HIV 2023: PreP/PEP and other pearls

Friday, November 10 Session ID: 168 Room: 517AB

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Presenter Disclosure

Presenter: Gordon Arbess

Relationships with financial sponsors:

- Any direct financial relationships, including receipt of honoraria: Gilead , Merck, Viiv
- Membership on advisory boards or speakers' bureaus: ViiV, Gilead, Merck
- Patents for drugs or devices: None
- Other:

Grants: OHTN, CIHR (Investigator)

Presenter Disclosure

Presenter: James Owen

Relationships with financial sponsors:

- Any direct financial relationships, including receipt of honoraria: None
- Membership on advisory boards or speakers' bureaus: None
- Patents for drugs or devices: None

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Objectives

1. Describe an approach to using HIV prevention tools (PrEP, PEP) applicable to the clinical setting

2. Describe steps to initial management of a patient with new HIV positive serology

3. Review common medications used in initial HIV management, including common side effects and interactions

WHO WE ARE?

UNITY HEALTH TORONTO

Caring hearts. Leading minds.

Family Physicians in an Academic Family Health Team (AFHT) in Downtown Toronto

- Physicians, RN, NP, Pharmacist, PT, Dietician, Addiction Counsellor, SW, Dentist, Income Counsellor, Linkage to care worker, Psychologist, Psychiatrist as part of a one stop Multidisciplinary health team
- Walk in/same day access
- Focus on Equity, QI
- 5 sites

- HIV patients: ~1500+

Show of hands!

Do you have people living with HIV or at-risk for HIV in your practice?

Have you prescribed HIV PrEP before?

Have you prescribed HIV PEP before?

What questions do you have for us?

HIV PrEP

PrEP: Indications

Recent CMAJ article on PrEP

(CMAJ 2022 September 6;194:E1164-70)

Review CPD

Pre-exposure prophylaxis for HIV: effective and underused

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

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

Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis | CMAJ. 2017

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE

A CLINICAL PRACTICE GUIDELINE

US Public Health Service: PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE, A CLINICAL PRACTICE GUIDELINE (cdc.gov)

Providing HIV preexposure prophylaxis. CFP 2022

RxFiles

Providing HIV preexposure prophylaxis

Taisa Trischuk PharmD Bradley Little MD Marlys LeBras PharmD ACPR

Transmission of HIV is an ongoing concern in Canada. Since 1990, there have been approximately 2000 to 2500 Canadians diagnosed with HIV per year.[1] Most of these infections are diagnosed among those identifying as gay, bisexual, or men who have sex with men (MSM), although regional differences exist.[1] Preexposure prophylaxis (PrEP) is a proactive HIV prevention strategy for HIV-negative individuals at increased ongoing risk. Preexposure prophylaxis involves taking medication before and after potential HIV exposure to prevent transmission. Other risk reduction strategies such as frequent HIV testing, condom use, and opioid agonist therapy can be used in combination with PrEP. Canadian guidelines on HIV PrEP and other resources are available; however, recent data suggest that many MSM who could benefit from this strategy are not currently using PrEP.[2-4] Family physicians are trusted by their patients and thus well situated to offer PrEP to those who may benefit. This article will outline considerations when prescribing PrEP for MSM.

Identifying individuals at risk of acquiring HIV

Individuals who are HIV negative and at elevated risk of HIV acquisition can be identified by taking a detailed sexual and drug use history. Both past and anticipated future risk should be considered. A trauma-informed, individualized approach should be followed based on sex, culture, and ethnic background. Prescribers may use the HIV Incidence Risk Index for MSM (HIRI-MSM) assessment tool to estimate an individual's HIV risk.[5] Validated in a Vancouver-based study, the HIRI-MSM tool found that scores of 10 or higher were associated with a 2% per year incidence of HIV, while scores of 25 or higher represented a 7% per year incidence of HIV.[6] A Canadian guideline on HIV PrEP endorses the HIRI-MSM assessment tool permission to ask Thomas some questions about his sexual history as part of your routine care. Thomas agrees to this.

Doctor: "To start with, do you have any questions about your sexual health?"

Thomas: "It's been a while since I had an STI test. Should I get tested more often now that my boyfriend and I decided to have an open relationship? We know we should wear condoms, but it doesn't always happen."

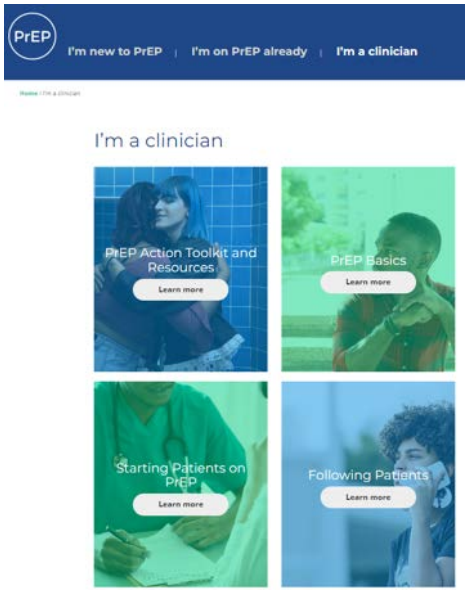
Doctor: "I recommend STI screening at least every 3 months given that you are sexually active. Since you have male partners, can I ask you some questions about your HIV risk? This will help me determine if a medication to prevent HIV transmission is worth considering, since many men underestimate their HIV risk."

You use the HIRI-MSM assessment tool, and based on Thomas' age (31 years, score of 5), number of male sexual partners (6 to 10 partners, score of 4), condomless receptive anal sex (1 or more times, score of 10), and use of poppers (alkyl nitrites; score of 3), you calculate his cumulative score to be 22. According to a Canadian guideline on HIV PrEP,[2] he has an indication for PrEP and could consider this strategy to protect himself from acquiring HIV.

Bringing evidence to practice: combination medications

Currently, there are 2 medications indicated for the prevention of HIV in MSM in Canada (**Table 1**). In a randomized controlled trial, participants receiving a combination of 200 mg–300 mg emtricitabine–tenofovir disoproxil fumarate daily reduced the relative incidence of HIV by approximately 50% in males at high risk compared with placebo over 1.2 years (event rate=3%

I'm a clinician - Ontario PrEP Clinics



PrEP: Indications

- "Recommended for persons engaging in condomless anal or vaginal sex either with partners of unknown HIV status or with partners with known transmissible HIV (i.e., detectable or unknown viral load)"
- "Additional risk factors such as previous use of HIV post-exposure prophylaxis and specific bacterial STIs are also useful in identifying people at elevated risk of HIV exposure"
- Tools for risk stratification exist: HIRI-MSM

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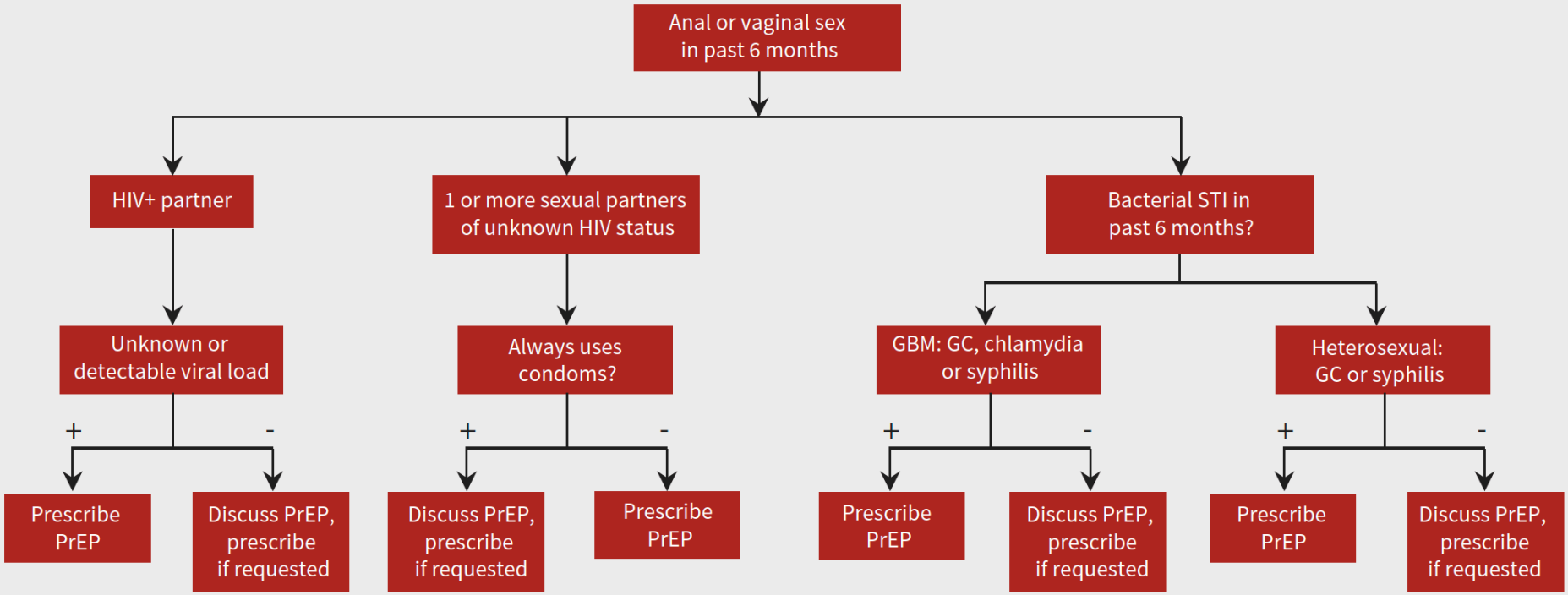
PrEP: Indications



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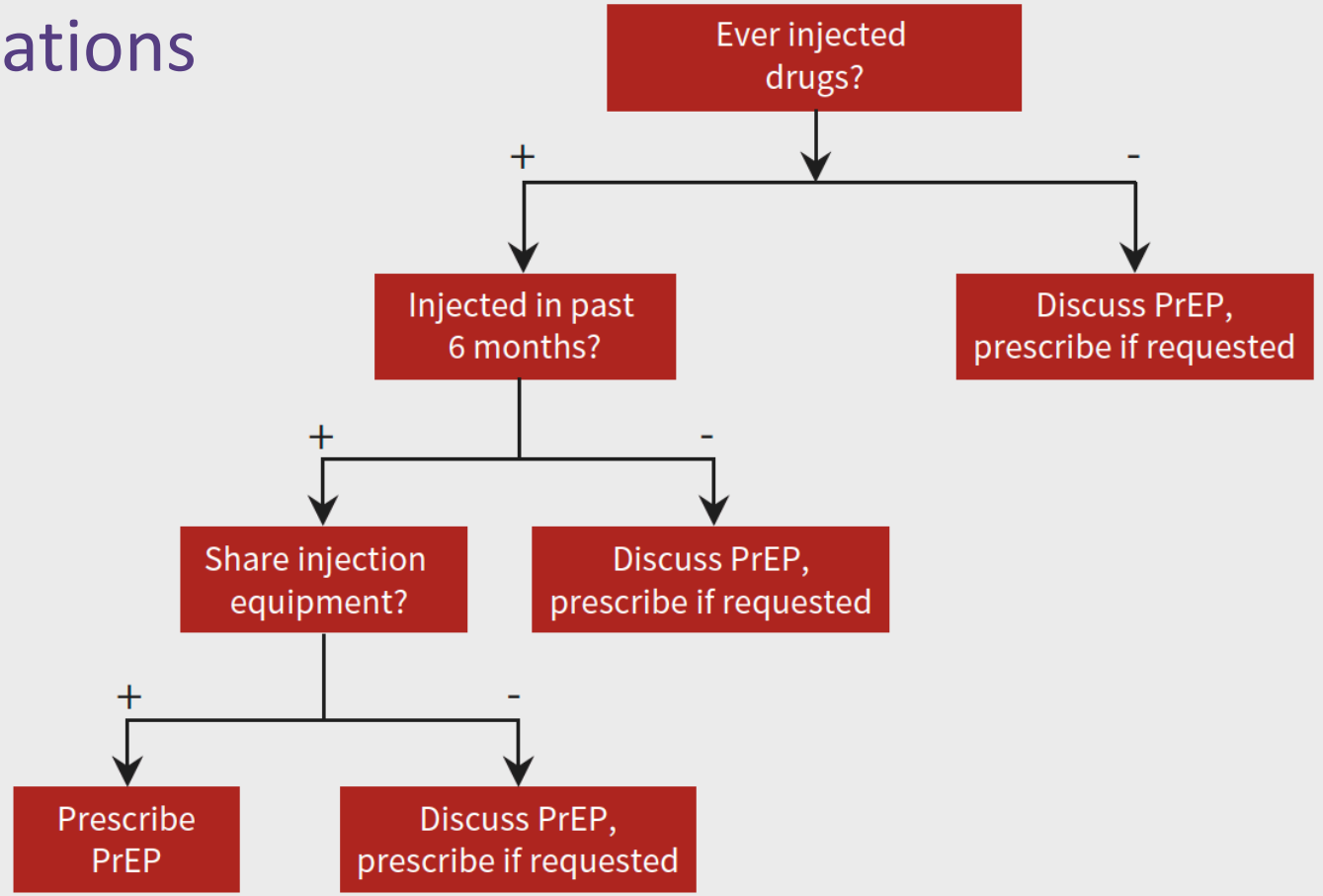
PrEP: Indications



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

Approaches - All are generally well-tolerated.

	Medication	Pros	Cons
Daily PrEP *(1 pill daily)*	Tenofovir disoproxil fumarate-emtricitabine (**TDF**+FTC, 300-200 mg)	- Generic available ($250 vs ~$900) - Most common form of PrEP administration	- Possible mild impact on eGFR & bone density (typically reversible upon discontinuation)
	Tenofovir alafenamide fumarate-emtricitabine (**TAF**+FTC, 25-200 mg)	- Smaller pill - More renal-and bone-friendly	- No generic available (=$$$) - Cannot be used for on-demand approach (can cause confusion for patients) - Not as readily covered on formularies - Less weight- and lipid-friendly
Intermittent/On-Demand PrEP (2-1-1…) (*Off-label; for gbMSM & trans women only; Method: 2 tablets taken together 2-24 hours before sexual activity, then 1 tablet daily until 2 days after last sexual encounter)*	Tenofovir disoproxil fumarate-emtricitabine (**TDF**+FTC, 300-200 mg)	- Generic available - Most cost-efficient approach with lowest pill burden - Available evidence thus far suggests noninferiority to daily PrEP	- Less robust evidence - May be confusing for patients - More GI side effects with 2-pill loading dose

Prescribing PrEP:

Important Points

- **Must document baseline HIV-negativity at PrEP initiation, and at follow-up tests every 3 months**
- Screen for other STIs minimum q3months
  - Remember these are patients who are by definition at high-risk for STIs
- Only prescribe 3 months of HIV PrEP at a time
  - I often limit fax renewal requests to small amounts that bridge until next appointment and/or lab tests
- Can be time-intensive
  - Consider supports (RN phone calls, templated email reminders, standing orders, providing multiple copies of requisitions in advance)

Suggested Counseling

PrEP-specific

- Adherence to PrEP & adherence supports (eg reminders)
- Side effects

Non-PrEP specific

- Brief sexual history
- Explore HIV risk reduction strategies
- Screen for STI symptoms
- Substance use and mental health screening

Always consider how you can do this in a non-stigmatizing way.

Laboratory Monitoring

Consider HIV serology & Cr/eGFR at ~1 month after PrEP initiation

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

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

CMAJ 2022 September 6;194:E1164-70

HIV PEP

PEP

- Identify high risk exposure to HIV
- Offer and counsel on PEP **within 72 hours of exposure**
- Do initial and post PEP testing
- Rx:

  TDF+FTC 300/200mg (Truvada®)1 pill daily

  PLUS one of

  Dolutegravir (Tivicay®) 50 mg daily

  OR

  Raltegravir (Isentress®) 400 mg BID

  OR

  Darunavir (Prezista®) 800 mg daily (boosted with ritonavir 100 mg)

  x 28 days

Need to counsel on PrEP?

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

Risk that a person has transmissible HIV infection

Substantial

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

Low but nonzero

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

Negligible or none

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

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

High

- Receptive anal intercourse
- Needle sharing

Moderate

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

Low

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

PEP – Testing

- First visit:
  - HIV, HAV, HBV, HCV, syphilis
  - ALT, Cr, CBC
  - NG/CT urine/swabs as appropriate, B-HCG as appropriate
- Week 2
  - Repeat ALT, Cr if symptomatic or abnormal at baseline
- Week 4
  - clinic visit and repeat HIV serology
- Week 12
  - HIV, HBV, HCV, syphilis

(Baseline HIV, viral hepatitis, STI testing of source patient if feasible)

CMAJ Nov 2017, 189 (47) E1448-E1458
DeHaan E. Post-Exposure Prophylaxis (PEP) to Prevent HIV Infection [Internet]. Baltimore (MD): Johns Hopkins University; 2020 Jun. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562734/

PEP - Resources

- Public Health Agency of Canada HIV Factsheet: PrEP vs PEP
- CATIE: Canadian AIDS Treatment Information Exchange– information for both providers and PATIENTS
- Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis
- St. Michael's Pocket P.E.P.
- Hillier M, El-Baba M and Owen J. "Just the Facts: HIV PEP". CJEM. 2021 Mar;23(2):150-152.

NEW HIV DIAGNOSIS

Janet

- 24 y/o cisgender woman
- Performs sex work; inconsistent condom use
- On Ontario Works (provincial social assistance)
- Last STI testing 9 months ago
- Describes recent flu-like illness 2 months ago

STI testing done:

- All bacterial STIs negative
- HIV result is POSITIVE

Your office contacts her and she is able to come to clinic tomorrow to discuss.

Initial reaction/discussion points

- Need to assess reaction/supports
- Disclosure to partners
- Who do they feel comfortable disclosing diagnosis to?
- Cultural/spiritual/psychological concerns
- Housing
- Supports to address mental health/substance use
- Coverage for medication
- Readiness to start antiretroviral medication

DHHS

Baseline Evaluations

Every patient with HIV entering into care should have a complete medical history (with a complete immunization history, including for SARS-CoV-2), physical exam, and laboratory evaluation and should be counseled regarding the implications of HIV infection

The initial evaluation should include discussion of benefits of ART for patient health and to prevent HIV transmission and strategies to optimize care engagement and treatment adherence (AIII)

Goals of Initial Evaluation
• Confirm HIV diagnosis • Obtain appropriate baseline historical and laboratory data • Ensure patient understanding about HIV infection and its transmission • Initiate care as recommended in guidelines

DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, March 2023. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed May 2023

DHHS

Baseline Evaluations

HIV infection should be confirmed, but other test results, including HIV RNA, CD4 count and resistance testing do not need to be available prior to ART initiation, unless the individual is planning to begin an INSTI-containing regimen and has had prior exposure to CAB-LA as PrEP

Recommended Laboratory Testing
Tests performed during initial patient visits can be used to stage HIV and guide ARV selection: • HIV antigen/antibody testing **(AI)** • CD4 count **(AI)** • Plasma HIV RNA **(AI)** • CBC, chemistry profile (including glucose), BUN, creatinine, liver enzymes and bilirubin, urinalysis, serology for hepatitis A/B/C† **(AIII)** • Serum lipids • HLA-B*5701 test (if ABC considered) **(AI)** • Genotypic resistance testing **(AII)**‡ – for patients with HIV RNA <1000 c/mL, viral amplification for resistance testing may not always be successful **(BII)**
Other tests (including STI screening, OI and cancer) as recommended in HIV primary care/OI guidelines

BUN, blood urea nitrogen; CBC, complete blood count; HLA, human leukocyte antigen; OI, opportunistic infection; RT, reverse transcriptase; PR, protease; PrEP, pre-exposure prophylaxis
†Screening for viral hepatitis should be done before starting ART, and if ART initiation occurs before results are available, a regimen that has activity against HBV should be selected.
‡Standard genotypic drug-resistance testing in ARV-naive people should focus on testing for mutations in RT and PR genes. If transmitted INSTI resistance is a concern in people with newly-diagnosed HIV or in people who acquired HIV after receipt of CAB-LA as PrEP, testing for mutations in the integrase gene also should be performed. It is not necessary to delay ART until results are available, but results should be reviewed as soon as possible in order to make adjustments to the regimen, if needed
DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, March 2023. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed May 2023

STARTING ARV THERAPY

Everyone should be initiated on antiretroviral treatment!

ISSUES TO CONSIDER:

- Patient Readiness
- Cost/coverage
- Co-morbidities
- Drug interactions
- Hepatitis Status
- Child Bearing Potential/Pregnancy

Initiate ART As Soon As Possible After HIV Diagnosis

Rapid start (including same day as diagnosis) ART, unless that patient is not ready to commit to starting therapy
  - Structural barriers should be removed

- Samples for HIV-1 RNA level; CD4 cell count; HIV genotype for NRTI, NNRTI, and PI; HLA-B*5701 testing; laboratory tests to exclude active viral hepatitis; and CBC, ALT, Cr should be drawn before beginning ART, but treatment may be started before results are available.
- NNRTIs (possible transmitted resistance) and abacavir (without HLA-B*5701 results) should not be used for rapid ART start
- ART should be started as soon as possible (but within 2 weeks) after diagnosis of most opportunistic diseases

Saag, Benson, Gandhi, et al, *JAMA*, 2020.

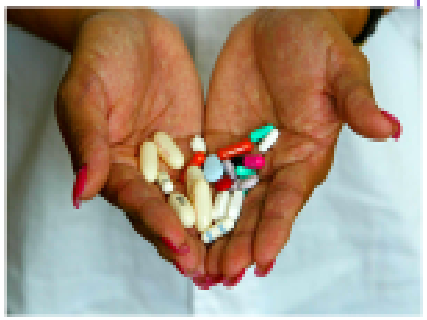
Goals of HIV Treatment

- maximally and durably suppress plasma HIV viral load,
- restore and preserve immunologic function (CD4),
- reduce HIV-associated morbidity and prolong survival,
- improve quality of life, and
- prevent HIV transmission.

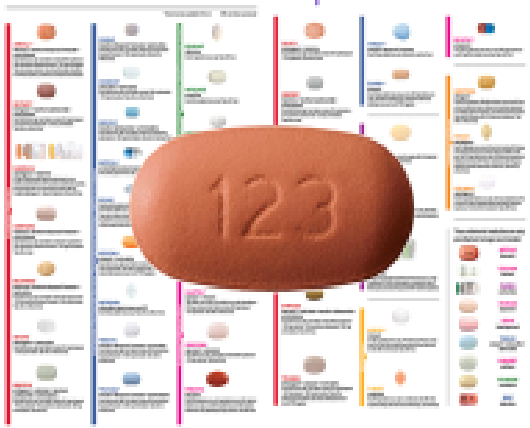
Scientific advancement of HIV-1 treatment

Increasingly effective, tolerable, simplified oral ART

1980 1990 2000 2010 2020



Multiple pills, multiple times per day



>30 FDA-approved antiretroviral options

Two injections monthly or bimonthly (2 drugs)

Recommended Initial Regimens for Most People With HIV: U.S. DHHS Guidelines (September 2022)

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use

For people who do not have a history of CAB-LA (CABENUVA) use as PrEP:

	Specifically recommended regimens	Rating of recommendation
INSTI + 2 NRTIs	BIC/FTC/TAF (BIKTARVY)	AI
	DTG/ABC/3TC (TRIUMEQ) (if HLA-B*5701 negative)	AI
	DTG + (TAF or TDF) + (FTC or 3TC)	AI
INSTI + 1 NRTI	DTG/3TC*	AI

*Except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

Rating of Recommendations: A = Strong; B = Moderate; C = Optional Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational

Coverage of Antiretroviral Medications

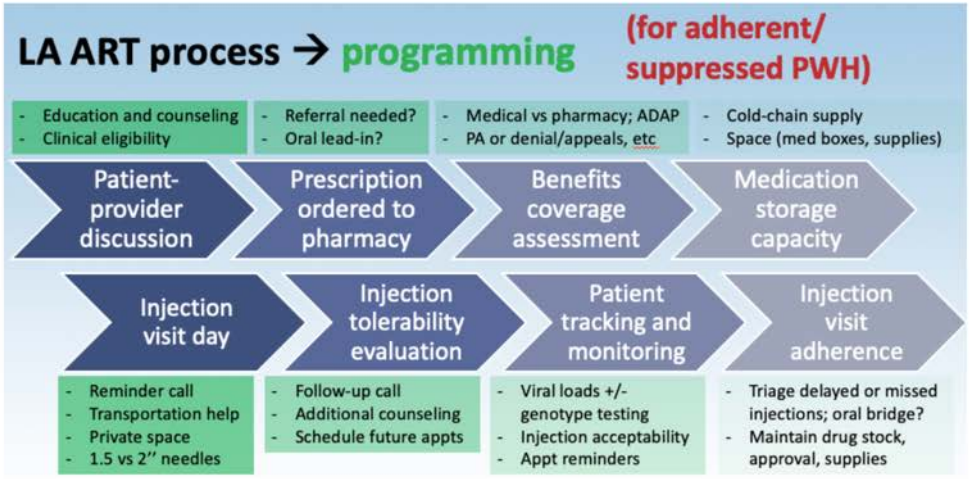
In Ontario:

- ODB (OW and ODSP) in Ontario or Provincial Coverage
- Non-Insured Health Benefits (NIHB)-for Registered First Nations/Inuit
- Trillium
- Private Insurance
- Clinical trial
- Patient Assistance Program (Max card from Gilead or Viiv Cares)

Long-acting therapy

- Provides the opportunity to transform the landscape of care for HIV treatment and prevention:
  - Alleviate pill fatigue
  - Improve adherence
  - Reduce stigma

- Need additional data in:
  - Youth ≤12 years old
  - Pregnant and breastfeeding
  - Patients with viremia



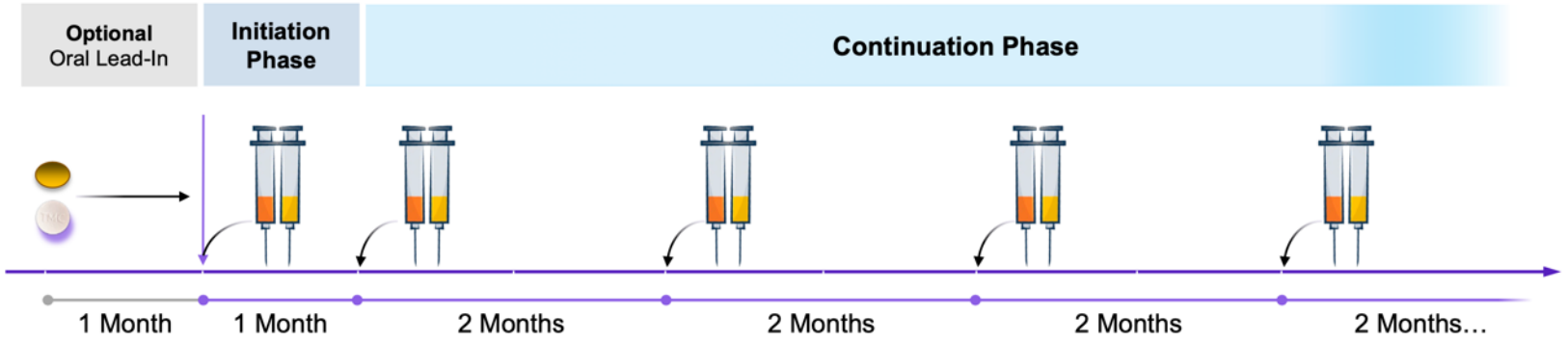
ACTG Protocol 5359

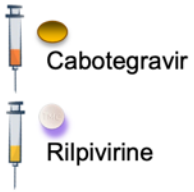
ACTG LATITUDE

Schedule for Every 2-Month Injectable Cabotegravir and Rilpivirine

Schedule for Injections*: First two injections given 1 month apart then every 2 months thereafter

Administer first injections on the last day of current antiretroviral therapy or last day of oral lead-in (if used)





Optional Oral Lead-In Dosing: Cabotegravir 30 mg PO daily and Rilpivirine 25 mg PO daily

***First Two Injections (Initiation Phase):** given 1 month apart, before transitioning to every 2-month dosing

***Dosing for All Injections** = LA Cabotegravir (600 mg): 3 mL IM and Rilpivirine (900 mg): 3 mL IM

Injections of rilpivirine and cabotegravir given as 2 separate IM injections at separate gluteal sites (opposite sites or 2 cm apart on same site)
Injections may be given up to 7 days before or after the scheduled date

Cabotegravir-Rilpivirine Prescribing Information; Illustration: David H. Spach, MD

Back to our case:

- Janet is surprised and upset by the result; you endeavour to reassure her this is something that can be managed, and she can take control
- Labs ordered
- Previous Hep B serology negative; urine pregnancy test negative
- You start bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) 1 pill daily at that visit
    - Fully covered by Ontario Works/ODB
- You arrange close follow-up

Fast forward 2 weeks…

- Janet is doing well with Biktarvy, no adherence issues
- Physical exam WNL
- Initial bloodwork:
    - HIV viral load 134,000 copies/mL
    - CD4 754 cells/uL
    - Metabolic labs normal
- You plan continue follow-up and labs and repeat HIV VL in 4-6 weeks

Adverse effects?

-Antiretroviral therapy is much better tolerated than in the past-simpler, less toxic, better tolerated choices

-Integrase Inhibitors-fatigue, CNS effects (mood, sleep), weight gain

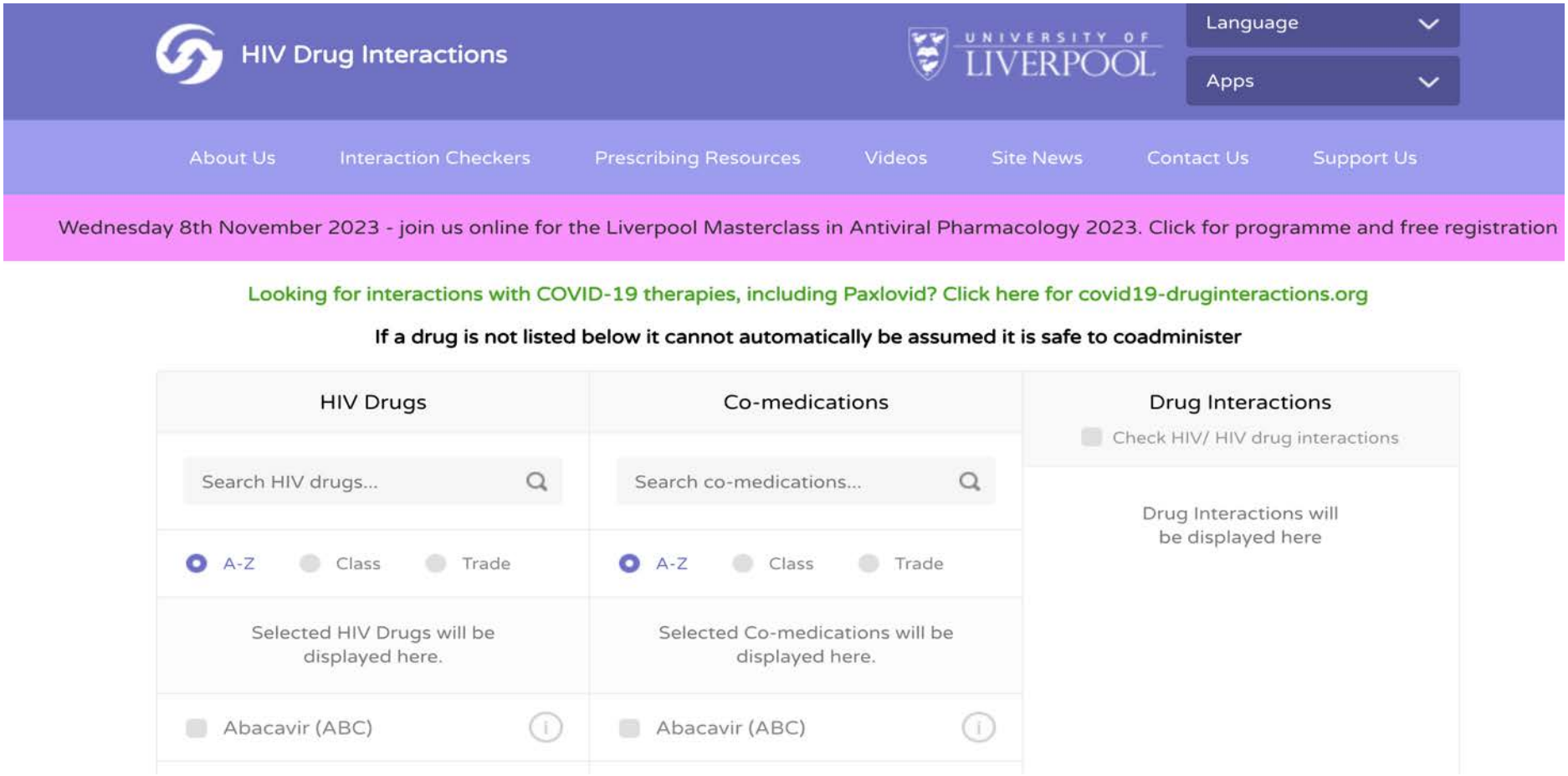
Tenofovir-impact on renal function, decreased bone density

-NNRTI-CNS effects/possible rash

-Protease Inhibitors (PI)-weight gain, hyperlipidemia, possible impact on Blood Glucose

-Abacavir-risk of hypersensitivity reaction (important to ensure HLAB*5701 negative)

Drug Interactions



Questions & Discussion

Objectives

1. Describe an approach to using HIV prevention tools (PrEP, PEP) applicable to the clinical setting

2. Describe steps to initial management of a patient with new HIV positive serology

3. Review common medications used in initial HIV management, including common side effects and interactions

Thank you!

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James Owen: james.owen@unityhealth.to

Questions?

RESOURCES

RESOURCES

Web:

- Guidelines (PrEP and PEP) and Review articles (PrEP)
- OHTN (Ontario HIV treatment Network)
    - PrEP training and resources (patient and provider)
- CATIE (Canadian AIDS Treatment Information Exchange): patients and providers
- Public Health Agency of Canada
- DHHS (Dept of Health and Human Services): HIV Treatment Guidlines
- BC Centre for Excellence in HIV: Education and Training

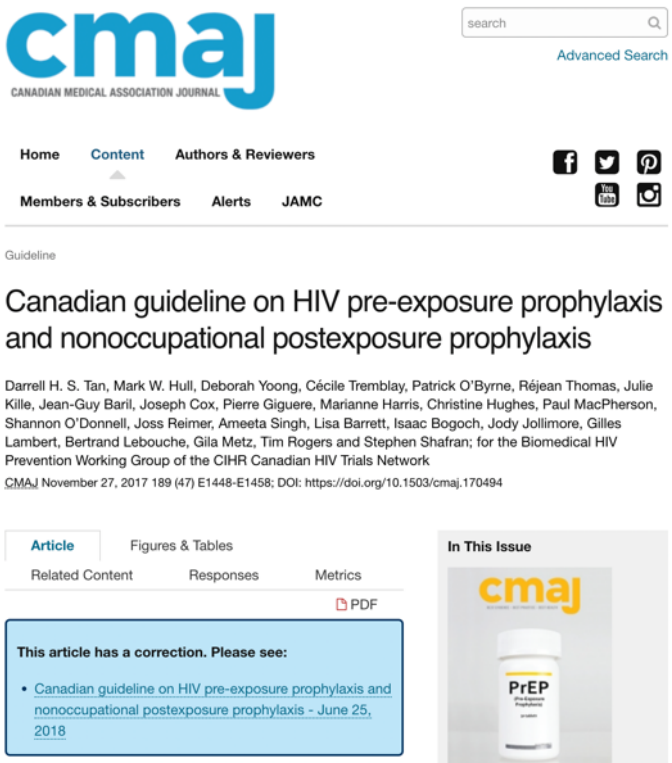
Apps:

- Canadian STI Guidelines app (Apple App store or Google Play)

Handout:

- Developed in conjunction with OHTN
- Our slides

Guidelines and Review Articles



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Guideline

Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis

Darrell H. S. Tan, Mark W. Hull, Deborah Yoong, Cécile Tremblay, Patrick O'Byrne, Réjean Thomas, Julie Kille, Jean-Guy Baril, Joseph Cox, Pierre Giguere, Marianne Harris, Christine Hughes, Paul MacPherson, Shannon O'Donnell, Joss Reimer, Ameeta Singh, Lisa Barrett, Isaac Bogoch, Jody Jollimore, Gilles Lambert, Bertrand Lebouche, Gila Metz, Tim Rogers and Stephen Shafran; for the Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network

CMAJ November 27, 2017 189 (47) E1448-E1458; DOI: https://doi.org/10.1503/cmaj.170494

Article Figures & Tables
Related Content Responses Metrics
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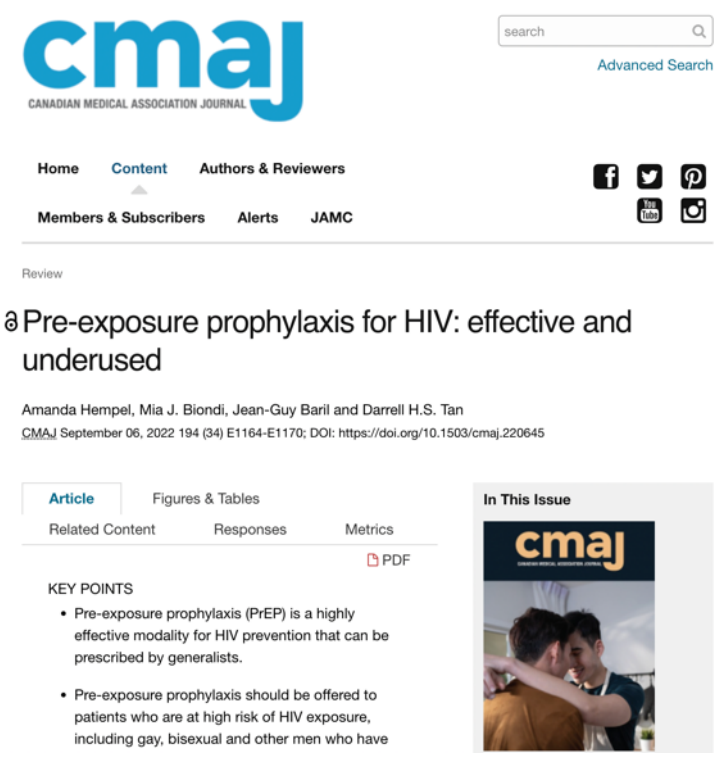
This article has a correction. Please see:

- Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis - June 25, 2018

In This Issue



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Review

Pre-exposure prophylaxis for HIV: effective and underused

Amanda Hempel, Mia J. Biondi, Jean-Guy Baril and Darrell H.S. Tan

CMAJ September 06, 2022 194 (34) E1164-E1170; DOI: https://doi.org/10.1503/cmaj.220645

Article Figures & Tables
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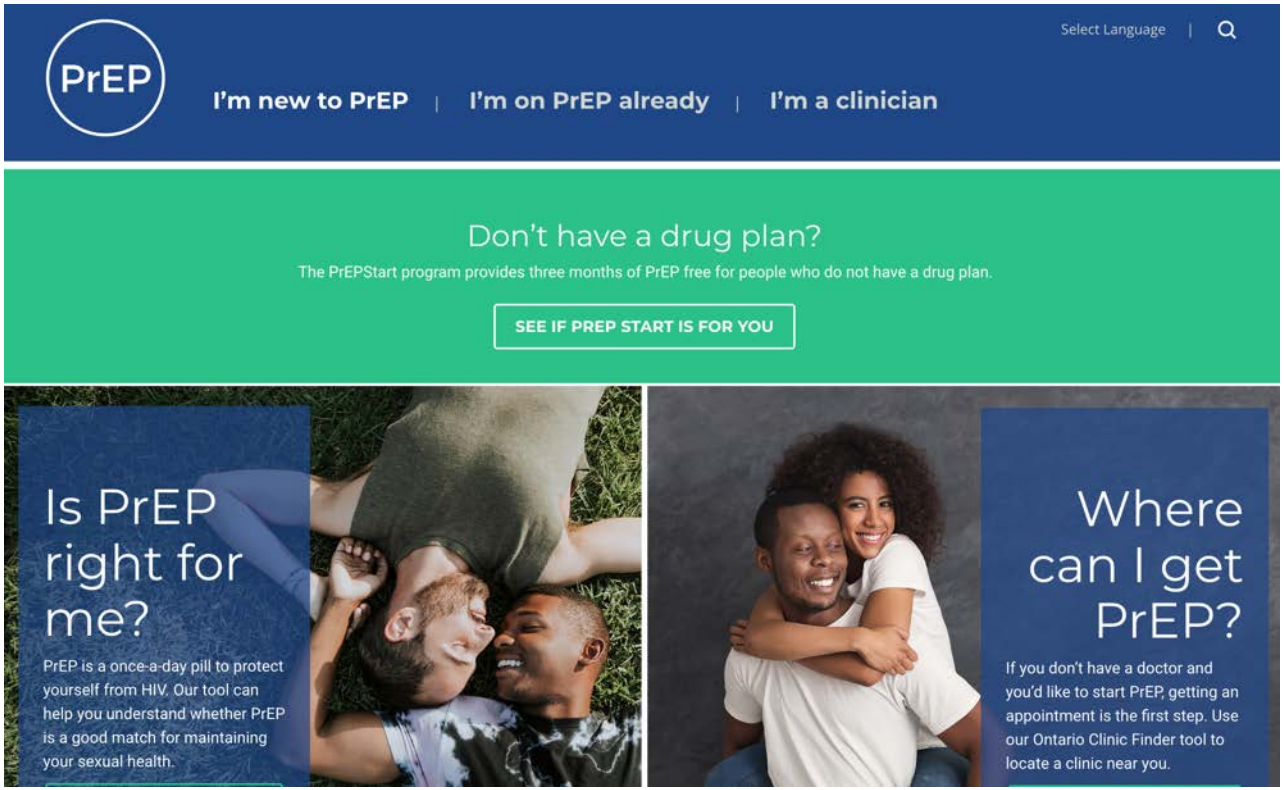
KEY POINTS

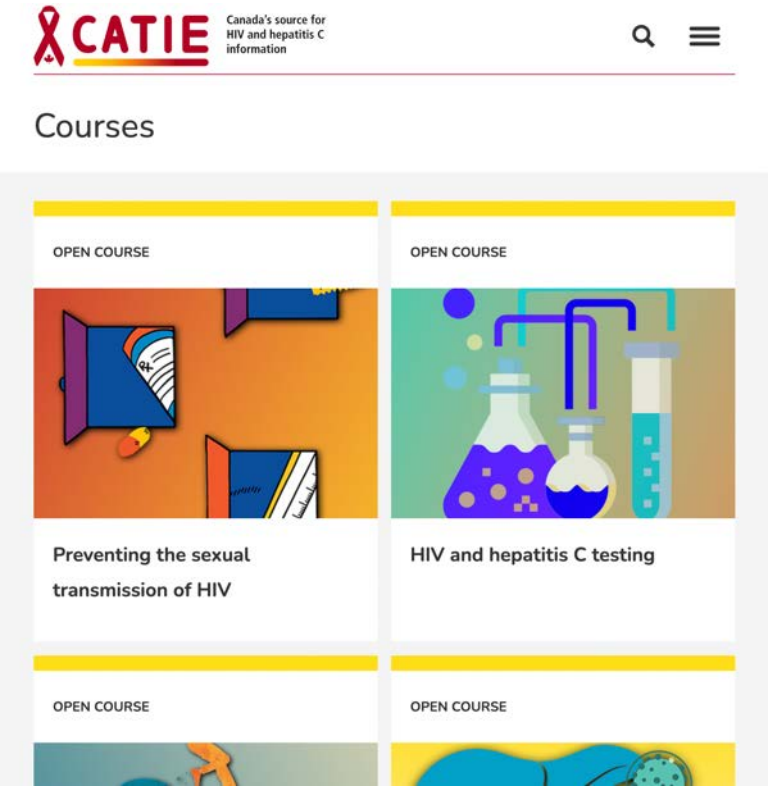
- Pre-exposure prophylaxis (PrEP) is a highly effective modality for HIV prevention that can be prescribed by generalists.
- Pre-exposure prophylaxis should be offered to patients who are at high risk of HIV exposure, including gay, bisexual and other men who have

In This Issue

Ontario PrEP - OHTN



CATIE:
Canadian AIDS Treatment Information Exchange



PHAC: Public Health Agency of Canada