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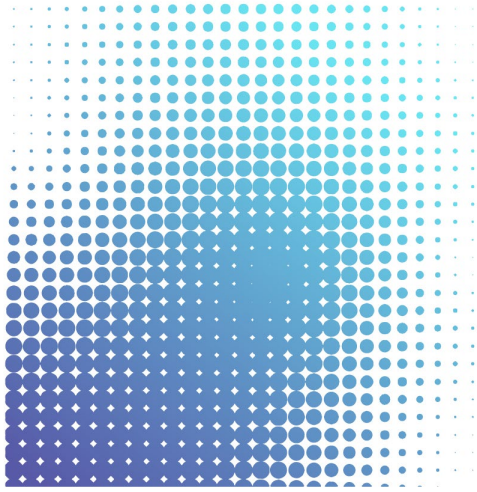
GAY MEN'S SEXUAL HEALTH ALLIANCE

Pre-exposure prophylaxis (PrEP) for Two-Spirit, gay, bisexual, trans and queer (2SGBTQ) men: Everything you need to know about PrEP



Frequently Asked Questions, and Glossary of Terms and Definitions on PrEP

2024

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About this document

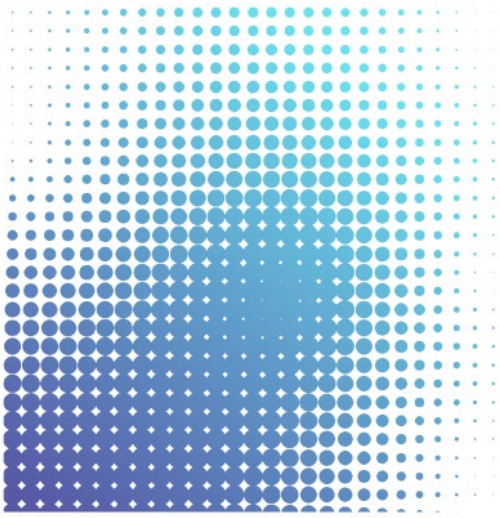
The document is intended for front-line, outreach staff, public health workers, and others providing sexual health care to the communities of Two-Spirit, gay, bisexual, trans and queer (2SGBTQ) men, as well as other men who have sex with men (MSM).

The FAQ document is a guide to the slides on various research studies on PrEP as well as other resources that encompass terms, definitions, medical or clinical reports, and additional information on medications, kidney functions, drug interactions, and references on PrEP.

To the best of our knowledge, we have incorporated the latest scientific information on PrEP in curating this document. It is highly recommended to go through the content, notes, and the wide range of information in this document to build a strong foundation of PrEP and its community, cultural and clinical competencies. The information in this document ranges from basic, intermediate to advanced knowledge of PrEP and clinical data. The document on PrEP is not an exhaustive list of all information and science on use of PrEP.

The information on PrEP is provided for informational or educational purposes only. The resource on PrEP is not a substitute for professional medical advice, diagnosis, or treatment. Always speak to a healthcare provider for further information on PrEP use.

For questions, please contact: dnambiar@gmsh.ca

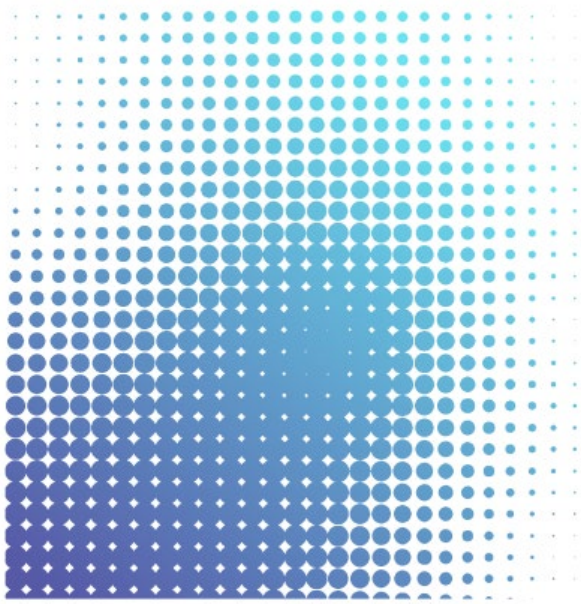


Please note: This guide is formatted to follow the slide number listed in the Power Point.

Recommended pre-reading on PrEP: Tan, D. H., Hull, M. W., Yoong, D., Tremblay, C., O'byrne, P., Thomas, R., ... & Shafran, S. (2017). Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *Canadian Medical Association Journal*, 189(47), E1448-E1458. https://doi.org/10.1503/cmaj.170494

Access the PDF file for free here: Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis (updated version, 2018).

CMAJ Podcasts: PrEP interview with Dr. Darrell Tan on Canadian guideline on HIV PrEP. In this interview, Dr. Darrell Tan takes listeners through the Canadian guidelines on HIV pre-exposure prophylaxis and nonoccupational post-exposure prophylaxis. (2018). Duration: 38.20 minutes. Listen here: https://soundcloud.com/cmajpodcasts/170494-guide



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Slide 4: What is PrEP?

It is an antiretroviral drug taken to prevent a person from acquiring HIV. The most commonly used type of PrEP is Truvada (brand name), which contains two medications: emtricitabine & tenofovir disoproxil fumarate. Tenofovir can also be used to treat hepatitis B.

All drugs are listed under different names such as trade, brand, and generic name. For example, the two common types of PrEP: Truvada (emtricitabine/tenofovir disoproxil fumarate) and Descovy (emtricitabine/tenofovir alafenamide). Vemlidy (tenofovir alafenamide) is also used to treat chronic (long-lasting) Hepatitis B with stable liver disease. Check this link out for more information about Vemlidy. If you would like to learn more about other types of liver diseases, check out the link here!

References:

1. RxList (2024, April 8). *Vemlidy Tablets (Tenofovir Alafenamide): Uses, Dosage, Side Effects, Interactions, Warning*. https://www.rxlist.com/vemlidy-drug.htm#description
2. Truvada (2024, May 13). *(Emtricitabine and Tenofovir Disoproxil Fumarate): Uses, Dosage, Side Effects, Interactions, Warning*. https://www.rxlist.com/truvada-drug.htm

Slide 5: Canadian guidelines on HIV PrEP (2017)

In 2017, the Canadian guidelines on the use of PrEP to reduce and prevent HIV infection was launched in Canada. For more information about these guidelines, check out: **Tan, D. H., Hull, M. W., Yoong, D., Tremblay, C., O'byrne, P., Thomas, R., ... & Shafran, S. (2017). Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *Canadian Medical Association Journal*, 189(47), E1448-E1458. https://doi.org/10.1503/cmaj.170494**

Check out the PDF file for free here: https://www.cmaj.ca/content/cmaj/189/47/E1448.full.pdf

Slide 6: Tenofovir Disoproxil Fumarate (TDF) vs. Tenofovir Alafenamide (TAF)

TDF and TAF are two different forms of the drug Tenofovir that is widely used in medications intended to treat HIV and Hepatitis B. Known as the old formulation of Tenofovir, TDF has always been safe but can have an impact on the kidneys and bone mineral density in certain people. TAF is a newer formulation of tenofovir and is regarded as a 'prodrug' where it gets converted into the active drug in higher concentrations in the body cells compared to TDF. Because of this, lower levels of the drug circulate in the blood, with lesser exposure for the kidneys, bones and other

organs in the body. (POZ, 2021). However, TAF does not have the same beneficial effect on blood lipids and may be linked to greater weight gain.

First approved in 2001, TDF is sold as the stand-alone medication Viread and is a component of the combination pills Truvada, Atripla, Complera, Delstrigo, Stribild and Symfi/Symfi Lo. TDF is now off patent, and there are cheaper generic versions available.

Approved in 2015, TAF is sold alone as Vemlidy and is a component of the combination pills Descovy, Biktarvy, Genvoya, Odefsey and Symtuza. TAF will remain under patent until 2022, and generic versions are not currently available. TAF was primarily developed to reduce the high blood levels of Tenofovir that impacted kidney function and cause bone mineral density loss in many people.

Reference:

1. Cairns, G. (2021). A large US study confirms that people switching from TDF to TAF experience rising blood fat levels. AIDSMap. https://www.aidsmap.com/news/oct-2021/large-us-study-confirms-people-switching-tdf-taf-experience-rising-blood-fat-levels

Slides 7: TDF, TAF, brand name, trade, and generic name

Drugs typically have two names. The ***brand name*** is given by the pharmaceutical company. It is often a short name, catchy and used to market the drug.

Generic names are assigned for a global market by the World Health Organization (WHO) and this name can be long. The generic name informs the pharmacist or doctor about the drug's pharmacological properties and chemical structure.

All prescription drugs approved in Canada and elsewhere have a brand name, trade name, and the generic name. When drugs are approved by Health Canada, it has a Drug Identification Number (DIN) and it is a registered drug with specific criteria for dosage, illness, treatment, drug interactions, etc. The drug has a patent by the pharmaceutical, and in Canada, patent terms are 20 years. When the patent expires, other pharmaceutical companies can manufacture the 'drug' as generic drugs. Generic drugs have same efficacy as brand-name drugs, but at a substantially lower cost.

Truvada® is the ***brand name*** of the generic medicine emtricitabine/tenofovir disoproxil fumarate.

References:

1. Highleyman, L. (2015) Tenofovir alafenamide equally effective but safer for kidneys and bones than current formulation. AIDSMap. https://www.aidsmap.com/news/feb-2015/tenofovir-alafenamide-equally-effective-safer-kidneys-and-bones-current-formulation

2. Lexchin, J, & Sud, A (2021) Generic drug names provide information for doctors, so why is Health Canada promoting the use of pharma brand names?. The Conversation. https://theconversation.com/generic-drug-names-provide-information-for-doctors-so-why-is-health-canada-promoting-the-use-of-pharma-brand-names-174087
3. Patented Medicine Prices Review Board (PMPRB): http://pmprb-cepmb.gc.ca/home
4. Common Drug Review (CDR) archieved: https://www.canada.ca/en/health-canada/services/health-care-system/pharmaceuticals/management/common-drug-review.html
5. Health Canada (2023) Prescription drug pricing and costs. Government of Canada. https://www.canada.ca/en/health-canada/services/health-care-system/pharmaceuticals/costs-prices.html
6. Health Canada (2023) Prescription drug management. Government of Canada. https://www.canada.ca/en/health-canada/services/prescription-drug-system.html

Slide 8: Descovy vs. Truvada vs. generic PrEP

All three forms of PrEP contain Tenofovir that is 99% effective as a HIV preventative medication. Descovy contains a new formulation **(**Tenofovir alafenamide (TAF) and emtricitabine (FTC)) and was approved for use as PrEP in 2019. However, this approval by the FDA only covered at-risk men and transgender women as there were insufficient data for cisgender women. Truvada contains tenofovir disoproxil fumarate (TDF) and FTC and was approved by the FDA in 2012. However, as described above, the TDF medication in Truvada can have implications for kidney function and bone mineral density over time. Generic PrEP is pretty much the generic version of Truvada – it contains both TDF and FTC. The production and sale of generic PrEP with FDA approval start happening more rapidly after Truvada's patent expired in 2020. The are no generics for Descovy as the patent has not expired yet.

Reference:

1. Broussard, J. (2019). *Side-by-side comparison: Truvada and Descovy for PrEP*. San Francisco AIDS Foundation. https://www.sfaf.org/resource-library/side-by-side-comparison-truvada-and-descovy-for-prep/
2. Carstens, A. (2022). Truvada or Descovy: which should I take for PrEP?. AIDSMap. https://www.aidsmap.com/about-hiv/truvada-or-descovy-which-should-i-take-prep

Slide 9:

Switching from TAF to TDF has shown benefits in the forms of reduced cholesterol and triglycerides, and improved lipid profile.

Reference:

Kauppinen, K. J et al. (2022). Switching from tenofovir alafenamide to tenofovir disoproxil fumarate improves lipid profile and protects from weight gain.
DOI: 10.1097/QAD.0000000000003245
https://pubmed.ncbi.nlm.nih.gov/35727143/

Slide 10: Question 1.

Answer: ***Reverse transcriptase***

Slide 11: How does tenofovir prevent HIV infection in the cell?

When a HIV virus infects a cell, it forces the cell to make many more copies of itself (by changing its genetic material from RNA to DNA via reverse transcription). To make these copies, the cell uses enzymes called reverse transcriptase. Tenofovir interferes with the reverse transcriptase enzyme to inhibit and/or reduce its activity, hence reducing and ultimately completely stopping the production of new HIV viruses by the HIV-infected host cells.

Click on the following links to learn more about:

- HIV
- Life cycle of HIV

Reference:

1. Hosein, SR. (2014). *Tenofovir (Viread)*. CATIE. https://www.catie.ca/tenofovir-viread

Slide 12: How does PrEP prevent HIV? PrEP Guide by CATIE

Watch the video for a better, illustrative idea of how PrEP prevents HIV:
https://www.youtube.com/watch?v=jyDHRJ_zwQ4

Slide 13: Intracellular levels of TDF & TAF

Intracellular means occurring or located inside a cell. Extracellular on the other hand means being located outside the cell. In the context of this slide, we discuss the levels of TDF and TAF inside the cells (intracellular).

The new formulation (TAF) was developed in response to concerns that the slow metabolism of TDF meant that high levels of tenofovir persisted extracellularly in the blood, causing side-effects of kidney dysfunction and bone demineralization linked to TDF.

There are 2 types of tenofovir.

- Tenofovir Disoproxil (TDF) & Emtricibine is 300mg/200 mg
- Tenofovir alafenamide (TAF) & Emtricibine is 25mg/200mg (a prodrug)

The TAF drug produced lower plasma (extracellular fluid) levels of tenofovir than TDF, but intracellular levels were four-fold higher with TAF. The steady state of tenofovir concentration was 91% lower with TAF compared to TDF.

What is a steady state? "*Steady-state concentration (C_{ss}) occurs when the amount of a drug being absorbed is the same amount that's being cleared from the body when the drug is given continuously or repeatedly. Steady-state concentration is the time during which the concentration of the drug in the body stays consistent*."

Reference:

1. https://www.nuventra.com/resources/blog/what-is-steady-state-concentration/

The intracellular concentration of tenofovir disphosphate reached when TAF was taken once every three days was 2.6 times higher inside peripheral blood mononuclear cells (PBMCs) than when using TDF daily.

PBMCs are the lymphocyte and monocyte cells in the immune system that are floating freely in blood and thus easy to extract; PBMCs include some of the T-cells which HIV mainly infects.

Reference:

1. One dose of TAF every three days. https://www.aidsmap.com/news/sep-2021/one-dose-taf-every-three-days-gets-more-drug-cells-daily-dose-tdf
2. Poz. (2022) TAF Versus TDF: What's the Difference? - POZ https://www.poz.com/basics/hiv-basics/taf-versus-tdf-difference

Slide 14: Question 2.

Answer: kidneys.

Slide 15: PrEP & kidney function

Tenofovir is excreted/eliminated from the body by the kidney in the urine through glomerular filtration and active tubular secretion.

- TDF can "damage the tiny structure known as proximal tubules- responsible for secreting waste products, reabsorbing water and keeping a stable book chemistry."

Creatinine levels and the kidney: Creatinine is a by-product of muscle metabolism. Specifically, "creatinine is a chemical compound left over from energy-producing processes in your muscles. Healthy kidneys filter creatinine out of the blood. Creatinine exits your body as a waste product in urine." (Mayo Clinic).

Creatinine turns to creatine phosphate (CP) in the body. "CP makes a substance called adenosine triphosphate (ATP) -which is used in the energy house of the cell-called the mitochrondria. ATP provides energy for muscle contractions." (WebMD,2020)

High levels of creatinine could mean the kidneys are not working well. It could be a one-time incident. It could also be due to dehydration, or large intake of protein supplements or taking creatine supplements for working out. "Creatine is thought to improve strength, increase lean muscle mass, and help the muscles recover more quickly during exercise." (WebMD,2020) Also, it may help with burst of energy and speed in some sports. If creatinine is of concern, the physician would do another blood test and urine test to rule out kidney problems.

For adults with "creatinine below 15 mL/min who are receiving chronic hemodialysis -one tablet of FTC+TAF once a day on days of hemodialysis." (FTC/TAF, 2021)

From Life Labs results: "An eGFR from 60-89 ml/min/1.73 m2 is consistent with mildly decreased kidney function. However, in the absence of other evidence of kidney disease, eGFR values in this range do not fulfill the KDIGO criteria for chronic kidney disease. Interpret results in concert with ACR measurement. KDIGO 2012 guidelines highlight the importance of eGFR and urine albumin creatinine ratio (ACR) in screening, diagnosis and management of CKD. For patients of African descent, the reported eGFR must be multiplied by 1.15." The rationale for this race difference was listed in 1999 and in 2020 it is being reviewed here and a task force set up to focus on the use of race to estimate GFR.

Nephrotoxicity is defining as rapid deterioration in the kidney function due to toxic effect of medications and chemicals. There are various forms, and some drugs may affect renal function in more than one way. Nephrotoxins are substances displaying nephrotoxicity.

Diagnosis and monitoring chronic kidney disease (CKD) and ACR:
"CKD is defined in KDIGO 2012 as an abnormality of the kidney structure or function, which is present for more than 3 months, with implications for the patient's health. Patients at high risk for CKD include those with clinical conditions, such as diabetes, hypertension, and those with a family history of kidney disease. The identification of the root cause for impaired renal function is important for the development of a patient management plan. A diagnosis of CKD is confirmed when:

- The eGFR is less than 60 mL/min/1.73 m, if duration exceeds 3 months.
- The ACR is equal to or greater than 3 mg/mmol creatinine, determined on 2 of 3 samples collected at least 3 months apart." OAML (2015)

*KDIGO Kidney Disease: Improving Global Outcomes

Reference:

1. Venter et al. 2018. An overview of tenofovir and renal disease for the HIV-treating clinician - PMC (nih.gov) South Afr J HIV Med. Doi: 10.4102/sajhivmed.v19i1.817
2. Ontario Association of Medical Laboratories. (2015). Community Laboratory Guidelines. https://oaml.com/wp-content/uploads/2016/05/OAMLeGFREPIGuidelineFinal2015.pdf
3. Al-Naimi, M.S., Rasheed, H.A., Hussien, N.R., Al-Kuraishy, H.M., & Al-Gareeb, A.I. (2019). Nephrotoxicity: Role and significance of renal biomarkers in the early detection of acute renal injury. Journal of Advanced Pharmaceutical Technology and Research, 10(3), 95-99.
4. Mayo Clinic (n.d). https://www.mayoclinic.org/tests-procedures/creatinine-test/about/pac-20384646
5. An Overview of creatinine Supplements. (2020) https://www.webmd.com/men/creatine
6. Energy. Lecture 17. (2005).http://www.uwyo.edu/bio1000skh/lecture17.htm
7. FTC/TAF. (2021). https://www.mayoclinic.org/drugs-supplements/emtricitabine-and-tenofovir-alafenamide-oral-route/proper-use/drg-20311650
8. Flawed Racial Assumption in eGFR have Care Implications in CKD. https://www.ajmc.com/view/flawed-racial-assumptions-in-egfr-have-care-implications

Slide 16: Question 3

Answer: True

Slide 17: How is tenofovir metabolized in the body?

Pharmacokinetics of drugs: In pharmacokinetics, drugs undergo four stages within the body. The four stages are absorption, distribution, metabolism, and excretion. After a drug is administered, it is absorbed into the bloodstream. The circulatory system then distributes the drug throughout the body. Then it is metabolized by the body. The rest is excreted out by the body.

Think of pharmacokinetics as a drug's journey through the body, during which it passes through four different phases: absorption, distribution, metabolism, and excretion (ADME). The four steps are:

- **Absorption:** Describes how the drug moves from the site of administration to the site of action.
- **Distribution:** Describes the journey of the drug through the bloodstream to various tissues of the body.
- **Metabolism:** Describes the process that breaks down the drug.

- **Excretion:** Describes the removal of the drug from the body."

Reference:

1. Genomind (2021, January 21). Introduction to pharmacokinetics: four steps in a drug's journey through the body. Genomind 360 Learning Center. https://www.genomind.com/360/an-introduction-to-pharmacokinetics-four-steps-of-pharmacokinetics

Slide 18: ADME

It stands for **A**bsorption, **D**istribution, **M**etabolism and **E**limination of drugs.

Slide 19: Question 4

Answer to #1 is true. Answer #2 is true

Slide 20: Side effects of Tenofovir

The common side effects of tenofovir are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, and rash.

Reference:

1. RxList. (2023, 30 March). Viread. https://www.rxlist.com/viread-side-effects-drug-center.htm

For more on Lactic acidosis, hep B, pancreatitis, visit: https://www.catie.ca/tenofovir-viread.

What is renal tubular acidosis? "Renal tubular acidosis (RTA) occurs when the kidneys do not remove acids from the blood into the urine as they should. The acid level in the blood then becomes too high, a condition called acidosis. Some acid in the blood is normal, but too much acid can disturb many bodily functions.

Reference:

1. https://www.niddk.nih.gov/health-information/kidney-disease/renal-tubular-acidosis

What is acidosis? "Extra acid in your blood and other body fluids and tissues, sometimes caused by your kidneys' failure to excrete acid into the urine." (National Institute of Diabetes, and Digestive and Kidney Disease)

As an anti-HIV drug, Tenofovir is processed, metabolized, broken down and is eliminated from the body by the kidney. "*The drug can damage tiny structures known as proximal tubules that are responsible for secreting waste products, reabsorbing water and maintaining stable blood chemistry. Impaired kidney function can cause slower clearance of creatinine, a by-product of muscle metabolism. This leads to increased creatinine levels in the blood and a decrease in estimated glomerular filtration rate (eGFR); an eGFR measurement below 60 indicates moderate loss of kidney function. Other signs of impaired kidney function include low phosphate levels in the blood and protein in the urine*."

Reference:

1. TAF Versus TDF: What's the Difference? - POZ

Some people experience decreases in eGFR and other unfavorable changes in kidney functions. The drug circulates in the kidney, blood (extracellular) and some of it is absorbed into the cells (intracellular). The circulating tenofovir may harm the kidney's tubules in the kidney. The dose is higher in TDF (300 mg) versus TAF (25mg). "The kidneys play a key role in this process by the fine regulation of calcium excretion. More than 95% of filtered calcium is reabsorbed along the renal tubules. In the proximal tubules, 60% of filtered calcium is reabsorbed by passive mechanisms."

References:

1. Kidney and Calcium Homeostasis: doi: 10.5049/EBP.2008.6.2.68
2. Https://www.cancer.gov/publications/dictionaries/cancer-terms/def/renal-tubule
3. Weinstein & Anderson. (2010). The Aging Kidney: Psychiological Changes. doi: 10.1053/j.ackd.2010.05.002

Slide 21: Side effects & contraindications of Tenofovir

Prenevir study*: Kidney Toxicity Rare With Daily or On-Demand (As-Needed) PrEP*: Kidney toxicity proved rare with either daily tenofovir/emtricitabine (TDF/FTC) preexposure prophylaxis (PrEP) or on-demand (as-needed) TDF/FTC PrEP in a 1253-person analysis from May 2017 to October 2020. https://www.natap.org/2021/EACS/EACS_17.htm

Prevenir study: "From May 2017 to October 2020, 499 Prevenir participants took TDF/FTC PrEP daily, 494 took TDF/FTC on demand, and 260 switched from one strategy to the other. Everyone had eGFR determined every 3 months."

The Prevenir investigators summarized the eGFR findings by stating that "on-demand PrEP dosing had a smaller impact on eGFR evolution than daily PrEP, but the difference was not clinically relevant."

"In this analysis Prevenir researchers aimed mainly to compare changes in kidney function with the two PrEP strategies as determined by eGFR. From the initial Prevenir population of 3067 people, mainly men who have sex with men (MSM), the investigators eliminated participants already taking PrEP at enrollment and those who did not have a baseline creatinine measure."

OPERA cohort study: "TDF, the older formulation of tenofovir, has been associated with an increased risk of developing chronic kidney disease, especially in people who receive tenofovir as part of a combination that includes a boosting agent (ritonavir or cobicistat). Tenofovir is known to have a harmful effect on the kidney tubules and boosting agents may raise levels of tenofovir in the kidneys, exacerbating the harmful effects of the drug."

Reference:

1. https://www.aidsmap.com/news/nov-2019/tenofovir-tdf-does-not-increase-risk-kidney-disease-people-low-risk

TDF, the older formulation of tenofovir, has been associated with an increased risk of developing chronic kidney disease, especially in people who receive tenofovir as part of a combination that includes a boosting agent (ritonavir or cobicistat):

Reference:

1. https://www.aidsmap.com/news/nov-2019/tenofovir-tdf-does-not-increase-risk-kidney-disease-people-low-risk

"Studies have found a raised risk of kidney disease in some people on TDF, but minimal risk in younger people, including in another study of OPERA, which is the cohort analysed for the new study. They have also found low rates of side effects in people taking TDF for PrEP, probably because they are on average younger than people on treatment. But TAF offers benefits for people who already have reduced kidney function, especially older people (kidney function naturally declines with age) and one study found switching to TAF improved bone mineral density in the over-60s."

Reference:

1. Cairns, G. (2021). Large US study confirms that people switching from TDF to TAF experience rising blood fat levels. AIDSMap. https://www.aidsmap.com/news/oct-2021/large-us-study-confirms-people-switching-tdf-taf-experience-rising-blood-fat-levels

Newer version of ARV- such as integrase inhibitor Dolutegravir has caused weight gain for some PLHIV. Further analysis showed, "that lower CD4 count and /or high viral load before starting

treatment was the strongest risk factor for substantial weight gain. Increases in weight may represent a 'return to health' effect."

Reference:

1. Alcorn, K. (2021) Older version of tenofovir used as PrEP linked to weight loss. AIDSMap. https://www.aidsmap.com/news/oct-2021/older-version-tenofovir-used-prep-linked-weight-loss

Contraindications. What is a contraindication regarding medications?

There are two types of contraindications:

- Relative contraindication means that caution should be used when two drugs or procedures are used together. (It is acceptable to do so if the benefits outweigh the risk.)
- Absolute contraindication means that event or substance could cause a life-threatening situation. A procedure or medicine that falls under this category must be avoided.

Reference:

1. Taber's Medical Dictionary Online website. www.tabers.com/tabersonline. Accessed March 15, 2023

Slide 22: Tenofovir in antiretrovirals (ARV) for PLHIV

Impaired blood vessel and kidney function underlie heart disease risk in PLHIV.

- Higher levels of creatinine in the blood, a marker of reduced kidney function, was related to lower blood vessel function among those who were HIV positive.
- Kidney function had a greater connection to blood vessel function in people with HIV than in people without HIV infection.
- To put this finding in perspective, a 1% lower flow-mediated dilation is associated with a 10% to 11% increased future cardiovascular disease risk for middle- and older-aged adults.

"Regardless," he said, "people can protect their kidneys and prevent cardiovascular disease by doing such things as controlling blood pressure and preventing diabetes."

Reference:

1. https://www.eurekalert.org/news-releases/576650

Slide 23: PrEP for Hepatitis B

Persons with chronic hepatitis B who are at risk of contracting HIV can receive a double benefit from oral PrEP tenofovir-based formulations that protect from HIV and reduce hepatitis B virus (HPV) load

Slide 24: What is eGFR?

Based on the 2017 PrEP guidelines:

"**Renal monitoring** - Underlying kidney disease should be ruled out before PrEP is started, using a urinalysis and serum creatinine. The estimated glomerular filtration rate should be > 60 mL/min for use of PrEP."

Reference:

1. https://www.niddk.nih.gov/health-information/professionals/advanced-search/explain-kidney-test-results

GRF- how well your kidneys are filtering: https://labs.selfdecode.com/blog/egfr/

Glomerular Filtration Rate (GFR) is the amount of blood filtered every minute by tiny filters in the kidneys called glomeruli. It measures how efficient your kidneys are functioning.

The job of kidneys is to remove waste and excess water from the blood. This becomes the urine. Kidneys process about 50 gallons (180 liters) of blood every day to produce about 50 ounces (1.5 liters) of urine. If the kidneys are not working well, this affects the filtration rate and it could indicate kidney damage.

GFR is affected by many factors, such as time of day, dietary protein intake, exercise, age, pregnancy, obesity, high blood sugar, antihypertensive drugs (to <HBP), acute and chronic kidney disease.

Slide 25: Kidney functions: Glomerular filtration rate

As per Canadian PrEP guideline, underlying kidney disease should be ruled out before PrEP is started, using a urinalysis and serum creatinine. The estimated glomerular filtration rate should be > 60 mL/min for use of PrEP.

A glomerular filtration rate (GFR) is **a blood test that checks how well your kidneys are working**. Your kidneys have tiny filters called glomeruli. These filters help remove waste and excess fluid from the blood. A GFR test estimates how much blood passes through these filters each minute.

Reference:

1. https://medlineplus.gov/lab-tests/glomerular-filtration-rate-gfr-test/

People with pre-existing kidney problems, including an eGFR below 60, should not take Viread, Truvada or other coformulations containing TDF. Many experts recommend that people at risk for kidney problems should also avoid TDF. The risk of kidney problems rises with age. People living with HIV—especially African Americans—are more likely to have chronic kidney disease than HIV-negative people using PrEP. Some people who are unable to take TDF because of preexisting kidney disease or risk factors can safely use Vemlidy, Descovy and other TAF coformulations.

Reference:

1. TAF Versus TDF: What's the Difference? - POZ

Slide 26: Race correction in estimates of kidney function

Calculations of eGFR using the Black "race correction," which have been widely used in Canada, can falsely increase eGFR up to 10%, which can lead to delayed diagnosis and thus poorer outcomes.**"**

Reference:

1. Elimination of race in estimates of kidney function to provide unbiased clinical management in Canada | CMAJ https://www.cmaj.ca/content/194/11/E421

In 2024 the task force on eGFR calculation published their final report. "In 2020, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) convened a Task Force to recommend an evidence-based race-free approach to estimated glomerular filtration rate (eGFR). After the rigorous review of more than 20 approaches, the NKF/ASN Task Force published the final report that recommended the implementation of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2021) equation for eGFR using creatine and expanded utilization of cystatin C testing." The full report is available here https://doi.org/10.1089/heq.2023.0038

Slide 27-28: Bone health

DEXA scans measure the mineral content in certain bones, such as the hip, spine and/or wrist.

Dual-energy x-ray absorptiometry (DXA) is the most accurate scan for diagnosing osteoporosis and other bone fractures. A DXA (DECK-sa) scan is a non-invasive procedure used to measure bone density, as well as mineral content in other parts of the body, including the hip.

DXA scans are the most accurate ways to diagnose:

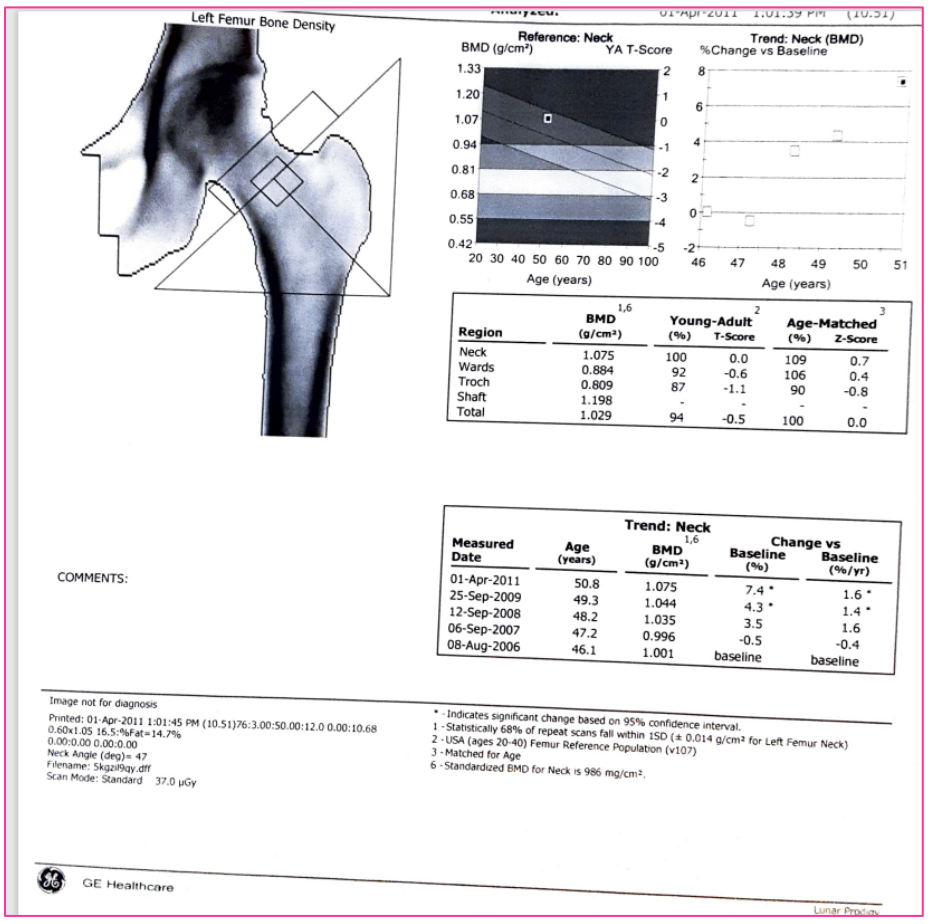
- The first stages of bone loss (osteopenia)
- Osteoporosis (PDF)
- The thinning of bones that can lead to bone fractures in aging men and women

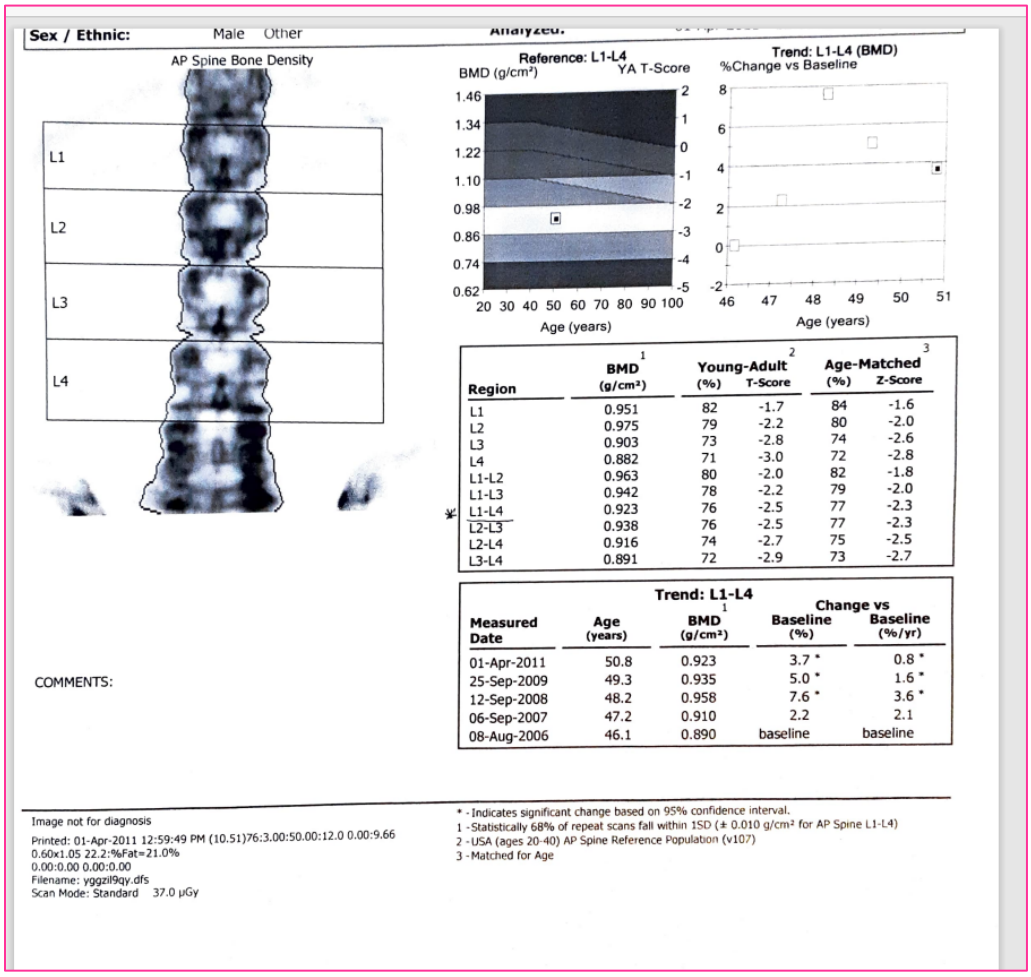
Bone loss, osteopenia, osteoporosis, can be more prevalent in PLHIV due to long term use of tenofovir (TDF) as antiretroviral therapy. Additional low testosterone levels in PLHIV can exacerbate the issue.

Bones need calcium, magnesium, sodium, phosphorus, copper, chloride, potassium, zinc, iron, manganese, chromium, organic factors.

Reference:

1. https://www.upmc.com/services/imaging/services/dual-hip-dxa





Region	BMD [1] (g/cm²)	Young-Adult [2] (%)	Young-Adult [2] T-Score	Age-Matched [3] (%)	Age-Matched [3] Z-Score
L1	0.951	82	-1.7	84	-1.6
L2	0.975	79	-2.2	80	-2.0
L3	0.903	73	-2.8	74	-2.6
L4	0.882	71	-3.0	72	-2.8
L1-L2	0.963	80	-2.0	82	-1.8
L1-L3	0.942	78	-2.2	79	-2.0
L1-L4	0.923	76	-2.5	77	-2.3
L2-L3	0.938	76	-2.5	77	-2.3
L2-L4	0.916	74	-2.7	75	-2.5
L3-L4	0.891	72	-2.9	73	-2.7

Trend: L1-L4				
Measured Date	Age (years)	BMD [1] (g/cm²)	Change vs Baseline (%)	Change vs Baseline (%/yr)
01-Apr-2011	50.8	0.923	3.7 *	0.8 *
25-Sep-2009	49.3	0.935	5.0 *	1.6 *
12-Sep-2008	48.2	0.958	7.6 *	3.6 *
06-Sep-2007	47.2	0.910	2.2	2.1
08-Aug-2006	46.1	0.890	baseline	baseline

Bone Mineral Density (BMD) Testing

“Osteoporosis is a disease characterized by low bone mass leading to fragile bones and increased risk of fractures. BMD testing measures bone loss due to osteoporosis and helps the patient and physician decide the risk of future fractures, determine the need for medical treatment and monitor the success of existing treatment.

Reference:

1. https://www.health.gov.on.ca/en/public/publications/ohip/bone.aspx

What does OHIP cover?

Medical experts recommend that BMD testing be carried out using only the 'axial DXA' machine which scans both hip and spine. This technique is clinically superior to all other testing methods and is the only method insured by OHIP.

Reference:

1. The 2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada can be found at: http://www.cmaj.ca/cgi/content/full/182/17/1864

Persons at High Risk for Osteoporosis
OHIP covers annual BMD tests for individuals at high risk for osteoporosis and future fractures.

Persons at Low Risk for Osteoporosis
Individuals at low risk are eligible for a baseline BMD test and a second BMD test 36 months after the baseline. Third and subsequent BMD tests for low-risk individuals are insured by OHIP once every 60 months.

Current recommendations by the Ontario Health Technology Advisory Committee (OHTAC) do not support the need for low risk individuals to be tested more often than every three to five years after baseline and at later intervals of seven to ten years when previous testing has shown a rate of bone loss of less than 1%. High risk patients (determined by the physician) will continue to receive annual access.Individuals and referring physicians must advise diagnostic facilities of the date of any previous BMD test so that the facility can verify that the planned test is insured. The Interactive Voice Response (IVR) system may also be used by physicians or clinics/facilities to determine the date of a previous BMD test. Instructions on the use of IVR can be found at: http://www.health.gov.on.ca/english/providers/pub/ohip/ohipvalid_manual/ohipvalid_manual_mn.html

What is not covered?

The following are not insured but may be provided at the patient's expense :

- BMD testing of low-risk persons provided more frequently than 36 months after the baseline test; and
- BMD testing of low-risk persons provided more frequently than 60 months after the second and subsequent tests.

This fact sheet includes material provided by the Osteoporosis Society of Canada (OSC). Further information at https://osteoporosis.ca/

Slide 29: PrEP 2-1-1

"On-demand" PrEP—also known as PrEP 2-1-1—is an alternative method of dosing that may speak to these concerns, making PrEP an option for more people than ever before. PrEP 2-1-1 is named for its schedule of dosing: 2 pills are taken 2-24 hours before sex, 1 pill 24 hours after the initial dose, and one final dose 24 hours later (find more info about this strategy). Clinicians only recommend PrEP 2-1-1 for people having anal sex, since the drug may not be present in levels high enough with PrEP 211 dosing to protect vaginal tissues.

For people having anal sex, PrEP 2-1-1 is effective at preventing HIV. Summary: In a study with more than 1,500 people followed for about 7 months, PrEP 2-1-1 was as effective as daily PrEP with neither strategy resulting in any HIV infections.

Reference:

1. https://www.sfaf.org/collections/beta/for-people-having-anal-sex-prep-211-is-as-effective-as-daily-prep/

Slide 30: PrEP for trans-feminine & trans-masculine persons

Referring to CATIE. Long acting cabotegravir -focus on transgender women

"Use of gender-affirming hormones did not result in significant increased weight in transgender participants during the study. Based on data from a sub-study of 53 transgender women, use of gender-affirming hormones did not affect cabotegravir levels in the blood.' Treatment Update 250. CATIE, 2024

"PrEP levels are generally measured in the blood whereas it is the mucosal and intracellular levels of PrEP that are assumed to matter when it comes to efficacy." This is explained in the Slide 31 in the UK guidelines that measure PBMC levels.

Reference:

1. CATIE Treatment Update 250. Long-acting cabotegravir -focus on transgender women. CATIE, 2024
2. iBREATHe- https://www.aidsmap.com/about-hiv/interactions-between-prep-and-gender-affirming-hormone-therapy
3. https://www.aidsmap.com/news/jul-2018/prep-does-not-lower-feminising-hormone-level-transgender-women

4. https://www.poz.com/article/underestimate-benefit-hiv-prep-trans-women

Other research on trans women and PrEP : "And standardized and real-life [feminizing hormone treatment] do not significantly impact on tenofovir and emtricitabine exposure among trans women at risk in a long-term follow up [Pharmacokinetic study]."

Reference:

1. Malone et al. (2021). LITE study (n- 1,293) An observational study of transgender women on PrEP. doi: 10.1097/QAI.0000000000002726

A second study by the same team looked at the effect of PrEP drugs on feminizing hormone levels. In this study, 33 women took TDF/FTC along with estradiol valerate and the testosterone blocker spironolactone. According to the study abstract, estradiol levels did not change significantly. Spironolactone levels decreased slightly but probably not enough to affect its effectiveness. "Our results reassure that oral PrEP and feminizing hormone therapy may be used concomitantly," the researchers concluded.

Reference:

1. https://www.aidsmap.com/news/oct-2021/cdc-prep-guidelines-should-include-specific-criteria-trans-women

Slide 31: 2024 UK guidelines for PrEP

In UK, as of February 2024 there has been some changes in PrEP based on absorption in blood levels of PrEP. In October 2024 a public consultation on PrEP was initiated. More here. The changes are based on recent studies that update our understanding of how PrEP works. Instead of needing to have good drug levels in vaginal or anal tissue, PrEP efficacy is now explained by drug levels in cells called peripheral blood mononuclear cells. (PBMC). More on PBMC here As the drug levels in PBMCs are not affected by sex or gender, there are now easier dosing options for cisgender women and for people who are transgender and non-binary.

The UK guidelines in 2024 might include additional recommendations that could make PrEP even easier. This includes that people who currently need 6-7 daily doses a week might only need 4 or more.

Event-based dosing can also now be used by everyone. This uses either 2:1:1 or 2:7 dosing (2 pills before sex and continue for 7 days).

2:1: 1 is two pills 2 to 24 hours before sex, and one pill for next two days.

2:7 is two pills at 2 to 24 hours before sex, and one pills for next even days

"***If you have sex several times over a few days, keep taking a pill each day. Continue for two days after the last day that you have sex."*** Examples of event-based 2:1:1 and 2:7 dosing | Guides | HIV i-Base

New clinical guidelines are coming up and when to start or stop PrEP and new versions of PrEP (TAF/FTC and injectables). Other studies show that everyone can now quick start PrEP with a double dose (two pills) to be protected within two hours.

In Canada we have not revised the PrEP guidelines and speak to your health care provider for updates.

Slide 32: 2:1: 1 dosing sex once

Slide 33: 2:1: 1 dosing more sex

Slide 34: 2 :7 for cis women and trans and non-binary people having receptive vaginal/frontal sex**.**

Slide 35: The relevance of pre-exposure prophylaxis in gay men's lives and their motivations to use it: a qualitative study (n=13, 2021)

These categories comprised ten themes, each of which had various repeating ideas. The ten themes were the following: (1) PrEP's social acceptability, (2) PrEP and HIV stigma, (3) PrEP and sexual relationships, (4) dissatisfaction with condoms, (5) negotiating risk, (6) peace of mind, (7) developing a relationship with PrEP, (8) putting yourself first, (9) PrEP awareness, and (10) PrEP logistics.

Reference:

1. Jorge L. Alcantar Heredia, Shelly Goldkland (2021). The relevance of pre-exposure prophylaxis in gay men's lives and their motivations to use it: a qualitative study - PubMed (nih.gov)

Slide 36: The PrEP-Stigma Paradox: Learning from Canada's first wave of PrEP users (n=16, 2018)

Reference:

1. Grace, D., Jollimore, J., MacPherson, P., Strang, M. J., & Tan, D. H. (2018). The pre-exposure prophylaxis-stigma paradox: learning from Canada's first wave of PrEP users. *AIDS patient care and STDs*, *32*(1), 24-30.

Slide 37: PrEP Whores and HIV Prevention

PrEP Whores and HIV Prevention: The Queer Communication of HIV Pre-Exposure Prophylaxis (PrEP) https://www.tandfonline.com/doi/full/10.1080/00918369.2016.1158012

The “PrEP whore” has come to designate the social value and personal practices of those taking PrEP. This study examines the “PrEP whore” discourse by using queer theory and quare theory. Within these theoretical vantage points, the study explicates four discursive areas: slut shaming, dirty/clean binaries, mourning the loss of condoms, and reclaiming the inner whore.

https://www.poz.com/article/queer-communication-prep “emphasized individual behavior change, population-based social marketing and education initiatives, and an emphasis on health care access and support services for people living with HIV including pregnant women. Individual behavior change has included, among others: abstinence-only initiatives, condom use, HIV testing, condom negotiation, needle exchange, HIV disclosure, sexual and drug-using risk reduction, HIV treatment adherence, and building supportive social networks. Population-based initiatives have included social marketing and educational initiatives.”

Sex-stigma emerged: as a complex theme in men's accounts of PrEP use across three overlapping domains: (1) PrEP-related stigma, including discussions of concealment and stigma from friends, family, and sexual partners, (2) PrEP as a perceived tool for combating HIV-related stigma, where some men said that they no longer discussed HIV status with sexual partners, and (3) PrEP as illuminating structural stigma, where it was attributed to unmasking stigma related to sex and sexuality.

We conducted small focus groups and individual qualitative interviews with 16 gay men in Toronto who were part of the ‘first wave’ of Canadian PrEP users. Participants were on PrEP for at least one year as part of a demonstration project (November 2014–June 2016). These participants accessed PrEP before regulatory approval by Health Canada in February 2016. The mean age of participants was 37.6 years (SD 11.02); 94% completed secondary education, and 69% were white

Slide 38: PrEP STIs and check up

Research has shown typically with PrEP use, most users have condomless sex. This increases prevalence of STIs, names syphilis, chlamydia, gonorrhea. It is important to get tested for STIs or be on doxycycline.

Slide 39: Danish Study

Slide 41: GMSH factsheets on syphilis, chlamydia, gonorrhea

Slide 41: GMSH factsheet on doxycycline for prevention of STIs

Slide 42: PrEP: Efficacy in clinical trials

Four studies on adherence and efficacy of PrEP. If taking daily efficacy is high. High adherence equals prevention.

Slide 43: PrEP: Low adherence correlates with poor efficacy

Trials where only a minority of subjects were adherent did not/could not demonstrate HIV protection.

Slide 44: Adherence to PrEP-urine test

Slide 45: Trends in PrEP uptake in Ontario (2015-2018) by Darrell H. S. Tan, Thomas M. Dashwood, James Wilton, Abigail Kroch, Tara Gomes & Diana Martins . *Canadian Journal of Public Health* volume 112, pages 89–96 (2021). https://pubmed.ncbi.nlm.nih.gov/32529552/

Results: The estimated number of individuals receiving PrEP increased 713%, from 374 in 2015 (Q3) to 3041 in 2018(Q2). Among PrEP users in 2018 (Q2), 97.5% were male, 60.4% were < 40 years, 67.7% obtained PrEP from a family physician, 77.2% used private insurance, and 67.0% were in Toronto. "PrEP-to-need ratios" (PNRs) were highest in 30–39-year-olds, males, Toronto and the Central East and West regions. Time series analyses found that Health Canada approval ($p = 0.0001$) and introducing generics/partial public drug coverage ($p = 0.002$) led to significantly increased use.

Conclusions: PrEP use has risen in Ontario in association with favorable policy changes, but remains far below guideline recommendations.

Slide 46: HIV testing and positive cases review March -May 2024 with no PrEP use

Slide 47: PARTNER 2 research:

PARTNER2 is a final results of multicenter, observational study

The level of evidence for HIV transmission risk through condomless sex in sero different gay couples with the HIV-positive partner taking virally suppressive antiretroviral therapy (ART) is limited compared with the evidence available for transmission risk in heterosexual couples. The aim of the second phase of the PARTNER study (PARTNER2) was to provide precise estimates of transmission risk in gay serodifferent partnerships.

The first phase of the study (PARTNER1; Sept 15, 2010, to May 31, 2014) recruited and followed up both heterosexual and gay serodifferent couples (HIV-positive partner taking suppressive ART) who reported condomless sex, whereas the PARTNER2 extension (to April 30, 2018) recruited and followed up gay couples only. The first phase of the PARTNER study (PARTNER1) estimated the risks for different types of sex and in a broader population. The study reported no linked transmissions in 888 serodifferent couples (548 heterosexual and 340 gay couples) who reported condomless penetrative sex during 1238 couple-years of follow-up when the HIV-positive partner was on virally suppressive ART.[8]

The primary aim of the second phase of the PARTNER study (PARTNER2) was to produce a similar level of evidence for transmission risk through condomless anal sex between men with suppressive ART (defined as HIV-1 RNA viral load <200 copies per mL) to that generated for heterosexual couples in PARTNER1. Aim of the second phase of the PARTNER study (PARTNER2) was to provide precise estimates of transmission risk in gay serodifferent partnerships.

Slide 48: PrEP cost at a glance

PrEP is free for people 24 years and under, free with OHIP & a prescription

PrEP is free if on ODSP, Ontario Works, over 65 years of age and on employee health benefits plan. A fee of $2.00 co-pay may apply in some pharmacies.

Paying for PrEP: Payment for PrEP can be paid via your employee health benefits/ health insurance

To pay by Trillium and Ontario Drug Benefit program (OHIP+ Trillium), apply for Trillium Drug Program, and pay a deductible. The deductible is based on household/personal income to offset cost of medications. The amount is verified from your income tax statements. Any unpaid deductible in a quarter will be added to the next quarter's deductible. (ODBF, p.55)

Trillium deductibles is divided into 4 payments. The payment is scheduled for August 1st November 1st, February 1st, May 1st .

Trillium at 1-800-575-5386. Trillium Drug program: Trillium Drug Program

Slide 49: Health Canada approves Cabotegravir the first long-acting injectable for HIV prevention

Cabotegravir (Apretude). 2024 August 4. Vol. 4. Issue 8 View of Cabotegravir (Apretude) | Canadian Journal of Health Technologies (canjhealthtechnol.ca)

FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention | FDA
https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention

The US FDA approved injectable PrEP on Dec 21, 2021. "The medication is Apretude (cabotegravir extended-release injectable suspension). Apretude is given first as two initiation injections –one month apart and then every two months thereafter. Patients can either start their treatment with Apretude or take oral cabotegravir (Vocabria) for four weeks to assess how well they tolerate the drug. Side effects occurring more frequently in participants who received

Apretude compared to participants who received Truvada in either clinical trial include injection site reactions, headache, pyrexia (fever), fatigue, back pain, myalgia and rash." FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention | FDA

EFR –extended-release formulation. Cabotegravir is a novel integrase inhibitor from ViiV Healthcare. Injectable cabotegravir (branded as *Vocabria*), along with rilpivirine (*Rekambys*), is also a component of the first complete long-acting regimen for HIV treatment.

The HPTN 083 trial enrolled more than 4000 cisgender men and transgender women who have sex with men in the US, Latin America, Asia and Africa. The study was halted ahead of schedule in May 2020 after an interim analysis showed that cabotegravir injections worked as well as daily pills. Further results showed that the injections were 69% more effective than TDF/FTC at preventing HIV acquisition. This is a remarkable finding, given that daily TDF/FTC reduces the risk of HIV by about 99% for gay and bisexual men who use it consistently.

A parallel study, HPTN 084, compared injectable cabotegravir PrEP versus daily TDF/FTC in more than 3000 mostly young cisgender women in sub-Saharan Africa. This trial was also stopped early after an interim analysis found that the injections were more effective. Researchers first reported that women who received the injections had an 89% lower risk of acquiring HIV than those who used daily pills. Further follow-up showed that injectable cabotegravir was even more effective—92%—after reclassifying a participant who was found to already have HIV when she started the study.

This is the highest efficacy ever seen in a trial of PrEP for women. Several prior studies have found PrEP pills to be less effective for women than for gay men. The superior efficacy of injectable PrEP for this population appears to be attributable to better adherence. https://www.aidsmap.com/news/dec-2021/us-approves-injectable-cabotegravir-prep

https://www.aidsmap.com/news/dec-2021/us-approves-injectable-cabotegravir-prep

Slide 50: PIP – PEP in Your Pocket

Slide 51: New research 2022: Biktarvy useful for HIV post-exposure prophylaxis (PEP)

Slide 52: Blood donation and PrEP and PEP and questions on deferring people who use PrEP/PEP. Their answer is this**:**

Pre-exposure prophylaxis (PrEP) is a highly effective medication regimen used for HIV prevention. In people taking PrEP or post-exposure prophylaxis (PEP), low levels of HIV may be missed in testing. We rely on accurate HIV testing as part of our multi-layered approach to safety. There needs to be more research on how PrEP and PEP affect HIV testing. Currently, individuals who take PrEP or PEP are unable to donate for 4 months from last use. This is an issue impacting blood operators worldwide. Tests used to detect HIV, and other viruses are manufactured by other companies, not Canadian Blood Services. Work to understand the true impact of PrEP and PEP

medication regimens on HIV tests can only be completed in collaboration with or directly by the manufacturers of the test, who hold the licensing for these products. Canadian Blood Services and other blood operators are highly interested in ongoing studies assessing impact of PrEP on testing assays.

. " Use of PrEP may interfere with testing for HIV by delaying seroconversion or giving unclear results in a positive donor. For this reason, it is important that donors who have taken PrEP in the previous three months are not accepted to donate, even if they do not have another blood safety risk."

The clinical rationale is as PrEP messes up HIV testing " “The clinical implications [of the findings] are currently unknown,” Custer said. “The potential or cause for concern is that ART and PrEP by definition are taken to alter the course of HIV infection; thus, the use of ART or PrEP could impact our ability to detect HIV infection in donated blood because blood tests for HIV measure the presence of viral RNA or antibodies to HIV infection.”

Reference:

1. https://www.healio.com/news/hematology-oncology/20200728/blood-donations-by-people-taking-drugs-to-treat-prevent-hiv-could-be-cause-for-concern

Similar guidelines on PrEP use and blood donation as CBS in UK:

1. https://www.transfusionguidelines.org/dsg/wb/guidelines/pre-and-post-exposure-prophylaxis-for-hiv#:~:text=Use%20of%20PrEP%20may%20interfere,have%20another%20blood%20safety%20risk