16th Ontario HIV Pharmacy Education Day

State of the Art HIV Treatment and Prevention Practices: A Case Scenario Approach for Pharmacists

Friday, October 18, 2024
Novotel, 45 The Esplanade, Toronto (Champagne Room)

Introduction

The 16th annual HIV Pharmacy Education day was centered on illustrating the pharmacists' role in HIV care and prevention with a clinical case-based approach. This event was held as a stand-alone education event. The Agenda included a plenary followed by two case scenarios, with a focus on treatment in the morning and prevention in the afternoon. Brief summaries are provided in this report.

Linda opened the day with a Land Acknowledgment and thanked all the partners and sponsors:

- Support: Ministry of Long-Term Care, HIV and Hepatitis Programs, and The Ontario HIV Treatment Network
- Planning committee: Linda Robinson, Sue Gill, Deborah Yoong, Alice Tseng and Pierre Giguere
- Sponsors: Gilead, ViiV Healthcare and Merck

First Plenary: Pre/Post Natal Care Update

Speaker: *Dr. Mona Loufty is an ID Specialist at Maple Leaf Medical Clinic and a Professor and Clinician Scientist at Women's College Hospital and University of Toronto. She founded the Women and HIV Research Program at the Women's College Research Institute, with a particular focus on pre-conception, pregnancy, parenthood, access to care, stigma, and women's and sexual and reproductive health.*

Practical cases review

Case #1: 34YO African woman, diagnosed with HIV in 2015, referred for pregnancy planning

- on TDF/FTC + DRV 800 mg/rtv 100 mg OD; VL<40 copies/mL and CD4=203 cells/L
- has been trying to get pregnant for 2y; low CD4 count might be causing fertility issues?
- send for quick referral to a Toronto Fertility Clinic where she did IVF[1]
- got pregnant in 2020: had a baby girl (HIV negative) whom she formula fed
- switched treatment to BIC/FTC/TAF; doing well and generally medically stable
- got pregnant again in 2023 and is due in 2024

Patient wants to change her treatment to a single tablet regimen and wants to breastfeed her baby: what would you recommend?

Case #2: 39YO woman living with HIV since 2003

[1]IVF in ON for women <43YO: everything covered, besides the hormonal treatment. Patient will get only 1 retrieval but can then receive as many embryo transfers as there were retrieved.

- presented with *Pneumocystis jiroveci* Pneumonia & esophageal candidiasis at diagnosis
- put on ABC/3TC OD + LPV/r BID at diagnosis, then switched to ABC/3TC + ETV 400 mg OD in 2007
- got pregnant in 2014 with a baby boy (HIV negative) whom she formula fed
- son diagnosed with autism: community felt it was because of formula and ARV
- got pregnant again in 2022 with a baby girl (HIV negative) whom she breastfed
- complex pregnancy management linked to complex medical history: PCOS; T2D; Hypertension; Obesity treated by laparoscopic gastric bypass; Postpartum depression
- other medications: Metformin 500 mg BID; Labetalol switched to Telmisartan/Amlodipine; Ferrous fumarate + IV Iron infusions; Vitamin B12 1000 mcg OD; Escitalopram 20 mg OD
- trouble with oral ARV adherence in 2023: VL=60 copies/mL
- switched to LA CAB/RPV (HepB negative; no medication history issue; Clade B virus)
- got pregnant in 2024

Patients wants to breastfeed this baby as well: what would you recommend? Would you keep her on CAB/RPV and, if so, switch to q1month? Or switch to an oral regimen and, if so, which one?

Dr. Mona's CAB/RPV checklist:

1. *Hep B status: Hep B surface Ab positive/Hep B negative*
2. *ARV history: CAB/RPV resistance associated mutations or INSTI/NNRTI mutations;*
3. *Virus subtype: CAB/RPV perform worse in subtype A1A6 virus (mostly found in Russia)*

(high BMI is not considered an issue anymore, based on clinical practice)

Context

Prenatal Care & HIV

All pregnant people living with HIV should be on ART and start ASAP (medical emergency)

Supported by data from French Perinatal Cohort (following the most parents/infants): no transmission between 2000 and 2017 in women undetectable before and throughout during and at delivery.

Recommended regimen: 2 NRTIs + Integrase Inhibitor (or Boosted PI/NNRTI as alternatives)

Presentation based on American DHHS Guidelines (updated annually) as Canadian SOGC Guidelines not on Open Access and are not updated regularly. Useful general statement from SOGC Guidelines: *Women living with HIV should generally continue to follow established regimens in pregnancy. There are uncommon situations where antiretroviral switching is indicated following specialist review.* There are often risks when switching regimen in pregnancy (e.g. side effects, adherence challenges) so preference is to not switch unless contraindication.

DHHS Guidelines recommendations (as of 31 Jan 2024) for regimens:

- Preferred: acceptable toxicity and ease of use; pregnancy specific PK data to guide dosing

Dual NRTI backbone	INSTI regimens	PI regimens
ABC/3TC – w/ HLA B5701 -	DTG + preferred dual-NRTI backbone	DRV/r bid + preferred dual-NRTI backbone – **ONLY IF TAKEN LA CAB FOR PREP PREVIOUSLY**
TDF/FTC		
TAF/FTC		

- Alternative: available da

Dual NRTI backbone	INSTI regimens	PI regimens	NNRTI regimens
ZDV/3TC	**RAL BID* + preferred dual-NRTI backbone**	**ATV/r* + preferred dual-NRTI backbone**	EFV/TDF/FTC
	TAF/FTC/BIC*	**DRV/r BID***	RPV + preferred dual-NRTI backbone

- Insufficient data**:** pregnancy specific PK/safety data too limited, i.e. 2 drugs regimens
  Note: may be appropriate to continue using them if patient fully suppressed and well tolerated, with potentially additional virologic monitoring

INSTI regimens	NNRTI regimens
• DTG/3TC • DTG/RPV • CAB + RPV LA	• DOR

- Not recommended**:** concerns with safety or PK data (e.g. EVG/c: 80%/90% concentration reduction during pregnancy)

INSTI regimens	PI regimens	NNRTI regimens
• EVG/c/TDF/FTC • EVG/c/TAF/FTC	• DRV/c • ATV/c • LPV/r	• NVP • ETR

BIC/FTC/TAF moved from *insufficient data* to *alternative* in 2024 because of recent PK studies in pregnancy and its safety of use:

- All BIC C_{24} remained above the BIC protein-adjusted EC_{95}, despite an AUC_{tau} reduction of 49% and 56% in the 2nd and 3rd trimesters (Powis et al., CROI 2023).
- BIC C_{trough} levels remained above the BIC protein-adjusted EC_{95}, despite an unbound AUC_{tau} reduction of 41% in the 3rd trimester, which is not considered clinically significant (Zhang et al., IAS 2023).
- APR[2]: N=539; rate of congenital anomalies=4.27%

DTG confirmed to be safe to use during pregnancy:

- APR: N=1052; rate of congenital anomalies=3.33%
- Tsepamo study in Botswana: increased rate of neural tube defect with DTG (4 cases; rate=0.94%) in 2018 but concern has gone away over time as 2022 update reported same rate as for the non-DTG group (rate=0.11%) (Zash et al. AIDS 2022).

CAB+RPV LA added in the *insufficient data* category in 2023 and recommendations were revised in 2024:

- 2023: shared care decision making with the patient; fine to use with more frequent biologic testing.
- 2024: if switching regimen, stop injections 1 year before conception to ensure drugs are fully eliminated. In patient with poor adherence history to oral drugs, switch may be associated with

[2] Antiretroviral Pregnancy Registry (APR): will report the rate of congenital anomalies if more than 200 cases have been recorded for a drug; rate is then compared to the Metropolitan Atlantic Congenital Defect Program (MACDP) and the Texas Birth Defect Registry (TBDR), which serve to represent the general population. A rate<4.5% is considered consistent with the general population.

increased risk of viral rebound and NNRTI resistance due to lack of adherence to a new oral regimen, so shared care decision making with patient is recommended (case series Coleman et al. AIDS 2022).
- PBPK modeling of CAB LA and RPV LA in pregnancy showed similar PK as in non-pregnant adults (Atoyebi et al, CROI 2022; Atoyebi et al. HIV Glasgow 2022).

CAB-LA now approved for PrEP and shown to be highly effective in women. Studies support that it can be continued during pregnancy:
- No difference in maternal and pregnancy outcomes when compared to FTC/TDF PO (Delany-Moretlwe. AIDS 2024).
- No drug concentration issue as C_{trough} remained far above the IC90 target (Marzinke et al. AIDS 2024).

Postnatal Care & HIV - Infant Feeding

DHHS Guidelines from 2019/21 did not recommend breastfeeding, which changed in 2023:
- people on ART with a consistently suppressed viral load should be counseled on both breastfeeding and formula feeding;
- only formula feeding eliminates HIV transmission risk;
- fully suppressive ART during pregnancy and breastfeeding decreases HIV transmission risk during breastfeeding to less than 1%.

Past Canadian recommendations were also against breastfeeding but changed in 2022 with CPARG consensus:
- exclusive formula feeding is the recommended method;
- free formula should be made available for the 1st year (e.g. The Teresa group in Ontario);
- all parents should benefit from detailed, comprehensive, multidisciplinary counselling (by adult ID, Ped ID and prenatal providers) on infant feeding options and risk;
- if parent meeting criteria (adherent to treatment) choses to breast/chestfeed, frequent monitoring is recommended;
- breast/chestfed infant should receive prophylaxis triple therapy[3] and get tested monthly;
- Child Protection Services does not need to be contacted.

Literature around the risk of HIV transmission through breastmilk is changing:
- Risk estimated at 6m used to be 1.08% (2016 WHO Guideline) but relied on older studies conducted in Africa with less effective ART and no evidence of viral suppression (Bispo, JIAS 2017).
- PROMISE trial estimated risk to be 0.3% at 6m and 0.7% at 12m, whether mother on ART or infant on ARV (Flynn et al., JAIS 2018). Update on the 2 cases of transmission that happened in the mother on ART group showed that one was not virally suppressed at time of transmission and the other was virally suppressed but had adherence challenges (Flynn et al., JAIS 2021). Latter case is why we can't say there is 0 risk of HIV transmission through breastfeeding.

[3] While Canada recommends 3 drugs for infant ARV prophylaxis, most other countries give only 1 or 2 drugs, and some none (e.g., Switzerland).

- Recent North America multisite study (including 3 Toronto Cases Series) reported no transmission in breastfeeding mothers, most on ART prior to pregnancy and undetectable at delivery (Levison et al, CID 2023; Nashid et al, JPIDS 2020).

Case follow-up

Case #1: Decided to not change her regimen, supported and counselled her on breastfeeding (with referral to SickKids). Patient gave birth to a 2nd baby girl and breastfed for 8 months.

Case #2: Took a person-centered shared care approach: patient worried about oral medication adherence and wants to stay on CAB+RPV LA. Haven't decided yet on dosing but will probably stay on q2.
CAB+RPV LA isn't preferred/alternative regimen in pregnancy so would be acceptable to switch regimen. However, would also be acceptable to keep it to limit exposure to multiple drugs: since it has such a long half-life, switching to oral regimen will result in infant being exposed to 5 different drugs.
For injection schedule, while drug concentration of many ARVs decrease in pregnancy, including for CAB/RPV, it has been shown to be higher in women. Monthly dosing is not recommended in the Guidelines, injection can be kept at q2 during pregnancy and more frequent VL testing can be considered.

Note: See Canadian HIV Pregnancy Planning Guidelines for tools on pregnancy planning – to be updated in 2025. To know more about Mona's counselling around breastfeeding, see the CATIE video.

Case Scenario 1: Treating Heavily Treatment Experienced Newcomers to Canada

Speaker: *Linda Robinson*

Context

HIV viruses can be very different around the world, depending on different drugs and situations they have been exposed to. A durable regimen relies on an adherent host and a drug with good PK for the known virus subtype. Pharmacofragility happens when insufficient pressure is put on virus, which leads to mutations and therefore resistance. While HIV can be kept at bay by being constantly exposed to enough drugs, this also leads to mutations and resistance building. ART resistance isn't going anywhere.

High income countries have access to very efficient regimens with high genetic barriers to resistance and forgiving PK if adherence challenges. This allowed Rapid Start to develop (i.e. start someone on ART at diagnosis before resistance testing). It also leads to modern treatments being ranked based on risk of failure and resistance building. People living with HIV advocate from themselves and are concerned about regimens strength and durability.

Changes are also happening in low income countries: i.e. Africa, 2018-2019, rolled out TLD in both treatment naïve and experienced patients (1 pill a day regimen (TDF/3TC/DTG) with high genetic barrier to resistance). Higher resistance levels than anticipated were observed, leading WHO recommendations for more viral load surveillance and resistance testing to follow prevalence and patterns. This is due to patients being put on TLD without baseline resistance testing or knowing ART history.

SIV and HIV phylogenetic tree is complex and keeps evolving, with many different clades and subtypes, some of which develop resistance more easily. In Canada in 2021, 1/3 of people who tested positive for HIV where migrants, which is more than 16% higher than in 2020. In Montreal, an increase in positive cases is largely due to migrants coming from countries where HIV is highly endemic.

Case example

40YO man, refugee from Rwanda with language barrier (EN speaking):

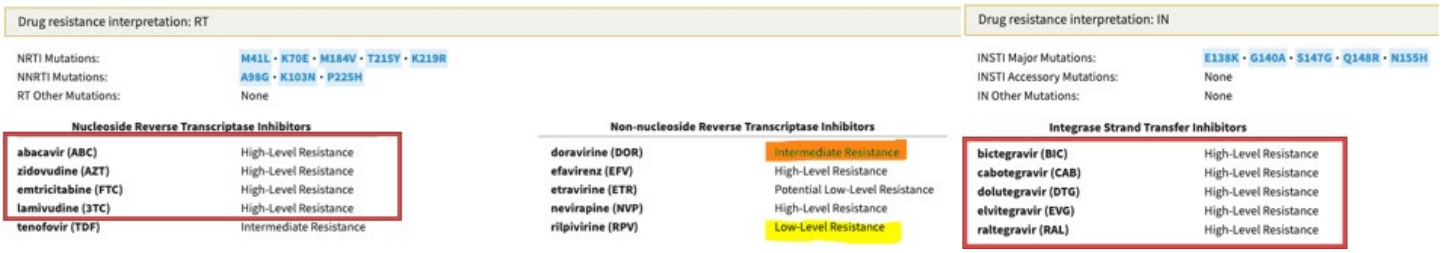
- received an HIV+ test in Dec 2023 in Saskatoon and referred to HIV care in Jan 2024
- claims it is a new infection and had a negative test result in 2021
- VL=308,000 copies/mL; CD4=319 cells/L; no HLAB*5701
- not on ART upon arrival and start postponed until TB status update (treatment impacts ART choice)

What would you recommend as treatment and how would you go about it?

Genotyping test conducted and showed growing mutations, which means virus has probably been exposed to ART in the past, possibly insufficiently strong since coming from a low-income country.

Clade C/Non R5 Tropic		
Viral Load	On intake: 308,000	4 weeks later: 524,000
NRTI	41L/wt ,70E/wt, 184V, 215NFY/wt 219R/wt	41L, 184V, 215Y
NNRTI	98wt/G, 103wt/N, 225H,	90G, 225H
PI	None	None
II	138EK, 140AG, 147GS, 148QR, 155HN	138K,140A,147G,148R,155H

Stanford database revealed high resistances in all drug categories and across all INSTI, which is unheard of. Resistance analysis showed 148R mutation common to all of them and resistance to all INSTI increased when combining 148R with other mutations, except for BIC. If first thought was to start patient on CAB+RPV LA, this shows the importance to really analyze mutations to avoid setting patient up for failure.



No resistance to PI, so regimen decided as follow:

- started on DRV/r + TDF/FTC once daily in February, as well as oral lead in for LEN (Capsid Inhibitor - using a new class for a high resistance profile)
- 2 weeks later, added LEN sc q6m
- VL=129 copies/mL in March
- added FTR BID (Attachment Inhibitor – works completely differently than the others)

Later removed FTR and patient remained virally suppressed. Ongoing talk about removing LEN as well and keeping only boosted PI regimen.

Takeaways

Fear of disclosure

Can be hard for migrants to disclose HIV status and/or full treatment history, out of fear of being deported/build unattractive profile for immigration. Language barrier also makes it very difficult to have an accurate history. Guaranteeing confidentiality in the clinic helps open up the conversation.

Treatment decision considerations:

- Today's mutations (if detectable viral load)
- Previous mutations (from available genotypes)
- Treatment history (help predict mutations prior to genotyping)
- Online calculator: Stanford University HIV Drug Resistance Database

Pay attention to newcomers

Several cases reported of new migrants having resistance testing showing breakthroughs, likely related to sub-therapeutic levels of second generation Integrates Inhibitors.

Case Scenario 1: ART after CAB+RPV LA failure

Speaker: *Pierre Giguere*

Context

CAB+RPV LA is the first long-acting IM ART. While it has great virologic success overall, it also has a small proportion of virologic nonresponse with background noise of resistance not attributed to adherence[4]:

- FLAIR Week 124: virologic outcomes at week 96 and 124 were 86.6% success/3.2% nonresponse and 80.2% success/14.8% nonresponse.

Risk factors for CAB+RPV LA failure

2 models developed (Orkin et al., CID 2023):

- From FLAIR, ATLAS, ATLAS-2M; N=1651; 1.4% confirmed virologic failure over more than 3y; incidence rate = 0.54 case per 100PY, i.e. will take up to 2y to see 1 case in 100 patients.
- Model #1 identified 3 baseline factors: preexisting resistance to CAB+RPV; subtype A6/A1 (but mostly A6); BMI>30 kg/m^2. Analysis showed significant risk of failure when patient has 2 or more baseline factors. However, difficult in clinic to do A6 genotype.
- Model #2 identified 2 baseline factors and considered drug concentration: preexisting resistance to CAB+RPV; subtype A6/A1; model-predicted low initial CAB trough and low initial RPV trough. Analysis showed significant risk of failure when patient has 3 or more baseline factors.
- Drug concentration and BMI are correlated and therefore both models gave similar results: Positive Predictive Value around 20% for both models, i.e. using these models will avoid virologic failure in 1 out of 5 cases and 4 out of the 5 cases would have been fine on CAB+RPV LA.

[4] Adherence is most of the time responsible for treatment failure in oral regimens.

Case example

Woman from Ethiopia:

- 2016, arrived in Canada: EFV/FTC/TDF; VL<40 copies/mL; CD4=891 cells/L – stable but complaining about dizziness
- 2017: switched to DTG/ABC/3TC; VL<40 copies/mL – stable but planning to get pregnant (risk of neural tube defect with DTG)
- 2019: switched to RPV/FTC/TDF; VL<20 copies/mL; CD4=937 cells/L – stable but wanted to switch to long-acting injectable
- Sep 2022: switched to CAB+RPV LA – complaining about pain related to injections more than usual
- Jan 2023 (2nd follow-up visit): asked to switch back to oral regimen and, incidentally, also had detectable viral load (VL=3120 copies/mL; CD4=476 cells/L) – started on BIC/FTC/TAF and genotype testing
- Mar 2023: resistance profile test results came back with K101E (susceptible to RPV, resistant to EFV and NVP); 148R (low level resistance to BIC and DTG, resistant to RAL EVG)
- Apr 2023: VL<20 copies/mL; CD4=818 cells/L – stable

What would you do: change the regimen base on the resistance profile or leave it as is?

In patients coming from low to middle income countries where the past history isn't known, a study supports offering CAB+RPV LA (Kityo et al, Lancet ID 2024):

- In Uganda, Kenya, South Africa, pragmatic switch in suppressed patients, stable on oral therapy, no history of virologic failure and without knowing baseline genotype testing results: about 97% virologic success whether patients kept on their oral regimen or switched to CAB+RPV LA. However, both groups had about 15% of resistance to CAB and to RPV.

This supports that positive predictive value of resistance testing is not 100% and offering CAB+RPV LA in these patients might still be an effective strategy.

Clinical trials identified several mutations responsible for CAB and RPV resistance[5], with crossed resistances for other drugs:

- NNRTI resistance: high level resistance to RPV with Y188L, M230M/L mutations; intermediate with K101E, E138A/K, Y181C; crossed resistance for DOR and ETR.
- INSTI resistance: L74I, N155H, Q148R, R263K, E138K, G118R mutations associated with CAB resistance; crossed resistance for DTG and BIC.

Studies have examined the effects of INSTI and NRTI resistance-associated mutations:

- Different mutations have different effects on medications; 1st generation INSTI tend to be lot more impacted than 2nd generation; BIC effect usually preserved in vitro (Smith et al, Retrovirology 2018).
- Edmonton Cohort (N=50): more than 90% patients on BIC/FTC/TAF and with several NRTI resistance-associated mutations remained virally suppressed after 18m (Shafran et al, HIV Med. 2023).
- Taiwan Cohort (N=72): very low rate of viral rebound with BIC/FTC/TAF in patients with NRTI resistance-associated mutations (Tsai et al, IJID 2023).

[5] Specific clade can only be known once treatment fails as cannot amplify virus when suppressed.

– Viking Study: DTG twice daily showed better results than once daily in patients with RAL treatment failure and achieved rapid and sustainable viral suppression, i.e. some INSTI can still have efficacy in patient with INSTI resistance-associated mutations (Eron et al, JID 2013).

Takeaways

Very little clinical data is available on strategy to adopt for treatment after CAB+RPV LA failure as it is uncommon (1-2%). Some information found in clinical trial reports showed that decisions based on genotypes and next regimens were PI-based. In general, the outcomes were good (i.e. virally suppressed).

5 cases of CAB+RPV treatment failure happened at The Ottawa Hospital (6-12m on average):

ID	Clade	BMI kg/m2	Treatment before CAB	VL @ CAB start	VL @ Cab failure	Resistance Associated mutation at CAB/RPV failure		Treatment post CAB failure	Last FU VL	duration
						NNRTI	InSTI			
1	C	37	RPV/FTC/TAF	<20	3120	101E	148R	BFTAF	<20	18 months
2	A	31	DTG/RPV	32.5	1290	90I 103N	138K, 148K	BFTAF	31	3 months
3	AG	30	DTG/ABC/3TC	<20	91300	138G, 230L	74I, 138E/K, 140A/G, 148K/Q/R, 230R/S	BFTAF	<20	15 months
4	C	25	BIC/FTC/TAF	<20	9340	181C, 221Y	138K 148R	BFTAF	<20	11 months
5	D	29	DTG/ABC/3TC	<20	1280	98G, 101E, 181C, 190A	118R	BFTAF	<20	6 months

For all of them, same strategy of switching to BIC/FTC/TAF resulted in virally suppressed/well controlled. However, the cost of treatment failure should be kept in mind as more of these cases have been happening.

PSG Networking

Speaker: *Sue Gill*

Keep in touch with other pharmacists working in HIV through different platforms:

- Ontario HIV Professional Specialty Group (PSG), Ontario specific
- Canadian HIV/AIDS Pharmacists Network (CHAP), pan-Canadian

We encourage you to join CHAP: Listserv for pharmacists to share cases; new Guidelines put out in 2024; regular Newsletters, and regular CHAP Chat webinars.

PSG wants to grow and is looking for new members for the Annual Education Day organizing committee (especially from outside the GTA), as well as volunteers to help set up a Listserv. An email from the OHTN will be sent, asking people in the PSG network to consent for their email to be added to the Listserv, and giving them the option to refer people.

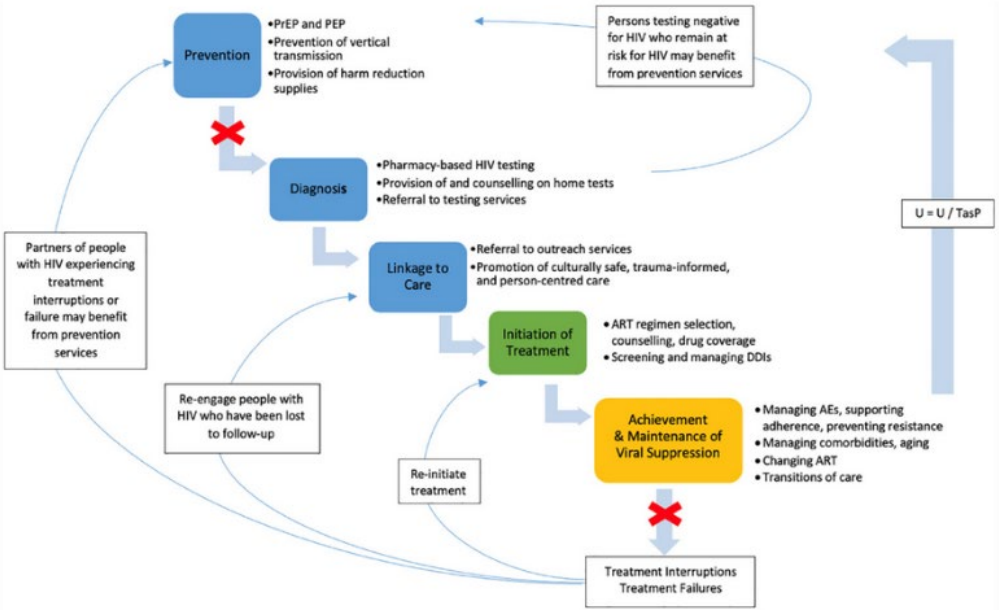
Second Plenary: Canadian PEP and PrEP[6] Guidelines Update

Speaker: *Deborah Yoong*

At the time of this presentation, the Guidelines were still in draft form.

The pharmacist's role

Pharmacists have an important role in HIV prevention and care – see Practice Guidelines (Tkachuk et al., CPJ 2024). By intervening at the top of the cascade, pharmacists can prevent all the rest from happening:



Because of their ubiquitous nature, pharmacists can interact with patients and have multiple opportunities to intervene: increase awareness around PrEP/PEP; HIV testing; linkage to care (start PrEP; deliver PEP; switch from one to the other); and the usual individual counselling and monitoring.
PrEP and PEP implementation should engage a broad range of healthcare providers and novel models of care (e.g. online) to increase awareness and access.

Guidelines development process

The panel includes 18 individuals from across the country, from different disciplines and groups. In addition, consultations were/are being held to gather feedback.

Decisions are made based on the GRADE methodology: ABCD for the evidence certainty (using PICO to frame clinical questions) and 123 for the recommendation type (linked to evidence but also to resource use, equity, effects, etc.).

Risk of HIV transmission is evaluated based on the likelihood the source has transmissible HIV (using population prevalence for unknown status) and the type of exposure. Compared to previous Guidelines, there is no evidence of increased risk transmission from people living with HIV who are undetectable but

[6] PrEP stands for pre-exposure prophylaxis and PEP for post-exposure prophylaxis.

with an STI. It is unknown if U=U applies in percutaneous exposures (e.g. needlestick) because of cell-associated virus. For sexual exposure, the window of transmission remains 24-72h.

Pharmacists' roles:

- Risk assessment: sexual history
- Testing: INSTI testing kits approved for Point-of-Care testing and at-home testing; 3rd generation tests and 99% accurate 3m after exposure. Laboratory testing uses 4th generation test and >99% accurate 42d after exposure. Ongoing monitoring to be done by laboratory testing, not INSTI test, as PrEP and PEP can delay development of detectable antibodies.
- Acute HIV infection: asking about symptoms

Pre-exposure prophylaxis (PrEP)

Who to prescribe PrEP to?

- Person requesting it: *"It is reasonable to prescribe HIV PrEP to adults and adolescents who request it."* Revised approach to avoid gatekeeping PrEP and increase access, recognizing that not everyone is comfortable disclosing their risk.
- Person screened by healthcare provider: *"Clinicians are encouraged to assess HIV risk (e.g. using HIV risk assessment tools) during routine health visits to identify people at increased risk of HIV who would benefit from PrEP, but who do not request it themselves."* Many people are not aware of PrEP, or underestimate their risk, the goal is to offer it to more people to avoid missed opportunities. No gold standard for which tool to use to assess HIV risk, clinicians can use whatever fits their setting.

Recommended regimens

Many new drugs have come out for PrEP since 2017. A systematic review of all PrEP trials was conducted and showed efficacy and safety profile of daily oral TDF/FTC is well established in all populations. In comparison:

- On-demand TDF/FTC (2-1-1) has similar side effects rates.
- Daily oral TAF/FTC has similar efficacy and side effects rates; renal and bone profile are more favorable (reversable) and metabolic less favorable.
- CAB-LA shows better efficacy; similar side effects rates, injection site reactions.

Population	Daily oral TDF/FTC	2-1-1 oral TDF/FTC	Daily oral TAF/FTC	Injectable CAB-LA
GBM* + transgender women who have sex with men	Strong recommendation for (Grade 1A)	Strong recommendation for (Grade 1A)#	Weak recommendation for (Grade 2A)	Strong recommendation for (Grade 1A)
Heterosexual cisgender women	Strong recommendation for (Grade 1A)	Strong recommendation against (Grade 1C)	Weak recommendation against (Grade 2B)	Strong recommendation for (Grade 1A)
Heterosexual cisgender men	Strong recommendation for (Grade 1A)	Weak recommendation for (Grade 2B)	Weak recommendation for (Grade 2B)	Weak recommendation for (Grade 2B)
People who inject drugs	Strong recommendation for (Grade 1A)	Strong recommendation against (Grade 1X)	Weak recommendation against (Grade 2X)	Strong recommendation against (Grade 1X)

*GBM = Gay, bisexual and other men who have sex with men
#avoid in those with active HBV and among those who may have difficulty adhering to the dosing regimen

Rational for *strong recommendation against*:

- On-demand TDF/FTC only studied in GBM and transwomen who have sex with men, not enough data available to know if dose is enough for ciswomen and people who inject drugs.
- Not enough data on use of CAB-LA in people who inject drugs.

Recommendations might change for specific populations/settings: hepatitis B, renal issue/bone loss, pregnancy, drug interactions, adherence issue, cost limitations (TDF/FTC would be the less costly because of the generic, especially on demand).

Monitoring

Pharmacists have a role in informing people about the various options available, as well as in monitoring:

- Adherence: dosing schedule and refill intervals.
- Renal function: TDF/FTC: every 3 to 6m; TAF/FTC: every 6 to 12m; CAB-LA: every 12m.
- Drug interactions: UGT inducer with CAB-LA and check with prescriber as needed.
- HIV testing: every 3m for oral therapy and 2m for injectable.
- Symptoms: if acute HIV infection suspected, connect with prescriber to suppress virus as soon as possible to avoid resistance from developing.
- Discontinuation: test 8w after stopping oral PrEP.

When discontinuing CAB-LA, oral PrEP should be taken for 1y after stopping the injections to avoid Long-acting Early Viral Inhibition (LEVI) syndrome: because of very long half-life, CAB-LA may delay detection of HIV seroconversion. Also associated with INSTI cross-resistance.

Guidelines suggests not routinely using HIV RNA testing to screen for incident HIV infection on CAB-LA as virus suppressed to such a low amount, test would not able to pick up on it and positivity will be delayed.

Post-exposure prophylaxis (PEP)

Who to prescribe PEP to?

Notion of non-occupational (sex/injection drug) Vs. occupational PEP (healthcare) was dropped as only setting changes but principle remains the same.

Status of source person	Exposure type			
	Percutaneous	Anal receptive Anal insertive Vaginal receptive Vaginal insertive	Oral sex (giving or receiving) Oral-anal contact	Blood or body fluid on compromised skin/mucosa
HIV+ with viral load >200 copies/mL OR HIV status unknown but high-prevalence population	Higher/moderate risk INITIATE PEP	Higher/moderate risk INITIATE PEP	Negligible risk GENERALLY DO NOT INITIATE PEP	Low risk CASE-BY-CASE DECISION
HIV+ with viral load <200 copies/mL	Low risk CASE-BY-CASE DECISION	No risk DO NOT INITIATE PEP	No risk DO NOT INITIATE PEP	Low risk CASE-BY-CASE DECISION
HIV status unknown but general population	Negligible risk GENERALLY DO NOT INITIATE PEP	Negligible risk GENERALLY DO NOT INITIATE PEP	Negligible risk GENERALLY DO NOT INITIATE PEP	Negligible risk GENERALLY DO NOT INITIATE PEP
Confirmed HIV negative	No risk DO NOT INITIATE PEP	No risk DO NOT INITIATE PEP	No risk DO NOT INITIATE PEP	No risk DO NOT INITIATE PEP

In cases of moderate to higher risk of HIV transmission, PEP should be given for 28d and within 72h after exposure. When risk is negligible or exposure happened more than 72h ago, PEP should not be given. For low risk exposure, a case-by-case evaluation and shared decision making is recommended.

The recommendations are based on observational data only, not randomized control trials. No certainty that PEP is even efficient past 24h after exposure. 72h window refers to sexual exposure rather than percutaneous, i.e. right into the bloodstream.

Recommended regimens

Systematic review of literature was conducted and recommendations made based on adherence (i.e. rates of therapy completion, side effects and discontinuation due to side effects).

Strong recommendation for	Weak recommendation for	Weak recommendation against
BIC/TAF/FTC	DTG + TAF/FTC	EVG/TDF/FTC/cobi
DTG + TDF/XTC*	RAL +TDF/FTC	EVG/TAF/FTC/cobi
	DOR/TDF/3TC	RAL +TAF/FTC
	DOR + TAF/FTC	RPV/TDF/FTC
	DRV/r + TDF/FTC	RPV/TAF/FTC
	DRV/r +TAF/FTC	
	DRV/cobi + TDF/FTC	
	DRV/cobi/TAF/FTC	

*XTC = lamivudine or emtricitabine

Regimens under *strong recommendation* could be suitable for wide use in the general population while *weak recommendation* may not be. Classification based on acceptability and feasibility rather than lack of efficiency (e.g. multiple pills, interactions, pregnancy, taken with food, coverage, etc.).

In case of imperfect PrEP use, *strong recommendation* regimens would be maintained because of their high genetic barrier to developing resistance. However, PI-based regimen recommended in the context of CAB-LA PrEP.

Implementation

Guidelines suggest:

- Starter Kits available in community for all individuals in whom PEP is initiated, followed by prescription for completion to allow modification based on needs/toxicity. This increases access and avoids delays. However, studies show risk of decreased PEP completion rate.
- PEP-in-pocket (PIP – prescription given in advance for self-initiation) can be considered for individuals with infrequent moderate to higher-risk exposures. This enhances autonomy and decreases barriers and delays to access first dose. Should be coupled with risk of exposure counselling.

Monitoring

Monitoring relies on adherence, side effects, interactions and testing (12w after exposure and 8w after PEP completion). High risk individuals should be encouraged to see provider for PrEP.

Case Scenarios 2: PrEP in Community Practice

Speaker: *Kishan Rana, Pharmacist at the PrEP Clinic*

Several tools are available to reduce HIV transmission: PrEP, PEP, U=U, and condoms. As per current guidelines, PrEP is recommended for Men who have Sex with Men (MSM) and transwomen who have unprotected anal sex, people in serodiscordant relationships with a detectable partner and who have unprotected front-hole/anal sex; and people who inject drugs, especially if sharing injection paraphernalia. In Canada, most people seen in community are MSM and transwomen.

Many reasons for people to not want PrEP. How to overcome barriers and increase access in community:

- Address stigma: create safer spaces for queer and trans folks; offer anonymous testing when clients don't want to share this information with their family doctor.
- Increase provider availability: create an interprofessional team with physician, pharmacists, NPs, etc.; make providers available for non-insured patients such as newcomers.
- Help with cost: pharmacists can help find financial assistance.
- Optimize timing: completely remote and in-person services available across Ontario; Rapid Start (same day negative rapid test for HIV and PrEP prescription) when needed.

Available PrEP options:

Drug	**FTC/TDF**		**FTC/TAF**	**LA-CAB**
Regimen	**Daily:** 1 tab PO daily	**On-Demand (2-1-1):** 2 tabs PO 2-24 hours before sex, then 1 q24h until 2 days after sex	1 tab PO daily	1 injection IM every month for 2 months, then 1 injection every 2 months **Optional:**oral lead-in
Indication	cis/trans folks	MSM	anal sex	cis/trans folks
Efficacy	up to 99%	at least 86%	up to 99%	at least 99%*
Adverse Effects	headache, N/V/D, **↓eGFR, ↓BMD**	headache, N/V/D, **limited ↓eGFR/BMD**	headache, N/V/D, **limited ↓eGFR/BMD, ↑lipids**	ISR, headache, limited N/V/D, **mood changes**
Drug Interactions	limit drugs that can impair **eGFR** (e.g. NSAIDs)	**Advisable** to limit drugs that can impair **eGFR** (e.g. NSAIDs)	**P-gp inducers** (St. John's Wort, anticonvulsants, antimycobacterial)	**UGT1A1/9 inducers** (anticonvulsants, antimycobacterial)
Drug	**FTC/TDF**		**FTC/TAF**	**LA-CAB**
Missed Doses	**Daily:** Take as soon as remembered If restarting, then 7 days before new anal sex or 21 days before new front-hole sex	**On-Demand (2-1-1):** Stratify risk by type of sexual encounter (oral < front-hole < anal < blood) If high risk, then recommend PEP within 72 hours of encounter from ER	Take as soon as remembered If restarting, then 7 days before new anal sex	Each dose must be +/- 7 days of target date If missing by >7 days, then start oral bridge within +/- 7 days of target date. 2 months max. Maintenance dose resumed if <1 month late, initiation doses restarted if >1 month late
Cost	Covered by ODB and most insurances, **~250$/m**	Covered by ODB and most insurances, **~250$/30 pills**	Covered by some private insurances, **~ 800$/m**	Not covered by most insurance yet, **~1000$/m**

FTC/TDF most used option: flexible, can be used in most people, lower cost (generic available). Side effects of oral PrEP include kidney function testing; product Monographs also mention bone density risk but not often tested as low risk and reversible upon discontinuation. Interactions mainly related to risk over kidney function (i.e. anti-inflammatories OTC).

When taken daily, PrEP offers 99% protection against sexually transmitted HIV. If patient does not wait the full 7 days, option to increase protection to 80% by taking 2 pills as soon as possible and continuing with daily dose. On-demand dosing is only used for planned sexual encounters. If unplanned high-risk sexual encounter and/or if patient doesn't take their PrEP on time, can refer for PEP within 72h. PEP-in-pocket should be a shared decision between provider and patient.

If patient doesn't have coverage, they can apply for:

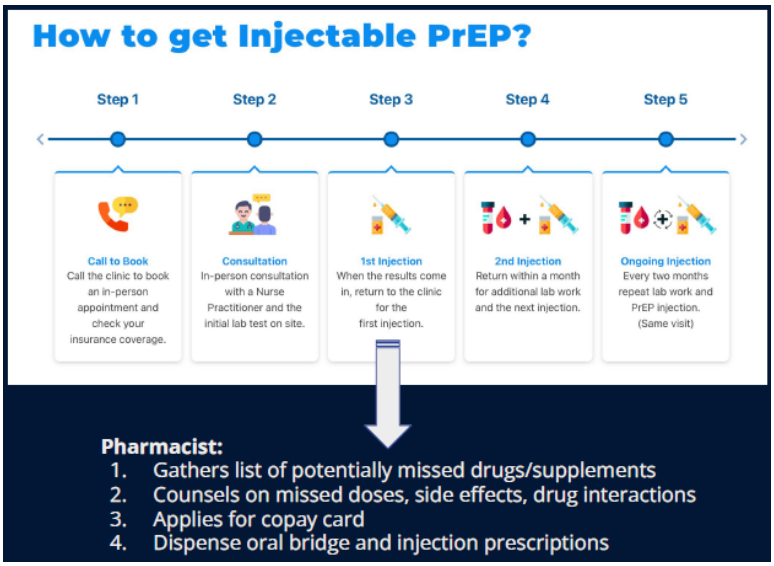
- Trillium: people who do not qualify for ODB and insurance not covering for 100% of the drugs (particularly useful for high cost drugs); application can be filled online.
- CoPay Cards: pharmaceutical companies' patient support program help pay for cost difference on brand name drug; providers can help patients sign up for ViiV's and Gilead's programs.

LA-CAB has been heavily anticipated by community:

- Advantages: no need for daily dosing so easier on adherence, no GI side-effects, no kidney function monitoring.
- Drawbacks: HIV testing every 2m instead of 3m, not referred in Clinical Guidelines yet, hesitations in regards to implementation, lack of coverage, 1y of oral PrEP after discontinuation.

interdisciplinary approach at PrEP clinic:

- NPs (prescription; injection)
- pharmacists (counselling)



Case Scenarios 2: GLP1-agonists for weight management

Speaker: *Alice Tseng*

Weigh gain with ART is common: clinic database study from Toronto General Hospital showed that 23% of ART-naïve patient (n=399) had ≥10% weight gain at 1y, associated with demographic factors but not regimen type.

GLP-1 RAs have multiple sites of action and therefore broad effects, not limited to weight loss. When used for obesity, weight loss effect can be similar to bariatric surgery (Is the weight over - Brown, CROI 2024). Also showed good results in people living with HIV:

- Observational cohort study showed that people lost on average 6.5kg, those with BMI≥40 lost significantly more, ART regimen did not impact weigh loss degree (Haidar et al., AIDS 2024).
- Retrospective cohort study had 44% participants with ≥5% weight loss and significantly associated with higher BMI at baseline and absence of diabetes (Nguyen et al., CID 2024).

Other effects of GLP-1 RAs in people living with HIV:

- Decrease markers of inflammation or immune activation associated with cardiovascular disease, independently of weight loss amount (Eckard et al., CROI 2024).
- Reduction in muscle volume but preserved physical function, can be compensated by high protein diet and resistance training (Ditzenberger et al., CROI 2024).
- Reduction in intrahepatic triglyceride (IHTG), in 30% of cases associated with complete resolution of metabolic dysfunction-associated steatotic liver disease (MASLD) (Lake et al., Ann Intern Med. 2024).

Lipohypertrophy, a side effect of older antiretroviral regimens, is a fat accumulation that changes the body shape. Not only cosmetically disfiguring and stigmatizing, but also associated with cardiovascular and metabolic complications.

Only treatment used to be Tesamorelin: growth hormone-releasing hormone analogue. Studies showed decrease of visceral fat (18%), hepatic fat and trunk-to-appendicular fat ratio (Russo et al., AIDS 2024) but no change in BMI or subcutaneous fat. However, only available in the US.

GLP-1 RAs could be used to treat lipohypertrophy associated with ARV: hypothesis few years ago (Culha et al., Med. Hy. 2016) but recent randomized double-blind trial with Semaglutide 1mg SC weekly, involving people without diabetes who have been on ARV for >10y, showed significant reductions in weight and BMI, as well as in visceral (>30%), subcutaneous and total abdominal fat, and total body, trunk and limb fat. No difference in outcomes linked to ART regimen and no significant differences in adverse events (Eckard et al., Lancet D&E 2024).

In the past, fat deposits that were surgically removed would come back. While GLP-1 RAs seem twice as efficient compared Tesamorelin, many questions remained: would higher dosing be more efficient (Semaglutide 2.4mg weekly dose now approved); are effects different based on type of weight gain; what happens when stopped; what effects on areas where fat is already lacking; etc.

In terms of potential drug interaction, some pharmacodynamics effect to keep in mind: GLP-1 RAs decrease gastric emptying rates and GI motility, which can affect gastric pH and can impact gastric pH dependent drugs, such as some ART (e.g. RPV). Viral load monitoring should be considered.
Ontario limiting access to GLP-1 RAs: currently in Limited Use for T2D and not available for weight loss.