Clinical Use of Antiretrovirals

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Objectives

1. Describe the indications for ART
2. Understand the principles of ART regimen building
3. Describe strategies to recognize barriers to and improve adherence
4. HIV Prevention

Clinical Management of Antiretrovirals

- Antiretrovirals are used in the treatment of HIV infection
- They prevent the replication of HIV particles in people with HIV infection which prevents disease progression and crucial for improving/maintaining health
- Used correctly ARVs result in complete viral suppression, the last step of the HIV Care Cascade
  - Improved health outcomes
  - No transmission of virus
- Treatment works only if taken daily, ongoing basis

Clinical Management of Antiretrovirals

- Many antiretroviral agents exist and are in common use
- Agents are used together in treatment regimens (ART) according to guidelines
- Many factors in choosing a regimen and ART is tailored for each patient

Indications for **ANTIRETROVIRAL** **THERAPY**

Indications

- **Everyone** infected with HIV!
- More urgent cases:
  - Pregnancy
  - AIDS-Defining illness/Opportunistic Infection
    - HIV-associated dementia (HAD), AIDS-associated malignancies
    - Cytomegalovirus retinitis, tuberculosis, toxoplasmosis, PCP pneumonia, Candidiasis, Mycobacterium avium complex, etc
  - Lower CD4 counts
    - Under 200-350
  - Early/acute HIV infection
  - Hep B and/or Hep C Coinfection
- Ultimately, patients start therapy **when they are ready**

Principles of **HIV** **REGIMEN BUILDING**

Guidelines - **DHHS**

- Follow the DHHS Guidelines
  - https://aidsinfo.nih.gov/guidelines
- Put out by the Panel on Antiretroviral Guidelines for Adults and Adolescents, a working group of the Office of AIDS Research Advisory Council
  - Frequently updated
- Provides HIV care practitioners with recommendations based on **up to date knowledge** of ARVs used to treat adults and adolescents with HIV

NRTIs - Nucleoside Reverse Transcriptase Inhibitors

Competitively binds viral reverse transcriptase to terminate DNA chain elongation, which terminates replication

- **TDF** (Tenofovir Disoproxil Fumarate)
- **TAF** (Tenofovir Alafenamide)
- **ABC** (Abacavir)
- **3TC** (Lamivudine)
- **FTC** (Emtricitabine)

NNRTIs - Non-Nucleoside Reverse Transcriptase Inhibitors

Prevent viral DNA chain elongation by blocking reverse transcriptase → stereochemical change that prevents nucleosides from being incorporated into viral DNA

- **RPV** (Rilpivirine)
- **EFV** (Efavirenz)

PIs - Protease Inhibitors

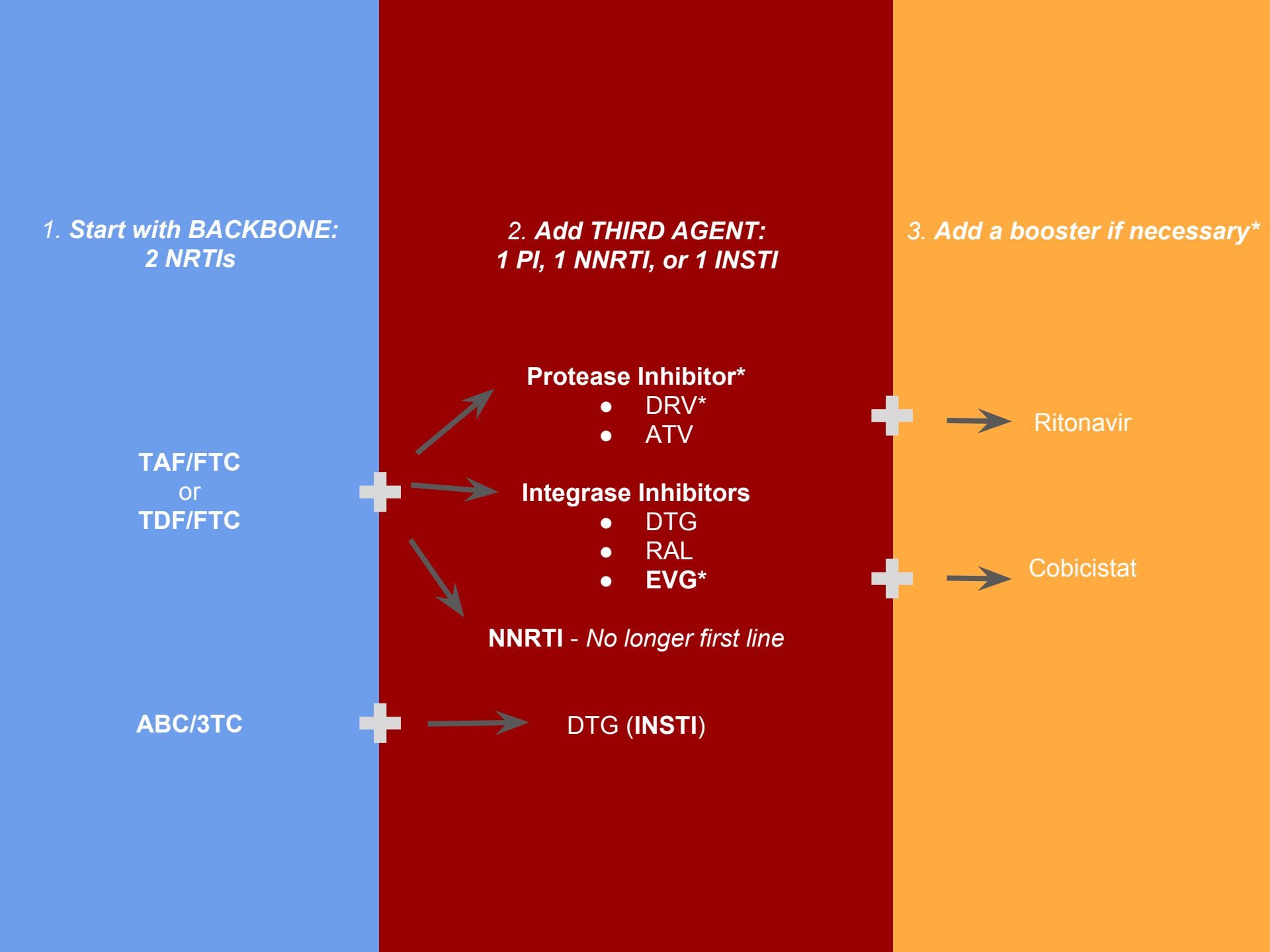
Inhibits polyproteins in HIV infected CD4 cells, which prevents HIV virus from maturing (leads to non-infectious immature virions)

- **DRV** (Darunavir)
  - Boosted with ritonavir or cobicistat
- **ATV** (Atazanavir)
  - Boosted with ritonavir or cobicistat

INSTIs - Integrase Strand Transfer Inhibitors ("Integrase Inhibitors")

Terminate viral replication by inhibiting strand transfer and binding of pre-integration complex into host cell DNA (can't bring viral DNA into the host nucleus)

- **RAL** (Raltegravir)
- **EVG** (Elvitegravir)
  - Boosted with cobicistat
- **DTG** (Dolutegravir)


1. Start with BACKBONE:
2 NRTIs
2. Add THIRD AGENT:
1 PI, 1 NNRTI, or 1 INSTI
3. Add a booster if necessary*
TAF/FTC
or
TDF/FTC
ABC/3TC
Protease Inhibitor*
DRV*
ATV
Integrase Inhibitors
DTG
RAL
EVG*
NNRTI - No longer first line
DTG (INSTI)
Ritonavir
Cobicistat

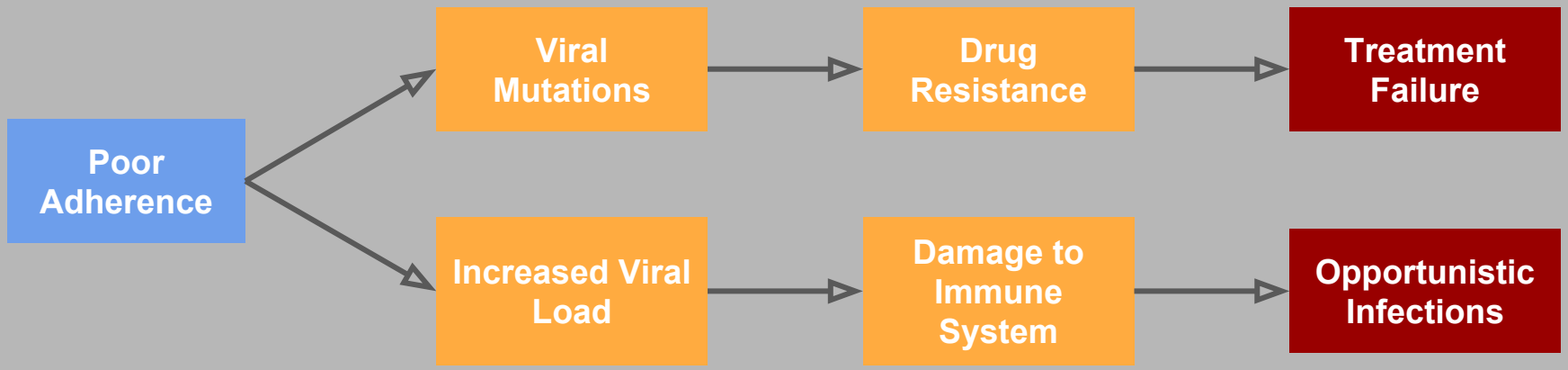
Optimal **ADHERENCE**

Adherence

- Both **adherence** and **persistence** to antiretrovirals are vital
  - **Adherence/compliance**: conforming to prescribed day-to-day treatment with respect to timing, dosage, and frequency
  - **Persistence**: the ability to take medications for their entire intended duration (in this case, **forever**)

Adherence

- Must take medications exactly as prescribed every day
- Do not miss **>2-3 doses/month** for optimal efficacy



Strategies to Improve Adherence

- Blister packing
- SMS/Text reminders
- Prescribe once-daily dosing regimens (and one-pill regimens if possible)
- Assess of readiness for adherence **before** initiating treatment
- Build up practitioner-patient relationships
- Address any substance abuse issues before starting therapy
  - Not a barrier to starting medication however
- Treat depression and other mental illnesses
- **Talk to your patients!!!**

Strategies to Improve Adherence

- Identify barriers and **do everything you can to help**
  - Cost
    - Saskatchewan Drug Plan
      - Social Assistance and Special Support
    - NIHB
    - Third Party/Manufacturer Payment Programs
  - Adverse effects
  - Chaotic life
  - Trouble swallowing
  - Addictions
  - Pill burden
  - Stigma
- **Refer** to other practitioners/organizations as necessary

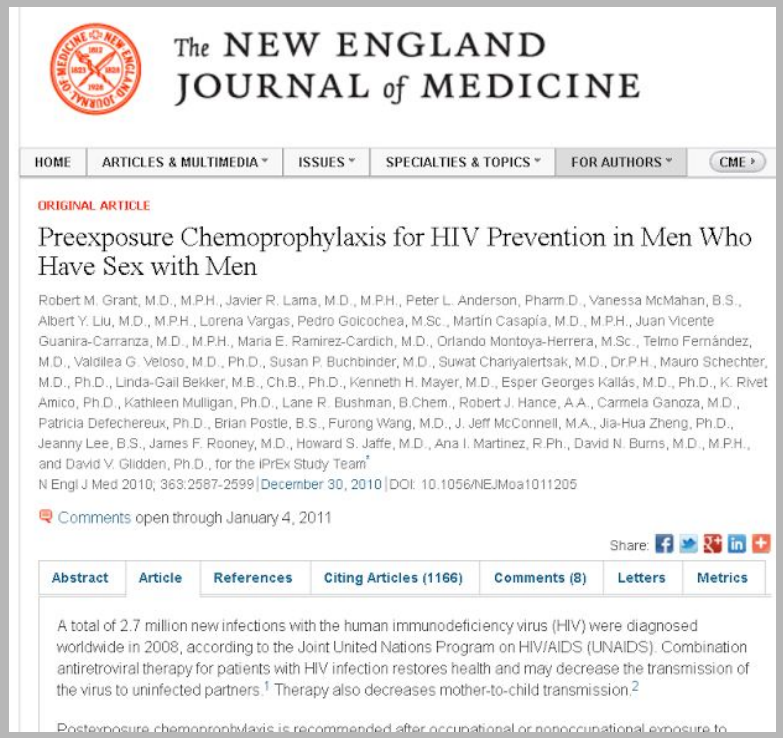
HIV **PREVENTION**

HIV Prevention

- No vaccine to prevent HIV transmission

- HIV can be prevented by implementation of behavioural and biomedical prevention strategies
  - PrEP
  - PEP
  - Condoms
    - 98-99% effective when used correctly
  - Treatment as Prevention (TasP)
    - Non detectable = Non Transmissible

Pre Exposure Prophylaxis (PrEP)



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ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

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N Engl J Med 2010; 363:2587-2599 | December 30, 2010 | DOI: 10.1056/NEJMoa1011205

Comments open through January 4, 2011

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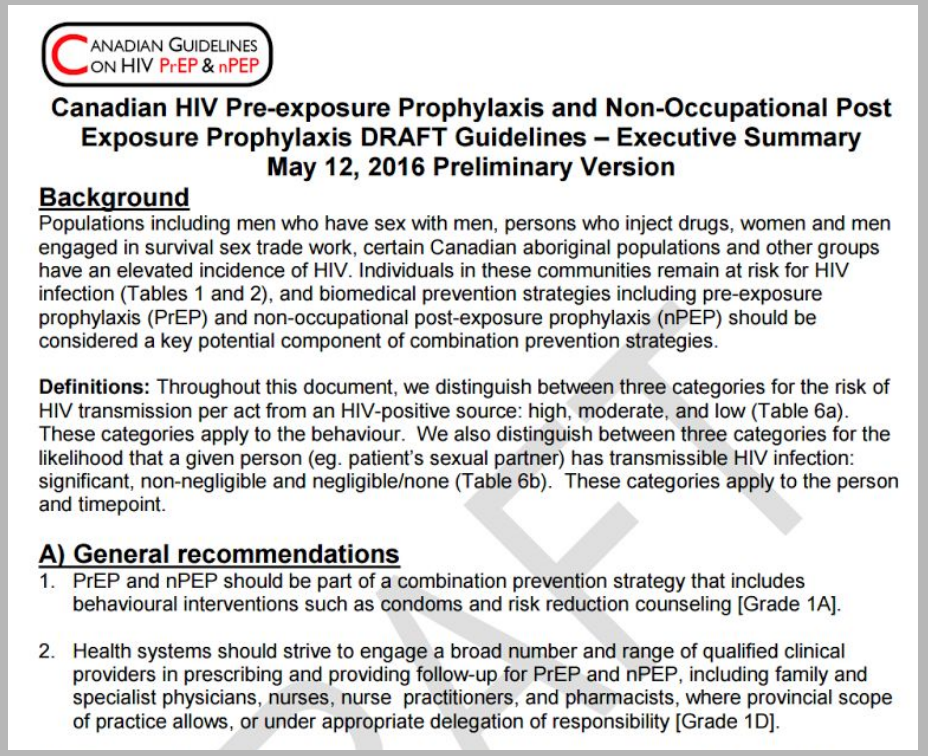
Abstract | Article | References | Citing Articles (1166) | Comments (8) | Letters | Metrics

A total of 2.7 million new infections with the human immunodeficiency virus (HIV) were diagnosed worldwide in 2008, according to the Joint United Nations Program on HIV/AIDS (UNAIDS). Combination antiretroviral therapy for patients with HIV infection restores health and may decrease the transmission of the virus to uninfected partners.[1] Therapy also decreases mother-to-child transmission.[2]

Postexposure chemoprophylaxis is recommended after occupational or nonoccupational exposure to

iPrex Study



CANADIAN GUIDELINES ON HIV PrEP & nPEP

Canadian HIV Pre-exposure Prophylaxis and Non-Occupational Post Exposure Prophylaxis DRAFT Guidelines – Executive Summary May 12, 2016 Preliminary Version

Background

Populations including men who have sex with men, persons who inject drugs, women and men engaged in survival sex trade work, certain Canadian aboriginal populations and other groups have an elevated incidence of HIV. Individuals in these communities remain at risk for HIV infection (Tables 1 and 2), and biomedical prevention strategies including pre-exposure prophylaxis (PrEP) and non-occupational post-exposure prophylaxis (nPEP) should be considered a key potential component of combination prevention strategies.

Definitions: Throughout this document, we distinguish between three categories for the risk of HIV transmission per act from an HIV-positive source: high, moderate, and low (Table 6a). These categories apply to the behaviour. We also distinguish between three categories for the likelihood that a given person (eg. patient's sexual partner) has transmissible HIV infection: significant, non-negligible and negligible/none (Table 6b). These categories apply to the person and timepoint.

A) General recommendations

1. PrEP and nPEP should be part of a combination prevention strategy that includes behavioural interventions such as condoms and risk reduction counseling [Grade 1A].

2. Health systems should strive to engage a broad number and range of qualified clinical providers in prescribing and providing follow-up for PrEP and nPEP, including family and specialist physicians, nurses, nurse practitioners, and pharmacists, where provincial scope of practice allows, or under appropriate delegation of responsibility [Grade 1D].

Draft Canadian Guidelines on HIV PrEP & nPEP -
http://www.catie.ca/sites/default/files/Canadian%20PrEP%20and%20nPEP%20Guidelines%20Executive%20Summary%20for%20circulation%20v0-5%20May%2012%202016.pdf

Pre Exposure Prophylaxis (PrEP)

- TDF/FTC (Truvada) highly effective at reducing rates of HIV transmission (86-100% efficacy in various studies)
  - Most trials in MSM
- For HIV-uninfected patients at high risk for acquiring HIV
  - Guidelines exist to assess risk
- Rigorous screening for HIV (and other STIs) at baseline, one month and every three months
  - Screens for kidney function for safety

Pre Exposure Prophylaxis (PrEP)

- Dosing:
  - TDF/FTC 300mg/200mg (Truvada) orally once daily
    or,
  - 2 tablets 2-4 hours before exposure and every 24 hours until 24 hours after last exposure

- Adherence is important as low blood levels of medication are associated with increased risk of HIV acquisition

Pre Exposure Prophylaxis (PrEP)

- Currently not reimbursed by Saskatchewan Drug Plan and Extended Benefits Branch
  - Listed in Formulary only for treatment of HIV
    - List price $27.703/tablet ($831.09/30 days)
  - Awaiting review from Pan-Canadian Pharmaceutical Alliance

- Open benefit on Non-Insured Health Benefits/First Nations and Inuit Health Branch Drug Benefit List
  - No charge to patients

Post Exposure Prophylaxis (PEP)

- Triple therapy ART regimen given to HIV negative patients after a known or high risk for HIV exposure: occupational or non-occupational
- Limited data but still widely accepted practice for prevention of HIV infection
- Guidelines exist to assess risk and algorithms exist for use in Saskatchewan

Post Exposure Prophylaxis (PEP)

- Efficacy decreases after 72 hours post exposure
- PEP ‘kits’ containing pre-printed orders and 3 days worth of medication (3TC/AZT + LPV/r) available at emergency departments throughout Saskatchewan
  - Patients receiving PEP must be referred for follow up evaluation by Infectious Diseases specialist
- If exposure is high risk a new prescription for total of 28 days to be given
  - Medications generally changed to once daily regimen such as DRV/r+TDF/FTC or DTG+TDF/FTC

Post Exposure Prophylaxis (PEP)

- Prescription should contain “For Post Exposure Prophylaxis” in order to process the claim at no cost to patient
  - Patient should have no remaining charge for medication

- If occupational exposure the claim will be processed by WCB

Questions?

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