


HIV PREP: THE NEXT STEP IN HIV PREVENTION
 Ariel L. Watriss NP-C, WHNP-BC
 Tufts University Health Services


DISCLOSURES

- None.




OBJECTIVES

- Learn about PrEP and its efficacy as an HIV prevention tool
- Describe common side effects of PrEP and prescribing criteria
- Discuss application of PrEP to case studies



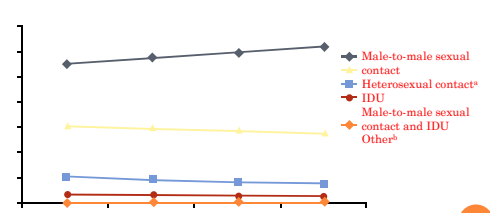
TERMS

- ART/ARV
- Cis-gender
- IDU or IVDU
- Microbicide
- MSM
- PEP
- PrEP
- RAI
- Seroconversion
- Trans
- Truvada
- Versatile or 'vers'
- Viral load or VL




THE NEED FOR HIV PREVENTION: CONTINUED HIV RISK IN THE US

- Estimated new HIV infections in the United States for the most affected subpopulations, 2008-2011




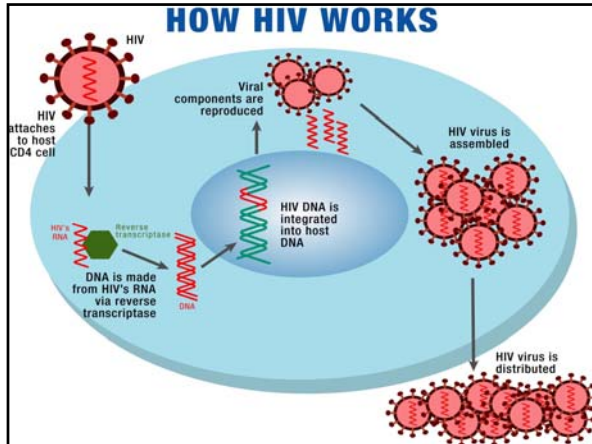
CDC. HIV in the United States: 2013.



PREVENTION- WHAT ALREADY WORKS?

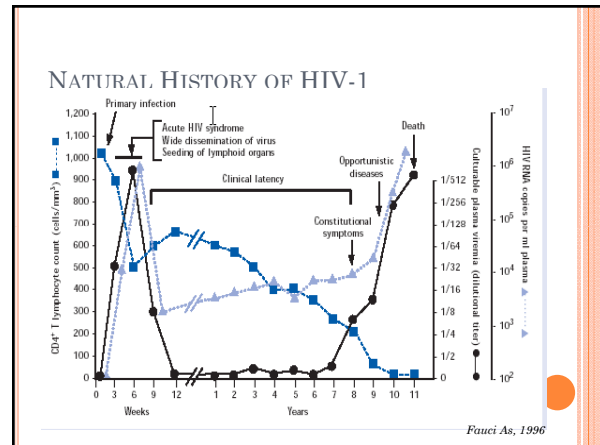
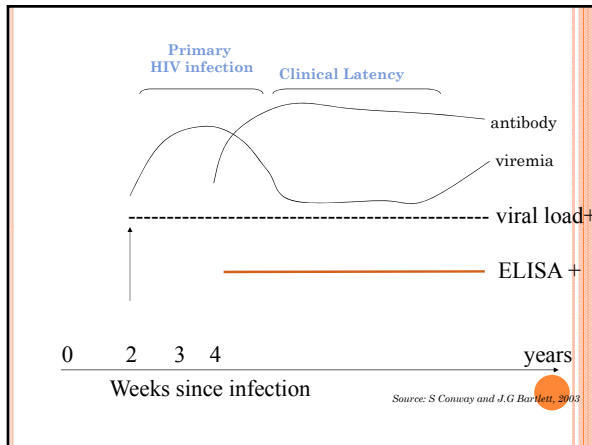
- Education
- HIV testing
- Behavioral changes
- Barrier methods
- PEP
- ART during pregnancy for HIV+ women
- Anything else?





PRIMARY HIV INFECTION

- The period immediately after infection characterized by high level of viremia (>1 million) for the duration of a few weeks
- Associated with a transient fall in CD4
- Nearly half of patients experience some mononucleosis-like symptoms (fever, rash, swollen lymph glands)
- Primary infection resolves as body mounts HIV-specific immune response
- After CD4 and viral load reaches plateau, patient enters "clinical latency"



ESTIMATED RISK OF SEROCONVERSION BY SEXUAL ACT

Type of Contact	Approximate Risk of Transmission
Receptive anal	1-30%
Insertive anal or receptive vaginal	0.1-10%
Insertive vaginal	0.1-1%

Landovitz NEJM 2009

HIV MEDICATION AS PREVENTION TOOL

- Idea of prophylaxis medication is not a new one.
- 1 pill daily of Truvada in conjunction with use of other prevention methods.

CIT leading the way in AIDS research

Nucleoside/Nucleotide Analogs (NRTIs)

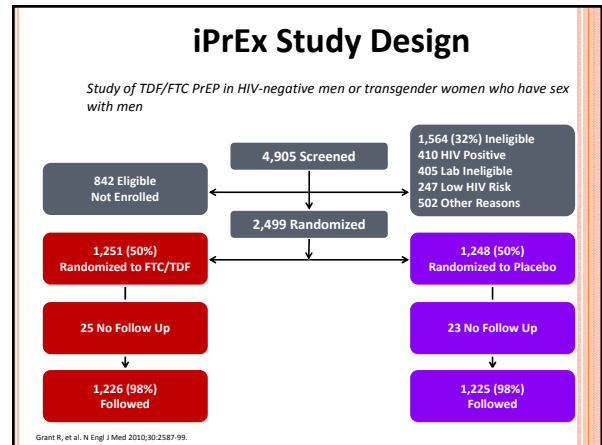
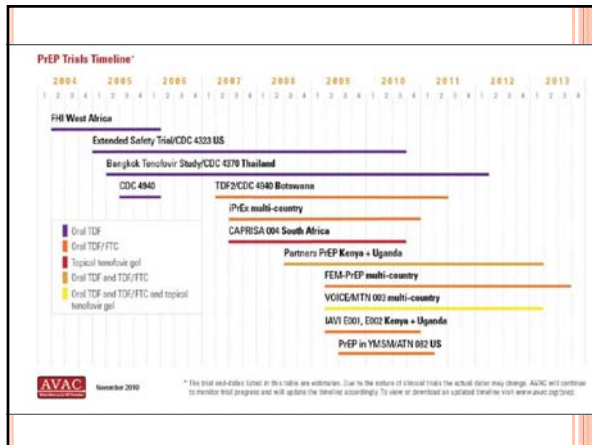
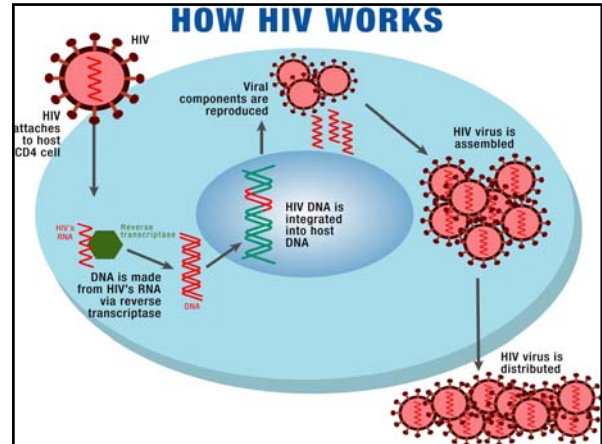
Abacavir (Zidovudine)	Lamivudine (3TC)	Emtricitabine (FTC)	Tenofovir Disoproxil Fumarate (TDF or TDF-ER)	Didanosine (ddI)	Zalcitabine (ddC)	Stavudine (d4T)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)
---------------------------------	----------------------------	-------------------------------	---	----------------------------	-----------------------------	---------------------------	-----------------------------	-----------------------------	-----------------------------	-----------------------------

Multi-Class Drug Combinations

Abacavir (Zidovudine)	Lamivudine (3TC)	Emtricitabine (FTC)	Tenofovir Disoproxil Fumarate (TDF or TDF-ER)	Didanosine (ddI)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)
---------------------------------	----------------------------	-------------------------------	---	----------------------------	-----------------------------	-----------------------------	-----------------------------	-----------------------------	-----------------------------

Protease Inhibitors (PIs)

Didanosine (ddI)	Emtricitabine (FTC)	Lamivudine (3TC)	Tenofovir Disoproxil Fumarate (TDF or TDF-ER)	Didanosine (ddI)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)	Zalcitabine (ddC)
----------------------------	-------------------------------	----------------------------	---	----------------------------	-----------------------------	-----------------------------	-----------------------------	-----------------------------	-----------------------------



iPREX: HIV BY GROUP AND DRUG DETECTION

Group	Drug Detection	HIV Infections	Incidence Density
Placebo	No	64	3.86
	Yes	3	0.35
FTC/TDF	No	33	4.04
	Yes	3	0.35

Relative Rate Reduction by use of FTC/TDF: 91%

- ### CHALLENGES/CONCERNS
- Side effects
 - Risk compensation
 - Resistance
 - How to identify acute HIV.
 - Adherence
 - Isolated use- PrEP includes Truvada but Truvada does not equal PrEP
 - Long term effects/Limits of current data
 - Cost
 - Possible drug interactions
 - Reception/Stigma

SIDE EFFECTS

- GI symptoms
- Renal issues
- Liver-Hepatitis challenge
- Bone density
- Long term effects?

RISK COMPENSATION

- Not seen in trials
- Opposite was noted.

RESISTANCE

- Resistance rare (consistent with subjects who acquired HIV not taking PrEP)
 - Exception: those with undiagnosed (seronegative) acute HIV infection at time PrEP was initiated
- Acute seroconversion

PREP SAFETY

- Rates of death, serious adverse events, and laboratory abnormalities (including renal dysfunction) low and not significantly different between those taking PrEP and those taking placebo
- PrEP was well tolerated
 - Adverse effects occurred in minority of subjects
 - GI adverse effects (eg, nausea) more common in those receiving PrEP than placebo
 - Occurred in < 10% and primarily during the first month only (PrEP "start up" symptoms)
- PrEP associated with a small change (~ 1%) in bone mineral density but without increased risk of fracture

LIMITATIONS OF CURRENT DATA

- Long-term adherence to PrEP and long-term health effects of TDF/FTC in HIV-negative persons and HIV seroconverters not known
- Adherence, risk behavior, and PrEP interest likely to be different now that PrEP HIV protection benefits known

COST

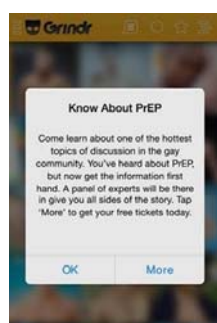
- ~\$1800/month
- Most insurance companies cover PrEP.
 - Co-pay can vary due to deductible/plan type.
- Assistance plans are available.

POSSIBLE DRUG INTERACTIONS

- Limited data available- Tenofovir only:
 - No significant effect seen with:
 - Buprenorphine
 - Methadone
 - Oral contraceptives
 - Renal monitoring for:
 - Acyclovir, valacyclovir, cidofovir, ganciclovir, valganciclovir
 - Aminoglycosides
 - High dose or multiple NSAIDs or,
 - Other drugs that reduce renal function or compete for active renal tubular secretion.

CDC PrEP Guidelines, 2014

TRUVADA = AWESOME...?



THE BIRTH CONTROL CONNECTION

- One of many options that will need to be revisited through their sexual lives-
- Birth control model- one size does NOT fit all, that's why there are so many types-
 - Fertility awareness
 - Condoms
 - Pills
 - Ring
 - Injections
 - ... to name a few.

CDC GUIDELINES

- Indications for PrEP use by MSM*-
 - Adult male
 - Without acute or ongoing HIV infection
 - Any male sex partners in last 6 months*
 - Not in a monogamous relationship with a recently tested HIV negative male
 - AND one of the following
 - Any anal sex (receptive/insertive) without a condom is last 6 months
 - Any STI diagnosed/reported in the last 6 months
 - Is in an ongoing relationship with an HIV positive male.

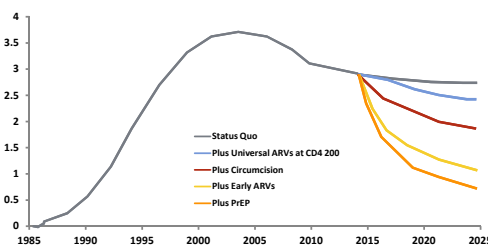
MONITORING AND FOLLOW UP

- Initial serology-
 - HIV test, Renal and hepatic (specifically looking for HBV) evaluation.
- Every three months*-
 - Repeat HIV test, assess for acute HIV, assess adherence, refill script, continue risk reduction education.
- Every six months-
 - Assess renal function, STI testing.
- Every 12 months-
 - Evaluate sexual health and HIV prevention needs

IN REVIEW

- ~91% Effective when taken accurately
 - Does not mean intermittent use.
- ~40% Effective when not taken consistently
- May not be the right method of prevention for everyone.
- Not meant to be used in isolation-
 - CDC recommends incorporating medication adherence counseling, HIV testing (3 mos), STI testing (3-6 mos), and condoms as part of the care around this PrEP method.
- Does not protect against other STIs.

HIV PREVENTION REQUIRES COMBINATION OF APPROACHES

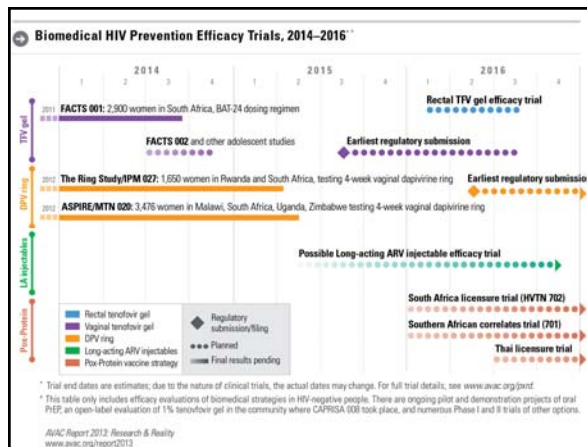


Conclusion: Different interventions together pack powerful prevention punch

Cohen J, et al. Science 2011;334:1614.

UPCOMING RESEARCH

- PrEP for other populations- PrEP adolescent trials
- Intermittent use of Truvada.
- Other drug combinations.
- Mode of delivery- injectable prep.
- RAI specific condoms.
- Other avenues of medication
 - Microbicides
 - Medicated lubricants and gels
 - Medicated vaginal ring- ARVs, plus contraception.



CASE STUDY #1

- 22 y/o MSM, has used PEP twice, moderate condom use. Small group of regular partners- all get tested regularly. Versatile. One of his partners mentioned PrEP.

CASE STUDY #2

- 21 y/o trans woman, here to start PrEP, found to have HIV on initial labs.

CASE STUDY #3

- MSM, symptomatic for STI(?)
 - Found to have gonorrhea.

CASE STUDY #4

- MSM/W, not sexually active for at least a year, heard about PrEP, eager to start.

CASE STUDY #5

- MSM in sexually monogamous relationship with partner of 2 yrs who is HIV positive. Partner is on ARVs medication, and has undetectable VL.

REFERENCES

- - Anderson PL, Ghadden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, McMahan V, Bushman LR, Casapia M, Montoya-Herrera O, Veloso VG, Mayer KH, Charvalertsak S, Schechter M, Bekker LG, Kallas EG, Grant RM; iPrEx Study Team. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med*. 2012 Sep 12;4(151):151ra125. PubMed PMID: 22972843
- - Krakower D, Mayer KH. What primary care providers need to know about preexposure prophylaxis for HIV prevention: a narrative review. *Ann Intern Med*. 2012 Oct 2;157(7):490-7. Review. PubMed PMID: 22821365
- - Liu AY, Vittinghoff E, Chillag K, Mayer K, Thompson M, Grohskopf L, Colfax G, Pathak S, Gvetadze R, O'hara B, Collins B, Ackers M, Paxton L, Buchbinder SP. Sexual risk behavior among HIV-uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States. *J Acquir Immune Defic Syndr*. 2013 Sep 1;64(1):87-94. doi:10.1097/QAI.0b013e31828f097a. PubMed PMID: 23481668
- - CDC PrEP Guidelines- <http://www.cdc.gov/hiv/prevention/research/prep/>
- HIV med chart- www.crime.org
- <https://www.ucsf.edu/news/2013/12/110831/no-link-between-hiv-prevention-pill-truvada-and-increased-sexual-risk-behavior>
- <http://myprepxperience.blogspot.com/2014/03/5-am-truvada-whore.html>
- Laegler T, et al. CROI 2011. Abstract 97LB. Grant RM, et al. *N Engl J Med*. 2010;363:2587-2599.
- Baeten JM, et al. *N Engl J Med*. 2012;367:399-410. (supplementary appendix). Thigpen MC, et al. *N Engl J Med*. 2012;367:423-434(supplementary appendix). Choopanya K, et al. *Lancet*. 2013;381:2083-209