Alberta HIV Pre-Exposure Prophylaxis (PrEP) Guidelines

February 17, 2021

Alberta Health Services

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Summary of Changes

Date of update	Chapter: Title	Subsection: Title	Page	Update
February 2021	Drug regimens for PrEP	Daily PrEP	8	F/TAF added
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February 2021	Appendix I added	Client Assessment & Checklist Prior to Initiation of HIV PrEP	31	Checklist added
February 2021	Appendix J added	HIV PrEP Flow Sheet	35	Flow Sheet added

.

Abbreviations

ACB - Afro-Caribbean Black population

CAB LA - long acting injectable cabotegravir

HAV/HBV/HCV-hepatitis viruses A, B and C respectively

HIRI-MSM-HIV incidence risk index

HIV- human immunodeficiency virus

HPV - human papilloma virus

MSM -men who have sex with men

nPEP -non-occupational post-exposure prophylaxis

POD - PrEP on-demand

PrEP- HIV pre-exposure prophylaxis

PWID - persons who inject drugs

STBBI – sexually transmitted and blood-borne infection

STI – sexually transmitted infections

TDF/FTC or F/TDF - Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg

TAF/FTC or F/TAF - Tenofovir alafenamide 25 mg/emtricitabine 200 mg

February 17, 2021

This document has been prepared by members of the Alberta STBBI-OSAP in partnership with PEP and PrEP working groups. The document has been updated by the scientific PrEP committee consisting of Jennifer Gratrix, Lindsay Rathjen, Dr. Caley Shukalek, Dr. Julia Carter, Dr. Ameeta Singh and Dr. Petra Smyczek.

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Introduction and Background

The newest addition to the list of existing HIV prevention strategies, **HIV pre-exposure prophylaxis (PrEP)**, when taken daily, is a highly effective pharmacologic means of preventing HIV infection.

PrEP should be used as part of a comprehensive HIV prevention strategy involving the care and treatment of HIV infected individuals, condom use, and behavioural strategies to minimize the risk of HIV acquisition with the goal of reducing or eliminating new HIV infections in HIV negative persons.

Medications for use as PrEP covered under the Alberta HIV PrEP program are daily generic F/TDF (Tenofovir disoproxil fumarate 300mg + Emtricitabine 200mg[1]) by persons at high and ongoing risk for HIV infection.

Early concerns about PrEP included selecting for HIV antiretroviral drug resistance and encouraging riskier sexual behavior thereby increasing the rates of other sexually transmitted infections (STIs):

- PrEP can lead to HIV drug resistance if a person initiates or continues PrEP when already HIV seropositive; this may arise when PrEP is initiated by persons with undiagnosed acute HIV infection. Resistance arising during PrEP use is rare, but was seen in the FEM-PrEP and VOICE trials in persons in whom medication adherence was questionable (Van Damme, 2012; Marrazzo, 2015). Six cases of PrEP failure have been reported in MSM who likely experienced primary HIV infection with strains resistant to F/TDF (Knox, 2017; Markowitz, 2017; Hoornenborg, 2017; Cohen, 2018; Colby, 2018; Thaden 2018).

- A meta-analysis by Traeger et al. 2018 suggests an increase in condomless sex and STI diagnoses in MSM on PrEP.This finding highlights the importance of counselling regarding condom use and other safer sex practices, and the central role of regular STI testing in patients taking PrEP.

- Linking regular STI testing to ongoing HIV PrEP provision will allow earlier detection and treatment of incident STIs, provision of hepatitis A/B and HPV vaccine to non-immune individuals, and is anticipated to reduce the burden of sexually transmitted and blood borne infections (STBBI).

[1]Brand name Truvada®

Guiding principles

The Alberta HIV PrEP program is designed to ensure equitable access to the full range of HIV prevention strategies (including PrEP) for people at risk of HIV infection. Access to PrEP is predicated on specific eligibility criteria based on the best available evidence. Eligibility is based on identifying those patients at high risk of acquiring HIV infection, who are therefore most likely to benefit from the intervention.

PrEP should be discussed and considered for all patients who fit the eligibility criteria and wish to optimize their HIV prevention strategies. PrEP should be accessible to all Albertans at risk of HIV infection regardless of geographic location, recognizing that patients in rural and remote areas of the province may have special challenges to gaining access to PrEP and appropriate follow-up.

Drug Regimens for PrEP

PrEP is generally prescribed as daily continuous prophylaxis, and the majority of the data is related to this use (Grant et al 2010, Grant et al 2014). Efficacy is highly dependent on adherence to the regimen, with highest efficacy seen among the most adherent patients (Grant et al 2014).

F/TDF (fixed drug combination Tenofovir 300 mg / Emtricitabine 200 mg[1]) one tablet daily, (continuous PrEP), received Health Canada approval in 2016 to reduce the risk of sexually acquired HIV infection in adults at high risk of exposure to the virus in combination with safer sex practices. In addition, available data supports the use of F/TDF for continuous PrEP for persons who inject drugs (PWID) and heterosexual persons.

F/TAF (fixed drug combination Tenofovir alafenamide 25 mg / Emtricitabine 200 mg[2]), one tablet daily (continuous PrEP) is an alternative option for PrEP with equal efficacy. F/TAF was approved in Canada in December 2020 and is not covered under the Alberta HIV PrEP program. F/TAF is not studied for persons at risk for HIV from receptive vaginal sex.

- **Daily PrEP**
    - F/FTC (for all eligible persons under the Alberta HIV PrEP program) one tablet daily
    - F/TAF one tablet daily

[2] Brand name Descovy®

There is some evidence to support intermittent ("on-demand") PrEP for some individuals; however, at present there is only evidence for the effectiveness of intermittent PrEP in MSM (no other risk factors) from a single randomized, placebo-controlled study (Molina et al.), showing an 86% efficacy. There is no efficacy data for any other risk category.

- **Intermittent PrEP**- PrEP On-Demand (POD): **MSM only***
    - F/TDF 2 tablets taken 2-24 hours before HIV risk activity, then one tablet daily until 48hr after last risk activity (*Note that this is not a Health Canada-approved indication*)

*quality data exists only for MSM (IPERGAY study; Molina et al 2015). The recommendation for On-Demand PrEP is rated as weak in the Canadian Guidelines (Tan et al 2017) due to uncertainty around its effectiveness in more sporadic exposures (< once weekly) and lack of data to guide recommendations in other risk populations. In particular, On-Demand PrEP is not recommended for women and Trans men having vaginal sex, due to the long time required to achieve protective vaginal drug levels. The data pertaining to "time on therapy to prevent HIV infection" is in evolution. Maximal intracellular levels of F/TDF are achieved after 7 days of dosing in rectal tissue, and at 20 days in cervico-vaginal tissue (Anderson PL et al 2011). **POD is not recommended for patients with chronic HBV infection due to the risk of exacerbating a disease flare caused by exposure to, then withdrawal from, F/TDF.**

- **Injectable PrEP**

Recent studies comparing long acting injectable cabotegravir (CAB LA) injected once every 8 weeks was superior to oral F/TDF for HIV prevention among cisgender men and transgender women who have sex with men (HPTN 083) https://www.hptn.org/news-and-events/press-releases/hptn-083-study-demonstrates-superiority-cabotegravir-prevention-hiv. **and cisgender women (HPTN 084)** The HIV Prevention Trials Network | Prevention Now (hptn.org). However, CAB LA is not currently approved for use in Canada for HIV PrEP.

PrEP Eligibility Criteria

(adapted from 2017 Canadian guidelines, Tan et al 2017)

1. **MSM, Trans Women and Gender Diverse People**
   - Condomless anal sex within the last 6 months **and** any of:
     - Infectious syphilis or bacterial STI (gonorrhea or chlamydia) in the past 12 months. This recommendation is expanded from the Canadian criterion specifying rectal bacterial STI given the limited uptake of extra-genital testing in Alberta).
     - nPEP (non-occupational HIV post-exposure prophylaxis) more than once
     - Ongoing sexual relationship with HIV-positive partner(s) with substantial risk of transmissible HIV (e.g. viral load detectable (>40 copies/mL*) or HIV status unknown but from a higher risk population, e.g. MSM, PWID)
     - HIRI-MSM risk score ≥ 11 (HIV Infection Risk Index for MSM; see Appendix A: HIRI-MSM risk assessment tool)
   - Not indicated for those in a monogamous relationship with a single partner with no or negligible risk of having transmissible HIV (e.g. HIV negative, HIV positive but virus suppressed with viral load ≤ 40 copies/mL*, or HIV status unknown but risk profile similar to the general population (Tan et al 2017)).
   - Gender diverse people are included in the eligibility criteria as incorrect assumptions can be made about the sexual practices of individuals.
2. **Heterosexual People**
   - Recommended for the HIV-negative partner in an ongoing relationship with an HIV-positive partner involving condomless vaginal or anal sex, where the HIV-positive partner has a substantial risk of having transmissible HIV (i.e. not on antiretroviral treatment)
   - Consider PrEP for the HIV-negative partner in similar situations where the HIV-positive partner has a lower, but non-negligible risk of transmissible HIV:
     - viral load detectable (>40 copies/mL*) or

- viral load usually undetectable* but concomitant STI present at time of exposure (recognizing that undetectable viral load gives a very low likelihood of transmission, but the presence of an STI may increase the presence of virus in ulcers (Boily MC et al 2009) or at mucosal surfaces), or

- HIV status unknown, but from a high-prevalence population- MSM, PWID, countries with high HIV prevalence (see UNAIDS AIDS info. http://aidsinfo.unaids.org. Accessed 22 Feb 2018). Also see Appendix B for Alberta HIV Epidemiology.

3. **PWID (People Who Inject Drugs)**

- PrEP may be considered when there is ongoing or anticipation of ongoing sharing of injection drug use paraphernalia (needles, syringes, spoons, foil, cotton filters etc.) with a person with a non-negligible risk of HIV infection:

  - Detectable viral load* **or**

  - HIV status unknown but from a high-prevalence population- MSM, PWID, countries with a high HIV prevalence.

*for the purposes of this document, an undetectable viral load is defined by 2 sequential measurements of HIV viral load <40 copies/mL on at least 2 occasions separated in time by 4-6 months.

Note: Although not validated in Alberta, the ARCH-IDU Risk Score (See *Appendix C: ARCH-IDU Risk Scoring Sheet*) may be a useful tool for assessing PWID for suitability for HIV PrEP.

PrEP and Specific Populations

- **Hepatitis B (HBV)**

  - F/TDF and F/TAF have activity against Hepatitis B virus (HBV). Careful consideration should be given to the safety of prescribing PrEP to patients with chronic HBV infection, as withdrawal can lead to serious, and potentially life-threatening flares of HBV activity. If PrEP is prescribed to a person with chronic HBV infection, monitoring for HBV should be done as per Canadian Hepatitis B treatment guidelines (Coffin CS et al, 2018) in consultation with a

Hepatologist or Infectious Diseases (ID) specialist experienced in treating HBV;

- In a patient with chronic HBV who is also receiving PrEP with F/TDF or F/TAF, when considering PrEP discontinuation the need for ongoing alternative HBV treatment must be assessed. If PrEP is discontinued and no other therapy for HBV is used, close monitoring of disease activity is advised, and the patient should be followed by a specialist experienced in chronic HBV management.

- **Pregnancy and Breastfeeding**

  - PrEP may be considered during pregnancy and breastfeeding after the benefits and risks have been discussed with the patient (Appendix D: Risks and Benefits of PrEP in the Patient who is Pregnant). Suggest management in conjunction with an HIV/ID specialist. F/TAF is not studied for persons at risk for HIV from receptive vaginal sex

- **Renal dysfunction/Osteoporosis:**

  - In general, PrEP with F/TDF is contraindicated in people with renal dysfunction (eGFR < 60 mL/min). In view of the possible effect of TDF leading to bone loss/osteopenia and/or in those with high fracture risk, careful consideration should be given to the risks and benefits of PrEP in such patients. In either case, if PrEP is contemplated, the patient should be managed in conjunction with an HIV/ID specialist.

  - In a recent large multi-center study, F/TAF showed more favorable changes in key markers of kidney function and bone mineral density. (Ogbuagu et al., 2020).

Starting PrEP

(*See Appendix E: Patient Education and Pre-PrEP Education*)

Starting PrEP:

- There are several pathways that can lead to any given patient being assessed for HIV PrEP:
  - Patient request
  - Physician recognizes that patient is in a risk category

  - Referral from other health care provider (includes nPEP program)
  - Referral from community-based organization
  - Patient already on PrEP from another jurisdiction

- The initial discussion between patient and PrEP prescriber must include (appendix I):
  - Ruling out existing HIV infection
    - HIV testing using a 4th generation HIV test (ideally within 2 weeks of initial PrEP visit).
    - Evaluating for symptoms/signs of an HIV seroconversion illness that might suggest patient is in early stage of HIV infection.
    - If the HIV test is positive, refer patient for HIV clinical care and follow-up.
    - If there is clinical concern about HIV seroconversion, delay initiation of PrEP until the results of HIV testing are available.
  - Review the indications for PrEP and estimate the risk for the individual patient.
  - Review the existing HIV prevention strategies that the patient is already using and provide counselling on additional strategies in addition to PrEP. (*See Appendix F: HIV/STI Risk Reduction Strategies*).
  - Evaluate for the presence of syndemic conditions that may increase the risk of HIV acquisition in that particular patient (*See Appendix G: Management of Syndemic Conditions*).
  - Discuss the vital importance of adherence to the PrEP regimen to obtain optimal protection against HIV infection. Assess motivation of patient to adhere at that point in time, and in the future (See Appendix H: Medication Adherence Support).
  - Review possible side effects and what the patient should do if any are experienced.

- If the provider and the patient agree that a course of PrEP is warranted, additional laboratory assessment as per ***Table 2- Laboratory*** below, including STI testing, is done at baseline then again with each visit for medication renewal.

- Once the baseline testing is done, if the patient is HIV negative with no symptoms/signs of acute HIV seroconversion illness, write a script for PrEP medication –1 tablet daily x 30 days, with an appointment for follow-up in 30 days to repeat the clinical and laboratory assessment, and to address any issues related to side effects (see ***Table 1- Clinical Assessments*** below) or adherence.

- After the 30 day visit, if there are no concerns, write a script for PrEP – 1 tablet daily x 3 months, with appropriate follow-up, as per Tables 1 and 2, every 3 months (appendix J).

- If the patient is being evaluated for PrEP during a course of nPEP involving F/TDF, and if the appropriate counselling and baseline testing has been done, the patient can be prescribed a full 3 months prescription and continued on PrEP with the usual follow-up. HIV testing should be repeated at 28 days as recommended after starting nPEP.

Stopping PrEP

PrEP should be discontinued immediately if the patient has a positive HIV test (to reduce the risk of antiretroviral drug resistance), and referred for active HIV care.

- PrEP should be discontinued electively if the patient no longer meets eligibility criteria, has a decline in renal function, or if the patient does not adhere to ongoing follow up requirements.

- If the decision has been made electively to discontinue PrEP, it should be continued for 28 days after the last risk exposure before stopping, with follow-up HIV testing at up to 8 weeks after discontinuation. At present, it is unclear how long PrEP should be taken after the last exposure. The IPERGAY trial (Molina et al 2015) suggests that a minimum of 2 daily doses is needed but insufficient data is available to be confident that more doses are not needed; in the absence of definitive data, the Canadian guidelines recommend continuing for up to 28 days after the last exposure (Tan et al 2017).

- If PrEP is to be restarted in the future, repeat HIV risk assessment and baseline laboratory testing before re-prescribing PrEP.

Designated PrEP Prescribers in Alberta

Patients who meet the eligibility criteria may wish to access PrEP through the government-funded Alberta program to have their PrEP paid for. To access this program, the patient must be seen and assessed by a Designated PrEP Prescriber. Designated Prescribers (currently physicians and nurse practitioners) will be authorized upon filling out an application form, and if approved by AHS, upon completion of a PrEP prescriber education module.

To see a list of Designated PrEP Prescribers, or to apply to become a Designated PrEP Prescriber, go to https://www.albertahealthservices.ca/info/Page16048.aspx

Initial Assessment for PrEP and Follow-up Reassessments

(adapted from Canadian PrEP guidelines; Tan et al. 2017)

Table 1 – Clinical Assessments

Clinical	Baseline	At 30 days	Every 3 months
Symptoms of HIV seroconversion?	X	X	X
Indications for PrEP	X	X	X
Using other HIV/STI prevention strategies? See *Appendix D- Risk Reduction Strategies*	X	X	X
Adherence assessment & support counseling See *Appendix E- Adherence Support*	X	X	X
Side effects Common: headache, nausea, flatulence, abdominal pain, decreased weight; typically resolve in a few weeks of starting TDF/FTC Less Common: see Truvada™ Product Monograph	X	X	X
HPV assessment + vaccine if indicated	X		
Syndemic conditions- presence/ Management See *Appendix F- Management of Syndemic Conditions*	X	X	X

Table 2 - Laboratory Assessments

Laboratory	Baseline	At 30 days	Every 3 months	Every 12 months
HIV test (4th generation test)[a]	X	X	X	
HAV immunity[b] (order HAV IgG)	X			
HBV screen[b] (order HBsAg, anti-HBs and anti-HBc total)	X			
HCV serology (order HCV antibody)	X			X
GC/Ct urine NAAT **and** rectal/throat NAAT	X		X	
Syphilis serology	X		X	
CBC	X			
Creatinine (serum)	X	X	X	
Urine R&M	X			
Pregnancy test	X		X	
Bone density assessment[c]				

[a] All Alberta laboratories currently use 4th generation HIV tests. HIV Point-of-care (POC) tests in Alberta are 3rd generation tests (INSTI HIV-1/HIV-2 Rapid Antibody Test) with a longer window period. At present, all positive POC tests are confirmed by standard HIV serology using a 4th generation test.

[b] Offer vaccine to all non-immune or unvaccinated patients.

[c] Not routinely recommended unless other factors for bone loss/fracture are present

Appendix A: HIRI-MSM risk assessment tool

Adapted from Canadian Guidelines on HIV PrEP and nPEP, version 2.1, November 13, 2017. Note that this tool has not been validated in Alberta and its performance characteristics are unknown in our population.

Question Number	Question	Response	Score
1	How old are you today? (years)	< 18 years 18 – 28 29 – 40 41 – 48 ≥ 49	0 8 5 2 0
2	How many men have you had sex with in the last 6 months?	>10 6 – 10 0 – 5	7 4 0
3	How many of your male sex partners were HIV positive?	> 1 positive partner 1 positive partner < 1 positive partner	8 4 0
4	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom?	≥ 1 time 0 times	10 0
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	5 or more times 0 – 4 times	6 0
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes No	5 0
7	In the last 6 months, have you used poppers (amyl nitrate)?	Yes No	3 0
		Total	

Appendix B: Alberta HIV Epidemiology

It is helpful to consider the subpopulations of Albertans who are at higher risk of acquiring HIV infection. Using subpopulation proportions from the 2011 Canada-wide data (Yang Q et al 2011), the 2019 Alberta HIV incidence data (http://www.ahw.gov.ab.ca/IHDA_Retrieval/), and recalculating from most recent Alberta population data; total population 4,371,324):

- Alberta population 15 years or older = 3,551,455
- Overall HIV incidence rate (2019) = 5.8/100,000
- **Men having sex with men (MSM)** population (2.6% of male population ≥15 years) = 46,295 MSM individuals
    - 64 new cases of HIV in MSM in 2019 for a rate of 138/100,000
- **People who inject drugs (PWID)** population (0.39% of total population) = 13,850 PWID individuals
    - 30 new cases of HIV in PWID in 2019 for a rate of 217/100,000
- **Indigenous population** (6% of the population ≥15 years) = 213,087 Indigenous individuals
    - 44 new cases of HIV in Indigenous people in 2019 cases for a rate of 21/100,000
- **Afro-Caribbean Black (ACB)** population (3.3% of the population ≥15 years) = 117,187 individuals
    - 86 new cases of HIV in ACB people in 2019 for a rate of 73/100,000 ACB individuals
- **Heterosexual people from an HIV endemic country** (2.5% of population ≥15 years) = 88,786 heterosexual individuals from HIV endemic countries
    - 20 new HIV cases in 2019 for a rate of 23/100,000
- There is no denominator data for the category **"Heterosexual/partner at risk"**, however its numerator magnitude is similar to that of "Heterosexual/HIV endemic country".
- **Sex workers** are not included as a discrete risk category, as their level of risk varies widely, and the Alberta data would suggest that virtually all people who identify "sex work" or "received money or goods for sex" as their HIV risk would have been eligible for PrEP consideration through another risk category.
- ACB are likewise not included as a discrete risk category; nearly three-quarters of new ACB cases were present at the time of arrival in Canada.

Appendix C: ARCH-IDU Risk Scoring Sheet

Only consider completing IDU risk index if individual has injected non-prescription drugs in the last 6 months; consider PrEP for scores >45

Age (yrs)	If < 30 If 30 – 39 If 40 – 49 If > 50	Score 38 Score 24 Score 7 Score 0				
Methadone maintenance in the past 12 months?	Yes No	Score 0 Score 31				
In the last 6 months:						
Inject heroin?	If 1 or more times If 0	Sub-score 1 Sub-score 0				
Inject cocaine?	If 1 or more times If 0	Sub-score 1 Sub-score 0				
Share a cooker?	If 1 or more times If 0	Sub-score 1 Sub-score 0				
Share needles?	If 1 or more times If 0	Sub-score 1 Sub-score 0				
Visit a shooting gallery?	If 1 or more times If 0	Sub-score 1 Sub-score 0				
Add down the 5 injection sub-scores above						
Composite injection score				If 0 If 1 If 2 If 3 If 4 If 5	Score 0 Score 7 Score 21 Score 24 Score 24 Score 31	
Add down the three entries in the right column to calculate the total score						**Total Score:**

Reference: Smith DK, Pan Y, Rose CE, Pals SL, Mehta SH, Kirk GD, Herbst JH. A Brief Screening Tool to Assess the Risk of Contracting HIV Infection Among Active Injection Drug Users. J Addict Med. 2015 May-Jun;9(3):226-32.

Appendix D: Risks and Benefits of PrEP in the Patient who is Pregnant

Q: I'm worried about getting HIV from my partner who is HIV-positive while I'm pregnant. How do we know that it's a good idea for me to take PrEP?

A: Taking PrEP with F/TDF can be considered in pregnancy and breastfeeding if the benefits outweigh the risks. F/TAF is not recommended for persons at risk for HIV from receptive vaginal sex. HIV infection may be more likely to occur in people at risk of HIV acquisition during pregnancy, depending on the partner's risk of having transmissible HIV. If HIV infection occurs in the mother while pregnant, the risk of HIV transmission to the infant during delivery may be significant. If HIV infection in the mother occurs while breastfeeding, the risk of infection to the neonate is increased due to very high viral load in the mother immediately after infection occurs.

Q: How do I know that PrEP is safe for me and my baby?

A: There is very little data on the safety of PrEP per se in pregnancy and breastfeeding (Mugo NR et al. 2014). Advice is therefore derived from studies of women who already are HIV-infected and take TDF-containing regimens during pregnancy for active treatment of HIV. Aside from startup side effects that may occur in any patient, observational studies of HIV-infected women treated with TDF during pregnancy did not demonstrate an association with any adverse outcomes in the mother. In one study of women who became pregnant while on PrEP (Mugo N et al 2014), there were no significant differences in rates of getting pregnant or in pregnancy outcomes related to taking PrEP.

Q: I've heard that babies of people who took PrEP during pregnancy have weak bones. Is that true?

A: Neonates born to HIV-infected mothers who received TDF during pregnancy had lowered bone mineral density by 12% (Siberry et al 2015), however the same group in a subsequent study did not find any effect (Siberry et al 2016). At present, there is insufficient evidence to implicate F/TDF/for PrEP in any clinically significant bone disease in the infant.

Q: If I'm taking PrEP during breastfeeding, is my baby exposed to high levels of the drugs?

A: The level of exposure of the neonate to F/TDF due to breastfeeding is detectable but very low, with levels of drug in breast milk between 0.3% and 2% of active treatment levels for infants. PrEP may therefore be considered in breastfeeding women at high risk for HIV acquisition.

Appendix E: Patient Education and Pre-PrEP Education

Education has been a key component of many PrEP trials. Educational interventions in the PROUD (McCormack et al 2016) study covered HIV prevention, HIV testing, treatment, side effects of F/TDF adherence, PEP, STI testing and other HIV prevention strategies. In services supporting PrEP use (generic, private or public funding), the following topics should be covered in brief to ensure the patient has sufficient knowledge before starting PrEP:

- HIV transmission;
- How PrEP works
- HIV testing and window periods
- Side effects of F/TDF or F/TAF
- Efficacy of PrEP and link to adherence
- Daily dosing and event-based regimens
- PEP for risks with suboptimal PrEP adherence
- Wider PrEP provision, including F/TDF or F/TAF
- STI testing/PrEP information resources
  - www.prepalberta.ca
  - Canadian AIDS Treatment Information Exchange (CATIE) http://www.catie.ca/en/prep
  - site has many online and printable resources for patient education
  - Center for Disease Control website has online educational resources https://www.cdc.gov/hiv/basics/prep.html
  - The World Health Organization (WHO) has an excellent module for patients considering PrEP http://apps.who.int/iris/bitstream/10665/258510/1/WHO-HIV-2017.31-eng.pdf?ua=1
  - There are apps available to help with remembering doses and scheduling appointments:
    - HIV Oral PrEP (Johns Hopkins/WHO)
    - MyPrEP (alarms and calendar notification of drug doses and follow up visits)
  - Harm reduction strategies and spaces, especially for PWID

Both internationally and within the UK PROUD study, uptake of PrEP has been greater amongst MSM with higher levels of formal education and associated socioeconomic resources (e.g. Caucasian, full-time employment). Educational needs of MSM beyond those seen in the PROUD study may be greater.

Similarly, it seems likely that other communities, particularly those who experience greater stigma or who have less engagement with HIV, may have significantly different and greater educational needs. More research is needed around knowledge, attitudes

and acceptability of PrEP within other groups at risk of HIV acquisition, especially, but not limited to, African/Black/Caribbean or trans people.

Key PrEP Messages for Patients

(adapted from WHO Implementation Tool for pre-exposure prophylaxis (PrEP) of HIV infection. Module 1: Clinical. Geneva: World Health Organization; 2017 (WHO/HIV/2017.17). Licence: CC BY-NC-SA 3.0 IGO)

Effectiveness

Message: PrEP is highly effective if you take it as prescribed.

Ways to support adherence

Message: Taking PrEP each day is easiest if you make taking the tablets a daily habit, linked to something else that you do every day without fail.

- There are many ways to support adherence. For example, considering daily habits that could be linked with taking PrEP tablets, such as brushing teeth, after the evening meal, watching a daily television program.
- Other ways to facilitate adherence include disclosing PrEP use to a partner or trusted person; using reminder devices, such as mobile phone alarms or medication reminder apps, can also be considered.

Message: If you forget to take a tablet, take it as soon as you remember. If it's less than 12 hours before the next dose, wait until the next dose. If you've forgotten a dose, don't take a double dose, as it will increase the likelihood of a side effect without giving you any additional benefit.

Message: PrEP tablets can be taken any time of day, with food or without food.

Message: PrEP can be taken with alcohol, although excess alcohol can impair memory and make it difficult to remember to take medication. If you are going to drink, plan ahead and set reminders.

Message: Taking PrEP is a responsible choice; it's responsible to protect yourself, your sex partners and your community.

- Not everyone will understand your decision to use PrEP.
- Seeking support from your friends and other people who use PrEP can be helpful.

Message: PrEP is safe and effective even if you are taking hormonal contraceptives, sex hormones or nonprescription medications.

- There are no drug interactions between the PrEP medicines and hormonal contraceptives or sex hormones so they can be safely taken together.

Message: In people taking PrEP, use non-steroidal anti-inflammatory medication (NSAIDs e.g. ibuprofen, naproxen, etc.) and other nephrotoxic drugs with caution due to the possibility of kidney injury.

Starting PrEP

Message: You should use additional HIV prevention measures for at least 7 days after starting PrEP.

- PrEP provides high levels of protection in people who take PrEP regularly.
- Time is needed to build up protective levels of the drug in the blood and other tissues (7 days for anal tissue, 20 days for vaginal tissue).
- Ways to lower risk during this period include: adopting safer sexual practices, such as, not having vaginal or anal intercourse, or using condoms for all vaginal and anal intercourse.

Stopping PrEP

Message: You can stop PrEP 2-28 days after your last possible HIV exposure. We don't know yet if 2 days post-exposure is really enough, so some experts recommend a full 28 days. People can consider stopping PrEP if they are no longer at substantial risk of acquiring HIV infection. Ways to lower risk include:

- adopting safer sexual practices, such as not having vaginal or anal intercourse, or using condoms for all vaginal and anal intercourse
- changing circumstances such as leaving sex work or stopping injection drug use
- For people in an ongoing relationship with an HIV-positive partner, there is effectively no HIV transmission risk when the HIV-positive partner is on HIV treatment and has a confirmed, sustained undetectable viral load (Tam T, Morrison H. Statement on behalf of the Council of the Chief Medical Officers of Health, issued 30 November 2017.

PrEP doesn't interact with recreational drugs or alcohol

Message: Taking alcohol or using substances (recreational drugs) such as heroin and other opioids, cocaine or methamphetamine will not reduce the effectiveness of PrEP.

No STI protection (other than HIV infection)

Message: PrEP does not prevent sexually transmitted infections other than HIV.

- PrEP does not prevent syphilis, gonorrhea, chlamydia, chancroid, Herpes, HPV, or trichomonas
- Correct and consistent use of condoms provides protection against many STIs, especially urogenital gonorrhea and chlamydia, which are transmitted through the exchange of fluids rather than by skin-to-skin contact.
- Seek medical attention if you develop:
    - discharge from urethra, anus or vagina
    - anal pain, burning with urination
    - oral, anal or genital sores
    - rash, especially on palms or soles of feet
- Regular testing for STIs is recommended at each PrEP prescription renewal, even if you don't have any symptoms

No contraceptive effect

Message: PrEP does not prevent pregnancy.

- PrEP medicines can be taken safely with all contraception methods
- If you want to become pregnant, ways to become pregnant safely should be considered.
- PrEP can be used in pregnancy and during breastfeeding if HIV risk continues to be substantial during this time.

Appendix F: HIV/STI Risk Reduction Strategies

Behavioural strategies for risk reduction

In the era of PrEP, behavioural methods of risk reduction retain their importance in preventing HIV infection and remain the pillar of STI prevention. F/TDF and F/TAF are approved for use as PrEP in both Canada and the USA "in conjunction with other safer sex practices". PrEP is an additional prevention strategy which can be added to other known effective methods of HIV prevention to reduce overall risk.

As part of the initial assessment of the patient being considered for PrEP, as well as at each follow up visit, it is prudent to evaluate the patient's use of other risk reduction strategies, and to promote their use along with PrEP to optimize that patient's overall risk reduction.

Discussion points on behavioural reduction of HIV and STI risk

Establish trust and two-way communication.

Provide feedback on HIV risk factors identified during sexual and substance use history taking.

- Take a good sexual history and substance use history
- Discuss known strategies to reduce risks associated with sex:
  - Limit number of partners
  - Know your partners, including HIV status and treatment/viral suppression status if positive
  - Discussion regarding the insertive vs receptive positions in penetrative sex as related to HIV transmission risk
  - Discussion of risk related to presence/absence of foreskin
- Elicit barriers to, and facilitators of, consistent condom use. Refer patient to: https://www.catie.ca/en/prevention/statements/condoms

- Elicit barriers to, and facilitators towards reducing substance abuse. Consider using the Information-Motivation-Behavioural Skills model (Fisher et al. 2003) for these assessments.
- In these discussions be aware of and sensitive to some of the potentially stigmatizing antagonism evolving between proponents of condom use and proponents of PrEP for HIV risk reduction.

Support risk-reduction efforts

- Help patient identify 1 or 2 feasible, acceptable, incremental steps toward risk reduction
- Identify and address anticipated barriers to accomplishing planned actions to reduce risk

Monitor medication adherence in a non-judgmental manner

- Acknowledge the effort required for behaviour change
- Reinforce success. If not fully successful, assess factors interfering with completion of planned actions and help patient identify the next steps (including PrEP prescriptions)

Refer patient for additional support:

- Community grassroots support/advocacy organizations
- Sexual health peer support
- Community behavioural change (e.g. motivational interviewing) or therapeutic change (e.g. counselling) services
- Drug & alcohol-related services- needle distribution, harm reduction, supervised consumption sites, opioid agonist therapy, and drug withdrawal and treatment programs.
- Community online support and trans specific clinics where available
- Mental health services, community counselling

Appendix G: Management of Syndemic Conditions

Definition: A syndemic, or synergistic epidemic, is the aggregation of two or more concurrent or sequential epidemics or disease clusters in a population with biological interactions, which exacerbate the prognosis and burden of disease (Singer M, 2009).

Known examples from the literature known to increase the risk of acquiring HIV infection (Stall R, 2003; Santos G-M, 2014; Wilson PA, 2014):

- Depression
- Substance use including alcohol
- Violence including intimate partner violence
- Sexual stigma- MSM, trans people, other gender diverse groups
- Homelessness
- Incarceration

Studies from Toronto showed high rates of depression (42%), problem alcohol use (37.5%) and problem drug use (34.5%) in MSM seeking or using PrEP (Tan 2016, Coleman 2015)

HIV risk is positively correlated with the number of coexisting syndemic conditions a given person suffers from- the more coexisting syndemic conditions, the higher the HIV acquisition risk.

Conversely, there are known mitigating factors, the so-called “Resiliency factors” (O’Leary A 2014):

- Social network size
- Connection to the gay community
- Cultural pride
- Optimism
- Education
- Income

It is important for clinicians to keep in mind that the presence of syndemic conditions and psychosocial comorbidities **are not exclusion criteria** for being on HIV PrEP. In fact, the presence of these conditions indicates increased risk and identifies patients who might most benefit from being on PrEP.

There are several validated and well-recognized screening tools available for assessing depression and substance-use disorders. These tools are not intended to be additional eligibility criteria, but instead to modify the degree of risk that any given patient might

experience, given that risk is directly correlated with the accumulation of coexistent syndemic conditions. Some examples of the most commonly used tools are given below:

Depression screen (CES-D; Centre for Epidemiologic Studies- Depression)
http://www.valueoptions.com/providers/Education_Center/Provider_Tools/Depression_Screening.pdf

Audit- Alcohol Use Disorders Identification Tool:
https://www.drugabuse.gov/sites/default/files/files/AUDIT.pdf

Dudit- Drug Use Disorder Identification Tool:
http://www.drugs.ie/NDRICdocs/protocol1/templates/DUDIT.pdf

Appendix H: Medication Adherence Support

Optimal adherence to the PrEP drug regimen is vital to getting the maximal effectiveness from taking PrEP. Prescribers should provide counselling to patients contemplating PrEP or who are taking PrEP regarding ways to maximize their adherence.

Establish trust and two-way communication and recognize factors that may indicate more intense adherence support requirements

- Person experiences high levels of stigma
- Abusive/violent relationships
- Young MSM
- Housing instability

Provide simple explanations and education

- Medication dosage and schedule
- Management of common side effects
- Relationship of adherence to the efficacy of PrEP
    - It is ideal to take daily PrEP at the same time of day to minimize significant fluctuations in drug levels
    - Although 7 daily doses/week is the ideal PrEP regimen, there is evidence that efficacy may be maintained with a few missed doses as long as 4-7 doses per week are taken (Grant 2014).
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence

- Identify and address barriers to adherence, including mental health issues and addictions
- Tailor daily dose taking to patient‘s daily routine e.g.
    - With tooth brushing, before bed etc.
    - Practice with one-a-day vitamin then replace with F/TDF
    - Strategize around remembering pill while travelling
- Identify reminders and devices to minimize forgotten doses
    - Alarms
    - Medication compliance apps
    - Storage options- key ring pill bottle, storing pills at home/work etc.

    - Help from partner(s) or trusted person
- Frequency of follow-up visits- may require more frequent visits to support ongoing adherence.

Monitor medication adherence in a non-judgmental manner

- Let patient know that monitoring (pill count, pharmacy records, self-report) is to help them with their adherence plan.
- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Plan with patient for management of missed doses:
    - If < 12 hours, take dose as soon as it's remembered
    - If > 12 hours, wait until next regularly-scheduled dose
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address these factors

Appendix I: Client Assessment & Checklist Prior to Initiation of HIV PrEP

Client Assessment & Checklist Prior to Initiation of HIV PrEP

Date: _____

Risk Evaluation & Eligibility Assessment for PrEP:

Currently on HIV PrEP ☐ No ☐ Yes, for how long:_____
Past use of HIV PrEP ☐ No ☐ Yes

Previous use of non-occupational PEP: ☐ No ☐ Yes, # of times: _____

Best describes gender identity:
☐ Cisgender man ☐ Cisgender woman ☐ Transgender man
☐ Transgender woman ☐ Self-describe _____

Race/Ethnicity:
☐ White ☐ Black ☐ Indigenous ☐ Latino ☐ Asian
☐ Other:_____
(Afro-Caribbean Black, Indigenous, and people from an HIV endemic country are at higher risk of HIV acquisition, refer to AB HIV PrEP Guidelines, Appendix B)

Identifies as:
☐ MSM, Trans, or gender diverse ☐ Heterosexual ☐ Person who injects drugs
☐ Other:_____

Sharing of drug use paraphernalia: ☐ No ☐ Yes

Sexual partner(s) who is/are HIV positive: ☐ No ☐ Yes ☐ Unknown

If yes, viral load of partner(s): ☐ Undetectable ☐ Detectable ☐Does not know
(AB HIV PrEP Guidelines: Undetectable viral load is defined by 2 sequential measurements of HIV viral load <40 copies/mL on at least 2 occasions separated in time by 4-6 months)

HIRI score (if MSM):_____
(HIRI score ≥11 would be an indication for PrEP; Refer to Canadian Guidelines on HIV PrEP, p. 13-14, AB HIV PrEP Guidelines Appendix A)

Condomless penetrative sex in the last 6 months: □ No □ Yes

Condom use: _____ out of 10

History of STI in last 12 months:
□ Chlamydia, site(s):_____
□ Gonorrhea, site(s): _____
□ Infectious syphilis

Symptoms of HIV seroconversion: □ No □ Yes, describe:_____
(Refer to Canadian Guidelines on HIV PrEP, Supplementary Box 1, p. 18. If HIV seroconversion suspected contact a HIV specialist.

Currently pregnant: □ N/A □ No □ Yes, # of weeks gestation: _____
(Refer to Canadian Guidelines on HIV PrEP, p. 22; AB HIV PrEP Guidelines, p. 8, Appendix D)

Currently breastfeeding: □ N/A □ No □ Yes
(Refer to Canadian Guidelines on HIV PrEP, p. 22; AB HIV PrEP Guidelines, p. 8, Appendix D)

Risks & Medical Management of PrEP:

Immunizations:

HPV vaccine complete:	□ No	□ Yes	□ Unknown
Hepatitis A vaccine complete:	□ No	□ Yes	□ Unknown
Hepatitis B vaccine complete:	□ No	□ Yes	□ Unknown

Is there a history of any of the following:

□ Kidney disease □ Medications affecting kidney function □ Hypertension

□ Liver disease (chronic Hepatitis B) □ Bone Density issues

_____

_____

_____

(Prescription of PrEP in chronic Hep B is best managed by a specialist, refer to Canadian Guidelines on HIV PrEP, p. 21-22; AB HIV PrEP Guidelines, p. 13)

Are there concerns with any of the following syndemic conditions?
(Risk of acquiring HIV infection and difficulty with adherence to PrEP may be increased in the presence of syndemic conditions. Refer to AB HIV PrEP Guidelines, Appendix C/G)

□ Depression □ Substance use including alcohol □ Violence (partner violence)

□ Housing/Homelessness □ Employment □ Incarceration □ Sexual stigma

_____

_____

Key Messaging & Education for PrEP Clients:

- □ HIV transmission, HIV testing, window periods
- □ How PrEP works
- □ Efficacy of PrEP and link to adherence
- □ How to take PrEP: daily dosing for greatest efficacy
- □ Required baseline testing (Refer to *Canadian Guidelines on HIV PrEP*, p. 39; *AB HIV PrEP Guidelines*, p. 13)
- □ Required ongoing lab monitoring & clinic appointments at 30 days and q 3 months thereafter (Refer to *Canadian Guidelines on HIV PrEP*, p. 39; *AB HIV PrEP Guidelines, Table 2*)
- □ Strategies to support adherence (e.g. linking to a routine daily activity, phone reminders such as alarms or medication reminder apps, social supports)
- □ Management of missed doses (If < 12 hours late, take as soon as remembered; if >12 hours late, wait until next dose)
- □ Length of time until effective (7 days for anal tissue, 20 days for vaginal tissue)
- □ 30 day initial prescription followed by 3 month prescriptions only with no automatic refills
- □ Potential side effects and how to manage (Common side effects include headache, nausea, flatulence, abdominal pain, decreased weight. Most side effects usually resolve in a few weeks of starting PrEP. Changing schedule may help, e.g. taking with a meal.)

Patient has a family physician: ☐ Yes ☐ No

☐ Discussed copying client's family physician on lab results:

_____

If client wishes that family doctor be copied, indicate name and location on Physician Flowsheet

☐ Discussed referral to a family physician:

_____

Discussed how to discontinue using PrEP:

☐ Discontinue PrEP 2-28 days after last HIV exposure

☐ Follow-up HIV testing 8 weeks after discontinuation

Risk Reduction Strategies:

☐ Discussed PrEP as a strategy to reduce HIV risk in conjunction with other safer sex practices

☐ Discussed other strategies to reduce HIV risk: *e.g. Reducing # of partners, knowing partners including HIV status and treatment/viral suppression status if positive, insertive versus receptive position for anal sex (MSM)*

☐ Discussed barriers to, and facilitators of, consistent condom use

Client eligible for HIV PrEP:

☐ Yes, would like to proceed ☐ Yes, but chooses not to proceed

☐ No:_____

☐ CT & GC testing done as per exposure

☐ Lab requisitions given for serology testing

Physician signature: _____Date:_____

Adapted from Sexual and Reproductive Health Clinics Calgary

Appendix J: HIV PrEP Flow Sheet

Alberta Health Services

HIV PrEP Flow Sheet

Patient Name
Date of Birth
PHN

Baseline Assessment

Date: _____

Indication(s) for PrEP: _____

Syndemic Conditions: _____

HPV vaccine complete: ☐ Yes ☐ No _____

Hepatitis A vaccine complete: ☐ Yes ☐ No _____

Hepatitis B vaccine complete: ☐ Yes ☐ No _____

Outstanding Issues: ***(√ when complete)***

Date/Issue: _____ ☐

Date/Issue: _____ ☐

Date/Issue: _____ ☐

☐ Copy results requiring f/u to family doctor: ☐ Yes ☐ No

Name: _____ Location: _____

PrEP Baseline Testing	Testing Date	Result	Additional Information/Notes	Initials
CBC		☐ Done		
Urinalysis		☐ Done		
Creatinine / eGFR		_____ umol/L / _____ mL/min		
Hepatitis A (HAV IgG)		☐ Done ☐ Not applicable		
Hepatitis B (HBsAg, Anti HBs, Anti HBc total)		☐ Done ☐ Not applicable		
Hepatitis C (Anti HCV)		☐ Done		
HIV		☐ Done		
Syphilis		☐ Done		
Chlamydia		☐ Done		
Gonorrhea		☐ Done		
Pregnancy		☐ Done ☐ Not applicable		
Other				

Adapted from Sexual and Reproductive Health Clinics Calgary

Alberta Health Services

Patient Name
Date of Birth
PHN

HIV PrEP Flow Sheet

Follow-up Assessments

Date Initial PrEP Rx Provided: _____

	Follow-up #1 (at 30 days) Date: _____	Follow-up #2 (4 month visit) Date: _____	Follow-up #3 (7 month visit) Date: _____	Follow-up #4 (10 month visit) Date: _____	Follow-up #5 (13 month visit) Date: _____
Assessment:					
Symptoms of HIV seroconversion	☐ None ☐ See chart note	☐ None ☐ See chart note	☐ None ☐ See chart note	☐ None ☐ See chart note	☐ None ☐ See chart note
Adherence (i.e. missed doses)	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note
Indication(s) for PrEP	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note
Side Effects	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note	☐ No concerns ☐ See chart note
Syndemic Conditions	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note	☐ No change ☐ See chart note
Pregnancy Test Required		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Comments					
Lab Tests:					
HIV	☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note
Syphilis		☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note
Chlamydia/Gonorrhea		☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note	☐ Done ☐ See chart note
Creatinine					
eGFR					
Hepatitis C (Anti HCV)					
Hepatitis B (HBsAg, Anti HBs, Anti HBc total) (Screen annually if unimmunized)					
Other Tests:					
Provider Signature					

Adapted from Sexual and Reproductive Health Clinics Calgary

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