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

PREVENTION- WHAT ALREADY WORKS?
• Education
• HIV testing
• Behavioral changes
• Barrier methods
• PEP
• ART during pregnancy for HIV+ women
• Anything else?

CDC HIV in the United States: 2013
**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**

<table>
<thead>
<tr>
<th>Type of Contact</th>
<th>Approximate Risk of Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptive anal</td>
<td>1-30%</td>
</tr>
<tr>
<td>Insertive anal or receptive vaginal</td>
<td>0.1-10%</td>
</tr>
<tr>
<td>Insertive vaginal</td>
<td>0.1-1%</td>
</tr>
</tbody>
</table>

**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.
iPrEx Study Design

Study of TDF/FTC PrEP in HIV-negative men or transgender women who have sex with men

- 4,905 Screened
- 2,499 Randomized
- 1,251 (50%) Randomized to FTC/TDF
- 1,248 (50%) Randomized to Placebo
- 23 No Follow Up
- 1,226 (98%) Followed
- 1,225 (98%) Followed

iPrEx: HIV by Group and Drug Detection

<table>
<thead>
<tr>
<th>Group</th>
<th>Drug Detection</th>
<th>HIV Infections</th>
<th>Incidence Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>No</td>
<td>64</td>
<td>3.86</td>
</tr>
<tr>
<td>FTC/TDF</td>
<td>No</td>
<td>33</td>
<td>4.04</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>3</td>
<td>0.35</td>
</tr>
</tbody>
</table>

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

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.

REFERENCES
- HIV medication: www.ctrr.org