PrEP: The New Morning
After Pill?

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Objectives:

At the end of this presentation the audience will be able to:

- Define PrEP
- Discuss current HIV incidence rates in Texas
- Review PrEP Guidelines and trials which contributed to current level of evidence
- Evaluate the adherence rate needed to decrease risk of HIV transmission
- Examine current literature as it relates to On-Demand PrEP dosing
Clinical Knowledge Check:

Which of the following are FDA approved for the use in pre-exposure prophylaxis (PrEP)?

A. emtricitabine (FTC) and tenofovir alafenamide (TAF) (Descovy®)
B. FTC (Emtriva®)
C. FTC and tenofovir disoproxil fumarate (TDF) (Truvada®)
D. dolutegravir (DTG) (Tivicay®)
E. lamivudine (3TC) (Epivir®)
Pre-exposure Prophylaxis (PrEP)¹

- emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF) [Truvada®]
- Fixed combination of 200 mg FTC and 300 mg TDF given once daily for the prevention of HIV
- Individual must be HIV seronegative to begin treatment
  - Serum Immunoassay is the preferred test
- HBV negative
- Common Side effects:
  - Headache, abdominal pain, GI upset, fat redistribution and weight loss
- Serious Side Effects:
  - Renal impairment (avoid nephrotoxic drugs)
    - eCrCl <60 mL/min
  - Bone mineral density decrease
  - Lactic acidosis
  - Severe hepatomegaly with steatosis
Patient Case

A 27 year old male is curious about this new medication called Truvada® been advertised on billboards. Patient wants to inquiry more about the medication and asks you (a pharmacist) to answer some questions about it.

What are some questions you would ask?
Epidemiology: New HIV Cases

https://gis.cdc.gov/grasp/nchhstpatlas/charts.html
Epidemiology: New HIV Cases

https://gis.cdc.gov/grasp/nchstpatlas/charts.html
Epidemiology: New HIV Cases

https://gis.cdc.gov/grasp/nchstpatlas/charts.html
### Current Guidelines\(^2\) (CDC 2014)

<table>
<thead>
<tr>
<th>Men who have sex with Men (MSM)</th>
<th>Heterosexual (Het) Women and Men</th>
<th>Injection Drug User (IDU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Eligible</td>
<td>Must be a candidate for FTC/TDF (Truvada(^\circ)) and have a documented HBV and vaccination series.</td>
<td></td>
</tr>
<tr>
<td>Prescription</td>
<td>Daily continuing oral dose of FTC/TDF (Truvada(^\circ)) &lt;90 Day supply</td>
<td></td>
</tr>
<tr>
<td>Follow-Up</td>
<td>3 Months: HIV test, pregnancy test (if indicated) adherence counseling, behavioral risk reduction support, side-effect management, STI symptom assessment</td>
<td>6 Months: Renal function and STI testing</td>
</tr>
</tbody>
</table>

See Appendix A for complete table guidelines
## Current Guidelines: MSM

<table>
<thead>
<tr>
<th>Trial</th>
<th>Outcome</th>
<th>Critique</th>
</tr>
</thead>
</table>
| iPrEX Trial\(^3\)            | • Efficacy of 44% in mITT<br>• Detectable Drug level concentration:<br>  • Efficacy of 92%                                      | • Multicenter randomized placebo-controlled study  
  • Adherence rates were determined by pill count, and drug level concentrations were only measured in HIV seroconversion  
  • Sexual methods reported |
|                             |                                                                         |                                                                                                                                          |
|                             |                                                                         |                                                                                                                                          |
| US MSM Safety Trial\(^4\)   | • 6 true seroconversions<br>• 3 in delayed arm<br>• 3 in placebo arm<br>• 0 in immediate arm | • US population  
  • Adherence rates differed between pill count and MEMs  
  • No drug level concentrations were taken  
  • Not a combination trial  
  • Sexual methods reported |

1. iPrEX Trial: 1.2 years follow-up  
   • MSM ages >17 years old  
   • South American, South Africa, Thailand, USA  
   • FTC/TDF vs. placebo  
   • n=2499  
2. US MSM Safety Trial: 24 month follow-up  
   • MSM ages 18-64 years old  
   • U.S. Cities: San Francisco, Boston, Atlanta  
   • 1:1:1:1 Design: TDF delayed vs. immediate vs. placebo  
   • n=400
## Current Guidelines: Heterosexual Women and Men

<table>
<thead>
<tr>
<th>Trial</th>
<th>Outcome</th>
<th>Critique</th>
</tr>
</thead>
</table>
| **Partner’s PrEP**<sup>5</sup>  
• 1.9 years  
• Discordant Male/Females ages >17 years old  
• Kenya & Uganda  
• 1:1:1 Design TDF vs FTC/TDF vs placebo  
• n= 4747 | • TDF 64% efficacy, 63% males & 71% females  
• TDF/FTC 75% efficacy, 84% males & 66% females  
• Detectable drug level concentration  
  • 90% TDF/FTC  
  • 86% TDF | • Populations affected with HIV  
• Longest follow-up years  
• Adherence rates were measured with pills counts  
• Males were the seronegative partner  
• Sexual methods not reported |
| **TDF-2**<sup>6</sup>  
• 1.1 years  
• Botswana  
• Male/female ages 18-39  
• FTC/TDF vs. placebo  
• n= 1563 | • Efficacy of 62.2% mITT  
• Detectable drug level concentration  
  • 77.9% efficacy | • No need to be in a discordant relationship  
• Similar male to female ratios  
• Low follow-up years  
• Adherence rates were measured with pill counts and self-reported surveys  
• Sexual methods not reported |
Current Guidelines IDU

<table>
<thead>
<tr>
<th>Trial</th>
<th>Outcome</th>
<th>Critique</th>
</tr>
</thead>
</table>
| Bangkok Tenofovir Study 7                  | • 48.9% efficacy mITT  
• Detectable drug level concentration  
• 73.5% efficacy            | • First study to show reduction in HIV transmission in IDU  
• Adherence rates were monitored with DOT and self-reported diaries  
• 80 % males  
• Limited sexual methods were reported |
| • 4 year follow-up  
• Reported ID use within the past year ages 20-60 years  
• Thailand  
• TDF vs. placebo  
• n = 2413 |                                                                          |                                                                          |
iPREX OLE\(^8\)

- Open Cohort Label 72 week study
- MSM/transgender women iPREX study, U.S. MSM Safety Trial
- Similar inclusion and exclusion criteria to iPREX study
- Outcomes
  - PrEP Uptake, Adherence, and Sexual Practices
- Design
  - Open Label, participants must use PrEP at 48 weeks after enrollment
  - Assessed drug concentration in dry-blood test at all time points in a case-cohort approach
ANRS-IPERGAY Study

- A multicenter double-blind randomized placebo-controlled trial
- MSM/transgender women greater than 18 years of age who have unprotected anal sex
- FTC/TDF on-demand dose protocol vs. placebo
- Dose protocol:
  - 2 tablets of FTC/TDF with food 2-24 hours prior to sexual intercourse
  - 1 tablet of FTC/TDF every 24 hours after loading dose for a total of 2 post-exposure doses
  - If consecutive sexual intercourse, individual will take 1 tablet of FTC/TDF every day of sexual activity with 2 post-exposure doses after last day of sexual activity
  - Loading dose will only be utilized if a week has passed since last FTC/TDF Dose
- Follow-Up Visits:
  - 4 weeks, and every 8 weeks after enrollment
ANRS-IPERGAY Study⁹ Cont’d.

- **Results:**
  - 86% efficacy
  - Median use of 15 pills per month

- **Critique**
  - First on-demand protocol trial
  - Median use equates to approximately 4 tablets/week
  - Cannot extrapolate to other groups
  - Study fails to investigate true on-demand protocol with 4 doses

![Graph showing cumulative probability of HIV-1 seroconversion](image)

*Figure 3. Kaplan–Meier Estimates of the Probability of HIV-1 Infection.*

The cumulative probability of HIV-1 acquisition is shown for the two study groups in the modified intention-to-treat analysis. The inset shows the same data on an enlarged y axis.
The 27 year old reports being a gay man who has casual male partners at this time and is not in a monogamous relationship. Patient practices safe sex often, but does admit to not using condoms when he drinks a little too much. Patient reports a sexual history of being treated for gonorrhea and positive for HSV-1.

Would you (the pharmacist) recommend on-demand or daily dosing PrEP for this patient?
Direction for Use of On-Demand vs Continuous Daily Dosing

- **MSM**: Only population studied
- **Sexual activity**: Greater than 2 sexual encounters/week
- **Adherence**: Individual with past adherence issues
- **Continuous Daily Dosing**: Daily PrEP is preferred due to limited studies
- **Possible Recommendation for On-Demand**: YES

**Flowchart:**
- MSM: NO -> Sexual activity: YES -> Adherence: NO -> Continuous Daily Dosing: NO
- MSM: NO -> Sexual activity: NO -> Continuous Daily Dosing: YES
Acknowledgements

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  - James Weems, R.Ph.
Questions
Abbreviations:

- PrEP: Pre-exposure prophylaxis
- HIV: Human Immunodeficiency Virus
- TDF: tenofovir disoproxil fumarate
- FTC: emtricitabine
- HBV: Hepatitis B Virus
- eCrCL: Estimated Creatinine Clearance
- MSM: Men who have Sex with Men
- IDU: Injection Drug Users
- Het: Heterosexual
- STI: Sexually Transmitted Infection
- HSV-1: Herpes Simplex Virus 1
## Table 1: Summary of Guidance for PrEP Use

<table>
<thead>
<tr>
<th>Detecting substantial risk of acquiring HIV infection</th>
<th>Men Who Have Sex with Men</th>
<th>Heterosexual Women and Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-positive sexual partner</td>
<td>HIV-positive sexual partner</td>
<td>HIV-positive sexual partner</td>
<td>HIV-positive injecting partner</td>
</tr>
<tr>
<td>Recent bacterial STI</td>
<td>Recent bacterial STI</td>
<td>Recent bacterial STI</td>
<td>Sharing injection equipment</td>
</tr>
<tr>
<td>High number of sex partners</td>
<td>High number of sex partners</td>
<td>High number of sex partners</td>
<td>Recent drug treatment (but currently injecting)</td>
</tr>
<tr>
<td>History of inconsistent or no condom use</td>
<td>History of inconsistent or no condom use</td>
<td>History of inconsistent or no condom use</td>
<td></td>
</tr>
<tr>
<td>Commercial sex work</td>
<td>Commercial sex work</td>
<td>Commercial sex work</td>
<td></td>
</tr>
<tr>
<td>In high-prevalence area or network</td>
<td>In high-prevalence area or network</td>
<td>In high-prevalence area or network</td>
<td></td>
</tr>
<tr>
<td>Clinically eligible</td>
<td>Documented negative HIV test result before prescribing PrEP</td>
<td>Documented negative HIV test result before prescribing PrEP</td>
<td></td>
</tr>
<tr>
<td>No signs/symptoms of acute HIV infection</td>
<td>No signs/symptoms of acute HIV infection</td>
<td>No signs/symptoms of acute HIV infection</td>
<td></td>
</tr>
<tr>
<td>Normal renal function; no contraindicated medications</td>
<td>Normal renal function; no contraindicated medications</td>
<td>Normal renal function; no contraindicated medications</td>
<td></td>
</tr>
<tr>
<td>Documented hepatitis B virus infection and vaccination status</td>
<td>Documented hepatitis B virus infection and vaccination status</td>
<td>Documented hepatitis B virus infection and vaccination status</td>
<td></td>
</tr>
<tr>
<td>Prescription</td>
<td>Daily, continuing, oral doses of TDF/FTC (Truvada) ≤90-day supply</td>
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<td></td>
</tr>
<tr>
<td>Other services</td>
<td>Follow-up visits at least every 3 months to provide the following:</td>
<td>Follow-up visits at least every 3 months to provide the following:</td>
<td></td>
</tr>
<tr>
<td>HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</td>
<td>HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</td>
<td>HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</td>
<td></td>
</tr>
<tr>
<td>At 3 months and every 6 months thereafter, assess renal function</td>
<td>At 3 months and every 6 months thereafter, assess renal function</td>
<td>At 3 months and every 6 months thereafter, assess renal function</td>
<td></td>
</tr>
<tr>
<td>Every 6 months, test for bacterial STIs</td>
<td>Every 6 months, test for bacterial STIs</td>
<td>Every 6 months, test for bacterial STIs</td>
<td></td>
</tr>
<tr>
<td>Do oral/rectal STI testing</td>
<td>Assess pregnancy intent</td>
<td>Access to clean needles/syringes and drug treatment services</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pregnancy test every 3 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

STI: sexually transmitted infection
References:

1. Truvada® [Package Insert]. 2017Gilead Sciences, Inc. Foster City, CA