; **or**<br>• Repeated courses of PEP; **or**<br>• HIRI-MSM score ≥10 | Reports condomless vaginal or anal sex **and** HIV-positive sexual partner not receiving stable ART **and/or** does not have a viral load consistently <200 copies/mL [a] | Reports sharing injection equipment **and** HIV-positive injecting partner not receiving stable ART **and/or** does not have a viral load consistently <200 copies/mL [b] |
| Clinically eligible | Documented negative Ab/Ag HIV test result within 15 days before prescribing PrEP<br>No signs/symptoms of acute HIV infection<br>Documented renal function[c]; no contraindicated medications<br>Documented hepatitis B virus infection status and vaccination status<br>Avoid TDF in patients with documented osteoporosis or osteomalacia[c] | | |

<table>
<tr><td>Prescription</td><td colspan="3">For daily, continuing therapy of emtricitabine/tenofovir DF; 30-day supply initially, then 90-day supply on a continuing basis if adherence, tolerability, and eligibility confirmed</td></tr>
<tr><td></td><td>For on-demand dosing, prescribe two tablets of FTC/TDF, 2 to 24 hours prior to anal sex, followed by one tablet daily until 48 hours after the last episode of anal sex. Prescribe 30 tablets initially, then enough to cover at least 90 days if adherence, tolerability, and eligibility confirmed (cisgender MSM only)</td><td></td><td></td></tr>
<tr><td>Other services</td><td colspan="3">Follow-up visits after 1 month and at minimum every 3 months thereafter,<br>to provide the following:<br>HIV test, assess renal function, medication adherence counselling, behavioural risk reduction support, side effect assessment, STI symptom assessment</td></tr>
<tr><td></td><td colspan="3">Assess vaccination status and recommendations for HPV, HAV, HBV, Mpox vaccines, and for routine vaccinations. Publicly funded vaccinations may be available.</td></tr>
<tr><td></td><td>Conduct urethral/oral/rectal STI testing as appropriate with reported sexual behaviour every 3 months</td><td>Assess pregnancy intent<br>Pregnancy test every 3 months<br>Conduct STI testing as appropriate with sexual behaviour</td><td>Access to clean needles/syringes and drug treatment services<br>Conduct STI testing as appropriate with sexual behaviour</td></tr>
</table>

[a] For individuals in a stable, monogamous relationship with an HIV-positive individual, the use of effective antiretroviral therapy by the HIV-positive individual as demonstrated by a sustained HIV viral load <50 [22] or <200 copies/mL [19] has been shown to reduce the risk of HIV transmission to very low or negligible levels. [b] The effectiveness of HIV treatment in reducing the risk of transmission through sharing injection equipment among PWID is unknown, but is assumed to be the same order of magnitude as for reducing sexual transmission. The added value of PrEP in these settings has not been evaluated. [c] May be eligible for FTC/TAF, see section 4 above. Recommendations for Cisgender men, transmasculine people and transfeminine people who have sex with men in whom FTC-TDF is contraindicated or who have experienced significant adverse reactions while taking FTC-TDF.

# TABLE 3: SUMMARY OF TESTING RECOMMENDATIONS DURING PrEP.†

| Assay Type | Baseline | After first month then Q3 months | Q 6 months |
|---|---|---|---|
| HIV Serology (4th Generation Ab/Ag Assay) | X | X | |
| HIV RNA NAAT Test (for those with symptoms of acute HIV) | X | X | |
| Hepatitis B Screen (Hepatitis B Surface Antigen, surface antibody, core antibody)* | X* | | |
| Hepatitis C Screen (Hepatitis C Antibody, if not known to be hepatitis C-positive) | X | | X (for PWID and MSM) |
| Gonorrhea screen^ (urine NAAT test, throat and rectal swabs for gonorrhea depending on type of sexual activity reported) | X | X (for MSM) | X |
| Chlamydia Screen ^ (Chlamydia urine NAAT test; throat and rectal swabs for chlamydia depending on type of sexual activity reported) | X | X (for MSM) | X |
| Syphilis Screen^ (*T. pallidum* EIA) | X | X (for MSM) | X |
| Creatinine and urinalysis or Urine albumin to creatinine ratio | X | X | |
| Pregnancy test (for people of child-bearing potential) | X | X | |

†Some recommended testing frequencies differ for CAB-LA. See CAB-LA section for details.
*Hepatitis B vaccination should be initiated in unvaccinated individuals who are anti-HBs Ab negative.
^Individuals diagnosed with concurrent STI should be offered standard therapy following Canadian Guidelines (32)

# IX REFERENCES


1. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. The New England Journal Of Medicine. 2010;363(27):2587-99.
2. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. The New England Journal Of Medicine. 2012;367(5):423-34.
3. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. The New England Journal Of Medicine. 2012;367(5):399-410.
4. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, et al. 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(9883):2083-90.
5. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. The New England Journal Of Medicine. 2015;373(23):2237-46.
6. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2016;387(10013):53-60.
7. US Food and Drug Administration. Truvada approved to reduce the risk of sexually transmitted HIV in people who are not infected with the virus 2012. Washington, D.C.: US Food and Drug Administration; 2012.
8. Gilead Sciences Canada I. Truvada® (emtricitabine/tenofovir disoproxil fumarate) tablets: (200 mg/300 mg) antiretroviral agent [product monograph]. In: Gilead Sciences Canada I, editor. Foster City, CA, USA2016.
9. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2017;189(47):E1448-E58.
10. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.
11. Sorge J, Consolacion T, Vijh R, Sereda P, Lima V, Wong J. HIV incidence and prevalence estimates for British Columbia and progress towards 90-90-90 HIV targets, 2020. British Columbia Centre for Disease Control;2023 https://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/HIV_2020estimates.pdf
12. Samji H , Moore D, et al.. HIV Incidence among Gay, Bisexual, and other Men who Have Sex with Men Attending Sexually Transmitted Infection Clinics in British Columbia. 25th Annual Canadian Conference on HIV/AIDS Research 2016 May 12- 15; Winnipeg, MB.

13. Lachowsky N, HL. A, Sereda P, Pan S, Bacani N, Olarewaju G, et al.. HIV Incidence and Associated Factors Among Men Who Have Sex With Men (MSM) in a Treatment as Prevention Environment: Benefits of a Prospective Cohort Study and Administrative Health Data Linkage. International AIDS Conference; 2018 July 21 -24; Amsterdam, The Netherlands.

14. Lachowsky N, Cui Z, Sereda P, Stephenson K, Rich A, Brown J, et al.. HIV Incidence Rate and Predictors Among Gay and other Men Who Have Sex With Men (MSM) in Vancouver: Additional Benefit of an Administrative Health Data Linkage. 25th Annual Canadian Conference on HIV/AIDS Research; 2016 May 12 - 14; Winnipeg, Canada.

15. Moore DM, Wang L, Lal A, Barath J, Montaner JSG, Hull M, Toy J, Lima VD, Sereda P, Hogg RS, Trigg J. Lachowsky NJ. Declines in HIV incidence among GBM in Vancouver, Canada: 2012-19 to 2017-23. Conference on Retroviruses and Opportunistic Infections, Denver, CO, USA. March 3 – 6, 2024.

16. Hull M, Lachowsky N, Moore D, et al. High incidence of subsequent HIV seroconversion amongst MSM accessing recurrent non-occupational post-exposure prophylaxis (NPEP) in Vancouver, BC. 25th Annual Canadian Conference on HIV/AIDS Research; 2016 May 12- 15 Winnipeg, MB.

17. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet. 2019;393(10189):2428-2438. doi:10.1016/S0140-6736(19)30418-

18. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. Journal of acquired immune deficiency syndromes. 2012;60(4):421-7.

19. Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. Lancet HIV. 2015;2(12):e512-9

20. Molina JM, Charreau I, Spire B, Cotte L, Chas J, Capitant C, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. Lancet HIV. 2017;4(9):e402-e10.

21. Antoni G, Tremblay C, Charreau I, Cua E, Rojas-Castro D, Hall N, et al., editors. On-demand PrEP with TDF/FTC remains highly effective among MSM with infrequent sexual intercourse: a sub-study of the ANRS IPERGAY trial. International Conference on HIV Science; 2017 July; Paris, France.

22. Noret M, Balavoine S, Pintado C, Siguier M, Brun A, Bauer R, et al. Daily or on-demand oral tenofovir disoproxil fumarate/emtricitabine for HIV pre-exposure prophylaxis: experience from a hospital-based clinic in France. AIDS. 2018;32(15):2161-9

23. Grant RM, Mannheimer S, Hughes JP, Hirsch-Moverman Y, Loquere A, Chitwarakorn A, et al. Daily and Nondaily Oral Preexposure Prophylaxis in Men and Transgender Women Who Have Sex With Men: The Human Immunodeficiency Virus Prevention Trials Network 067/ADAPT Study. Clin Infect Dis. 2018;66(11):1712-21.

24. Consolation T. Unpublished Provincial HIV Surveillance Data. Vancouver, BC: BC Centre for Disease Control.; 2017.

25. Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, van Lunzen J, et al. 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(2):171-81.

26. Kerr T, Shannon K, Ti L, Strathdee S, Hayashi K, Nguyen P, et al. Sex work and HIV incidence among people who inject drugs. AIDS. 2016;30(4):627-34.

27. Anderson PL, Kiser JJ, Gardner EM, Rower JE, Meditz A, Grant RM. Pharmacological considerations for tenofovir and emtricitabine to prevent HIV infection. J Antimicrob Chemother. 2011;66(2):240-50.

28. Patterson KB PH, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. Sci Transl Med. 2011;3()(112):112 - 4.

29. Hayashi K. Unpublished data from VIDUS cohort. Vancouver, BC: BC Centre for Excellence in HIV/AIDS; 2017.

30. Wood E, Kerr T, Marshall BD, Li K, Zhang R, Hogg RS, et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. BMJ (Clinical research ed.) 2009;338:b1649.

31. Coffin CS, Fung SK, Alvarez F, Cooper CL, Doucette KE, Fournier C, et al. Management of Hepatitis B Virus Infection: 2018 Guidelines from the Canadian Association for the Study of Liver Disease and Association of Medical Microbiology and Infectious Disease Canada. Canadian Liver Journal. 2018;1(4):156-217.

32. Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections Ottawa, ON: Public Health Agency of Canada; 2016 Revised 2008.

33. Mulligan K, Glidden DV, Anderson PL, Liu A, McMahan V, Gonzales P, et al. Effects of Emtricitabine/Tenofovir on Bone Mineral Density in HIV-Negative Persons in a Randomized, Double-Blind, Placebo-Controlled Trial. Clin Infect Dis. 2015;61(4):572-80.

34. Liu AY, Vittinghoff E, Sellmeyer DE, Irvin R, Mulligan K, Mayer K, et al. Bone mineral density in HIV-negative men participating in a tenofovir pre-exposure prophylaxis randomized clinical trial in San Francisco. PloS one. 2011;6(8):e23688.

35. McComsey GA, Tebas P, Shane E, Yin MT, Overton ET, Huang JS, et al. Bone disease in HIV infection: a practical review and recommendations for HIV care providers. Clin Infect Dis. 2010;51(8):937-46.

36. Seifert SM, Chen X, Meditz AL, Castillo-Mancilla JR, Gardner EM, Predhomme JA, et al. Intracellular Tenofovir and Emtricitabine Anabolites in Genital, Rectal, and Blood Compartments from First Dose to Steady State. AIDS Res Hum Retroviruses. 2016;32(10-11):981-91.

37. Updated Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new.

38. Cohen S VE, Philip SS, et al., editor Quarterly STI Screening Optimizes STI Detection Among PrEP Users in the Demo Project. . Conference on Retroviruses and Opportunistic Infections 2016 February 22-25; Boston, MA. .

39. Lachowsky NJ CJ, Cui Z, et al., editor Prevalence and incidence of hepatitis C virus infection among HIV-negative and HIV-positive gay and other men who have sex with men in Vancouver. 26th Annual Canadian Conference on HIV/AIDS Research; 2017 April 6-9; Montreal, QC.

40. Seifert SM GD, Meditz AL, et al. Dose response for starting and stopping HIV preexposure prophylaxis for men who have sex with men. . Clin Infect Dis. 2015;60 804-10.

41. Mayer KH, Molina JM, Thompson MA, Anderson PL, Mounzer KC, De Wet JJ, DeJesus E, Jessen H, Grant RM, Ruane PJ, Wong P, Ebrahimi R, Zhong L, Mathias A, Callebaut C, Collins SE, Das M, McCallister S, Brainard DM, Brinson C, Clarke A, Coll P, Post FA, Hare CB. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. Lancet. 2020 Jul 25;396(10246):239-254. doi: 10.1016/S0140-6736(20)31065-5. PMID: 32711800; PMCID: PMC9665936

42. Ogbuagu O, Ruane PJ, Podzamczer D, Salazar LC, Henry K, Asmuth DM, Wohl D, Gilson R, Shao Y, Ebrahimi R, Cox S, Kintu A, Carter C, Das M, Baeten JM, Brainard DM, Whitlock G, Brunetta JM, Kronborg G, Spinner CD; DISCOVER study team. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet HIV. 2021 Jul;8(7): e397-e407. doi: 10.1016/S2352-3018(21)00071-0. Erratum in: Lancet HIV. 2021 Dec;8(12): e734. PMID: 34197772.

43. Gilead Sciences Canada I. Descovy® (emtricitabine/tenofovir alafenamide) tablets: (200 mg/25 mg) antiretroviral agent [product monograph]. In: Gilead Sciences Canada I, editor. Foster City, CA, USA2022

44. ViiV Healthcare . Apretude® (cabotegravir) tablets: (30 mg), (cabotegravir) Extended Release Injectable Suspension 200 mg cabotegravir/mL (600 mg/3mL)antiretroviral agent [product monograph]. In: ViiV Healthcare ULC, editor. Montreal, QC, Canada 2022

45. Landovitz RJ, Donnell D, Clement ME, Hanscom B, Cottle L, Coelho L, et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. N Engl J Med. 2021 Aug 11;385(7):595–608.

46. Landovitz RJ, Hanscom BS, Clement ME, Tran HV, Kallas EG, Magnus M, et al. Efficacy and safety of long-acting cabotegravir compared with daily oral tenofovir disoproxil fumarate plus emtricitabine to prevent HIV infection in cisgender men and transgender women who have sex with men 1 year after study unblinding: a secondary analysis of the phase 2b and 3 HPTN 083 randomised controlled trial. Lancet HIV. 2023 Dec 1;10(12):e767–78.

47. K. Junine Toy, Raquel M. Espinoza (2025 March 9-12), Characteristics of Persons Diagnosed with HIV in a Population-Based PrEP program in British Columbia, [Abstract]l San Francisco, CA https://www.croiconference.org/abstract/3499-2025/

48. Delany-Moretlwe S, Hughes JP, Bock P, Ouma SG, Hunidzarira P, Kalonji D, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. Lancet Lond Engl. 2022 May 7;399(10337):1779–89.

49. Gandhi RT, Landovitz RJ, Sax PE, et al. Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society–USA Panel. *JAMA.* 2025;333(7):609–628. doi:10.1001/jama.2024.24543

50. ViiV Healthcare, APRETUDE (cabotegravir 200mg/ml extended release injectable suspension) Dosing and Administration Guide, ViiV, USA, 2024

51. Eshleman et al. The LEVI syndrome: Characteristics of early HIV infection with Cabotegravir for PrEP, Conference on Retroviruses and Opportunistic Infections, Seattle, Washington, Feb 19-22 2023

52. Gandhi RT, Landovitz RJ, Sax PE, et al. Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society–USA Panel. *JAMA.* Published online December 01, 2024. doi:10.1001/jama.2024.24543

53. RJ Landovitz *et al.* Performance characteristics of HIV RNA screening with long-acting injectable cabotegravir (CAB-LA) pre-exposure prophylaxis (PrEP) in HPTN. International AIDS Conference. Tuesday, July 23, 2024.

54. Meyers K, Nguyen N, Zucker JE, Kutner BA, Carnevale C, Castor D, et al. The Long-Acting Cabotegravir Tail as an Implementation Challenge: Planning for Safe Discontinuation. AIDS Behav. 2023 Jan;27(1):4–9

55. Shaik JSB, Ford SL, Lou Y, et al. A Phase 1 Study to Evaluate the Pharmacokinetics and Safety of Cabotegravir in Patients With Hepatic Impairment and Healthy Matched Controls. Clin Pharmacol Drug Dev. 2019;8(5):664-673. doi:10.1002/cpdd.655