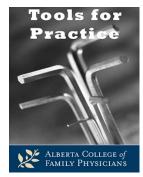
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Pre-Exposure Prophylaxis (PrEP): Are you PrEP'd for the future of HIV prevention?

Clinical Question: In patients at higher risk of contracting HIV, can daily antiviral therapy prevent infection?

Bottom-line: Tenofovir/emtricitabine (PrEP) once daily reduces the risk of HIV by ~50%, preventing infection for ~1 in 50 per year. A year of therapy costs ~\$12,000 and ~1 in 34 develop nausea/vomiting due to the drug.

Evidence:

- PrEP is tenofovir 300 mg (TDF) +/- emtricitabine 200 mg (FTC) once daily.
 - o Three systematic reviews¹⁻³ with 6-15 Randomized Controlled Trials (RCTs), new HIV infection statistically significantly reduced:
 - Meta-analysis (10 RCTs, 17,423 patients): 51% relative risk reduction (RRR).¹
 - Others^{2,3} similar.
 - Event rates over ~1 year: 2 2% PrEP versus 4% placebo, Number Needed to Treat (NNT)=50.
 - Adherence matters: Adherence >70%, RRR=70% but adherence <40%, effect not significant.¹
 - Seven primary RCTs (total 18,582 patients):
 - High-risk groups studied: Homosexual men (two RCTs);^{4,5} Heterosexual couples with one HIV positive (one RCT);⁶ Single heterosexuals –Africa (one RCT);⁷ IV drug-users –Thailand (one RCT);⁸ Women –Africa (two RCTs).^{9,10}
 - All similar with NNT=16-67 over ~1 year, 4-8 except:
 - Two RCTs of African women: 9,10 No effect but adherence very low.
 - o Example: ≤30% had drug in serum when tested. 10
 - o Other aspects:
 - Condom use ~80% and generally similar between groups. ^{4,6,7,10}
 - TDF effect likely similar to TDF+FTC,¹ but TDF+FTC most studied.
 - Adverse effects: Generally increased nausea/vomiting³ (example 8% versus 5%, NNH=34).⁸
 - Serious adverse events not increased.⁴⁻¹⁰

Context:

• CDC guidelines suggest PrEP (TDF+FTC) be considered if high risk of HIV infection. 11

- o Before starting PrEp, check renal function, hepatitis B, pregnancy, and (if at risk) osteoporosis.
- o Monitor renal function and for HIV (stop if positive).
- o Resources available http://www.catie.ca/en/prevention/statements/prep.
- Although cost is \$12,000/year, PrEP can be cost effective.¹²
- Modeling study: Homosexual men contracting HIV annually: 13
 - o 10.9% if no PrEP or condom use.
 - o ~3% if excellent PrEP or condom adherence.
 - o 0.9% if excellent PrEP and condom adherence.
- Unclear if PrEp increases risk behaviour:
 - Most research suggests not,¹ but one RCT found more PrEP users had multiple partners without condoms (21% versus 12%)⁵ and cohort study found 41% of men used condoms less.¹⁴

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Disclosures:

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References:

- 1. Fonner VA, Dalglish SL, Kennedy CE, et al. AIDS. 2016; 30(12):1973-83.
- 2. Jiang J, Yang X, Ye L, et al. PLoS ONE. 2014; 9(2):e87674.
- 3. Okwundu CI, Uthman OA, Okoromah CAN. Cochrane Database Syst Rev. 2012; 7:CD007189.
- 4. Grant RM, Lama JR, Anderson PL, et al (iPrEx). N Engl J Med. 2010; 363:2587-99.
- 5. McCormack S, Dunn DT, Desai M, et al (PROUD). Lancet. 2016; 387:53-60.
- 6. Baeten JM, Donnell D, Ndase P, et al (Partners PrEP). N Engl J Med. 2012; 367:399-410.
- 7. Thigpen MC, Kebaabetswe PM, Paxton LA, et al (TDF2). N Engl J Med. 2012; 367:423-34.
- 8. Choopanya K, Martin M, Suntharasamai P, et al (Bangkok Tenofovir). Lancet. 2013; 381:2083-90.
- 9. Van Damme L, Corneli A, Ahmed K, et al (FEM-PrEP). N Engl J Med. 2012; 367:411-22
- 10. Marrazzo JM, Ramjee G, Richardson BA, et al (VOICE). N Engl J Med. 2015; 372:509-18.
- 11. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States. CDC 2014. Available from: https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf. Last accessed July 2, 2016.
- 12. Gomez GB, Borquez A, Case KK, et al. PLoS Med. 2013; 10(3):e1001401.
- 13. Smith DK, Herbst JH, Rose CE. Sex Transm Dis. 2015; 42:88-92.
- 14. Volk JE, Marcus JL, Phengrasamy T, et al. Clin Infect Dis. 2015; 61:1601-3.

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