PrE-Exposure Prophylaxis (PrEP)  
A Tool at Your Hand to Fight HIV

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Disclosures

• I have no relevant financial disclosures
Objectives

1. To understand the rationale for PrEP
2. To review PrEP efficacy data
3. Summarize CDC Guidelines on HIV PrEP
4. Review some case scenarios of PrEP candidates and strategies
5. Review documentation and billing approaches for various patient populations
6. Review future directions for PrEP
### 39,782 • Total HIV Diagnoses in 2016

#### HIV Diagnoses Trends from 2011–2015

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Black MSM</th>
<th>Hispanic/Latino MSM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>down 16%</td>
<td>stabilizing</td>
<td>up 14% all ages</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>up 19% age 13–24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>up 21% age 25–34</td>
</tr>
</tbody>
</table>

#### Percentage HIV Diagnoses in 2016

Blacks/African Americans accounted for 44% of HIV diagnoses, though they comprise only 12% of the US population.

- **67%**: Gay and bisexual men (MSM)
- **24%**: Heterosexual
- **6%**: People who inject drugs (IDU)
- **3%**: MSM/IDU

*American Indian/Alaska Native: 0.6% • Asian: 2.5% • Native Hawaiian/Other Pacific Islander: 0.1% • Multiple races: 2.2%

Source: Centers for Disease Control and Prevention
Lifetime Risk of HIV Diagnosis by Race/Ethnicity

- African American Men: 1 in 20
- African American Women: 1 in 48
- Hispanic Men: 1 in 48
- Hispanic Women: 1 in 227
- White Men: 1 in 132
- White Women: 1 in 880

Source: Centers for Disease Control and Prevention
Context

• By the time I finish talking today, 5 new people in the United States will have contracted HIV

• In Jackson, if you are a black man who has sex with men (MSM), your lifetime risk of contracting HIV is 1 in 2

• Among metropolitan areas in the United States, Jackson ranks #4 for new HIV diagnoses

Sources: Centers for Disease Control and Prevention
Mississippi State Department of Health
So how does PrEP work?

• Rationale: Having HIV drugs present at the site of exposure should reduce the risk of infection
• Recommended for high-risk individuals by the CDC and World Health Organization (WHO)
• There is currently one FDA approved medication for HIV PrEP
Drugs used to treat HIV

- **Protease Inhibitors (PI)**
  - Saquinavir (Invirase)
  - Fosamprenavir (Telzir)
  - Darunavir (Prezista)
  - Ritonavir (Norvir)
  - Atazanavir (Reyataz)
  - Tiprinavir (Tipranavir)
  - Indinavir (Crixivan)
  - Fosamprenavir (Telzir)
  - Atazanavir (Reyataz)
  - Tiprinavir (Tipranavir)
  - Darunavir (Prezista)
  - Nelfinavir (Viracept)

- **Integrase Strand Transfer Inhibitors (Insti)**
  - Raltegravir
  - Elvitegravir
  - Dolutegravir (Tivicay)
  - Bictegravir

- **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
  - Nevirapine
  - Delavirdine
  - Efavirenz (Sustiva)
  - Etravirine (Intelence)
  - Rilpiverine (Edurant)

- **Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**
  - Zidovudine (Retrovir)
  - Didanosine (Videx)
  - Stavudine (Zerit)
  - Lamivudine (Epivir)
  - Abacavir (Ziagen)
  - Tenofovir (Viread)
  - Emtricitabine (Emtriva)

- **Entry Inhibitors**
  - Enfuvirtide (Fuzeon)
  - Maraviroc (Selzentry)
Truvada®
(entecitabine and tenofovir disoproxil fumarate)
Tablets
30 tablets
Rx only

Distributor: Each time Truvada® is dispensed, give the patient the attached Medication Guide.
PrEP Medication

• Tenofovir disoproxil fumarate – Emtricitabine (TDF-FTC) was FDA approved in 2012 for HIV PrEP

• TDF-FTC is used in many daily regimens among HIV-positive patients in combination with either an integrase inhibitor (INSTI) or a protease inhibitor (PI)

• Currently, it is the first (and only) medication approved for PrEP by the FDA
Timing of Prevention Opportunities

Cohen et al., JCI, 2008
Cohen et al., JIAS, 2008

UNEXPOSED
Behavioral, Structural
STDS, Circumcision, Condoms, Sexual Health Education

EXPOSED (precoital/coital)
Vaccines, ART PrEP, Microbicides, Antibodies

EXPOSED (postcoital)
Vaccines, ART PEP

INFECTED
Treatment Of HIV to Reduce Infectivity

YEARS
HOURS
72h
YEARS
## PrEP: Results from Clinical Trials

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Participants</th>
<th>Number</th>
<th>Drug</th>
<th>mITT (^a) efficacy of % reduction in acquisition of HIV infection (^b)</th>
<th>Adherence-adjusted efficacy based on TDF detection in blood (^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>iPrEx</td>
<td>Men who have sex with men (MSM)</td>
<td>2499</td>
<td>TVD</td>
<td>42 (15-63)</td>
<td>92 (40-99)</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>HIV discordant couples</td>
<td>4747</td>
<td>TDF</td>
<td>67 (44-81)</td>
<td>86 (67-94)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TVD</td>
<td>75 (55-87)</td>
<td>90 (58-98)</td>
</tr>
<tr>
<td>TDF 2</td>
<td>Heterosexually active men and women</td>
<td>1200</td>
<td>TVD</td>
<td>63 (22-83)</td>
<td>85(^d)</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study</td>
<td>IDU</td>
<td>2413</td>
<td>TDF</td>
<td>49 (10-72)</td>
<td>74 (17-94)</td>
</tr>
<tr>
<td>Fem-PrEP</td>
<td>Heterosexually active women</td>
<td>1951</td>
<td>TVD</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>VOICE</td>
<td>Heterosexually active women</td>
<td>5029</td>
<td>TVD</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

\(^a\) Modified Intent to Treat
\(^b\) Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
\(^c\) The percentage of reduction in HIV incidence among those with TFV detected in blood, compared with those without detectable TFV
\(^d\) Finding not statistically significant

Potential PrEP Providers

- STD care providers
- Primary care providers
- HIV uninfected at substantial risk
- HIV care providers
- Drug Treatment Providers
CDC Guidance on Prescribing PrEP

- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, screen/treat for STDs, screen/vaccinate for Hep B; pregnancy test) and r/o acute infection
- Prescribe tenofovir-emtricitabine 1 tablet by mouth daily x 90 days
- Provide condoms, adherence and risk-reduction counseling or referral
- Monitor
  - HIV status every 3 months
  - Renal function at 3 months and every 6 months
  - Risk reduction, condoms, STI assessments /Rx
Labs to order in every PrEP visit

- HIV antibody/antigen
  - LAB 5933
- RPR
  - LAB 494
- C. trachomatis/N. gonorrhoeae PCR, Urine
  - LAB 1376 (urine pipetted into yellow Cobas tube)
- N. gono PCR, throat
  - LAB 5899 (Aptima swab and medium, physician/nurse collected)
- N. gono PCR, rectal
  - LAB 5899 (Aptima swab and medium, patient collected)
- C. trach PCR, throat
  - LAB 5903 (Aptima swab and medium, physician/nurse collected)
- C. trach PCR, rectal
  - LAB 5903 (Aptima swab and medium, patient collected)
- Creatinine or BMP
- Urinalysis after initiation and annually
PrEP Implementation Concerns
Financing of PrEP: Billing

A 25 yo male presents concerned about condomless anal sex with another man and request an HIV test. MD notices that the patient is also due for a well visit this visit and performs it. MD Decides to perform a preventive medicine visit exam, spends 35 min counseling including PrEP and performs a rapid HIV test as well as screening for syphilis, CT/GC including extra-genital sites, and orders a serum creatinine. Patient has been vaccinated for HBV.

<table>
<thead>
<tr>
<th>Service</th>
<th>ICD-10 Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Medical Exam (WV)</td>
<td>Z0000</td>
</tr>
<tr>
<td>Special screening for other specified viral disease (HIV screening)</td>
<td>Z1159</td>
</tr>
<tr>
<td>HIV Counseling</td>
<td>Z717</td>
</tr>
<tr>
<td>High Risk Sexual Behavior</td>
<td>Z7251</td>
</tr>
</tbody>
</table>
Financing of PrEP: CPT codes for prevention counseling

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99401</td>
<td>Prevention Counseling (15 minutes)</td>
</tr>
<tr>
<td>99402</td>
<td>Prevention Counseling (30 minutes)</td>
</tr>
<tr>
<td>99403</td>
<td>Prevention Counseling (45 minutes)</td>
</tr>
<tr>
<td>99404</td>
<td>Prevention Counseling (60 minutes)</td>
</tr>
</tbody>
</table>
## Financing of PrEP: Billing Codes

<table>
<thead>
<tr>
<th>ICD-10*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z72.5</td>
<td>High risk sexual behavior</td>
</tr>
<tr>
<td>Z20.82</td>
<td>Contact with and (suspected) exposure to other viral communicable diseases</td>
</tr>
<tr>
<td>Z20</td>
<td>Contact with and (suspected) exposure to communicable diseases</td>
</tr>
<tr>
<td>Z20.2</td>
<td>Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission</td>
</tr>
<tr>
<td>Z20.6</td>
<td>Contact with and (suspected) exposure to HIV</td>
</tr>
<tr>
<td>Z77.21</td>
<td>Contact with and (suspected) exposure to potentially hazardous body fluids</td>
</tr>
<tr>
<td>W46</td>
<td>Contact with hypodermic needle: “the appropriate 7th character is to be added to each from category W46” A-initial encounter, D-subsequent encounter, S-sequela</td>
</tr>
<tr>
<td>W46.0</td>
<td>Contact with hypodermic needle (hypodermic needle stick NOS)</td>
</tr>
<tr>
<td>W46.1</td>
<td>Contact with contaminated hypodermic needle</td>
</tr>
</tbody>
</table>
Gilead will provide Truvada for PrEP at no cost for individuals who qualify for the assistance program

<table>
<thead>
<tr>
<th>Program Element</th>
<th>Truvada PrEP Medication Assistance Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility Criteria</td>
<td>US resident, uninsured or no drug coverage, HIV-negative, low income</td>
</tr>
<tr>
<td>Drug Fulfillment</td>
<td>Product dispensed by Covance Specialty Pharmacy, labeled for individual patient use and shipped to prescriber (30 day supply); no card or voucher option</td>
</tr>
<tr>
<td>Recertification Period</td>
<td>6 months, with 90 day status check</td>
</tr>
</tbody>
</table>
PrEP Assistance Program
www.start.truvada.com

TRUVADA for a Pre-Exposure Prophylaxis (PrEP) Indication

TRUVADA is indicated, in combination with safer sex practices, for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

Click here for factors that place an uninfected adult at high risk

Click here for factors to consider before prescribing TRUVADA for PrEP

Resources for Healthcare Providers

REMS Resources
Download important Risk Evaluation Mitigation Strategy (REMS) materials for healthcare providers before prescribing TRUVADA for a PrEP indication for uninfected individuals at high risk of sexually acquired HIV-1.
Read important REMS materials

HIV Testing
Read important information about safely prescribing TRUVADA for a PrEP indication, and answer a post-training questionnaire to qualify to offer HIV testing at no cost to uninsured or financially needy individuals.
Qualify to offer HIV testing at no cost to uninsured or financially needy individuals

Medication Assistance Program
Help eligible uninfected individuals taking TRUVADA for a PrEP indication receive assistance paying for the medication.
Download medication assistance form

For Uninfected Individuals

Condoms
If you are an uninfected individual at high risk taking TRUVADA for a PrEP indication, you can obtain condoms at no cost.
Open condom ordering form

Safety Information for Uninfected Individuals
Review information for uninfected individuals at high risk.
Review material for uninfected individuals
Family Planning Waiver

Eligibility Criteria:
• Family income is at or below 194% of the federal poverty level (FPL)
• Must be capable of reproducing ages 13-44 years of age.
• Must not have had a procedure that prevents them from reproducing.
• Must not have Medicare, CHIP, or any other health insurance or third party medical coverage

Benefits:
• Family planning and related services
• One annual visit and up to three subsequent visit (not to exceed four visits per federal fiscal year.
• Effective January 1, 2015, beneficiaries enrolled in the Family Planning waiver demonstration program may have a prescription for contraceptives and/or medications to treat a sexually transmitted infection (STI)/sexually transmitted disease (STD) written by any Medicaid participating provider filled at their local Medicaid participating pharmacy.
Assistance for Insured Patients

1. Gilead Advancing Access Co-pay Card
   gileadcopay.com
   877-505-6986
   - $3,600 max/calendar year
   - No income restrictions
   - Covers co-pays, deductibles and co-insurance
   - 12-month enrollment, reapply
   - Proof of US residence (utility bill, etc.)
   - Not used with state/federal plans, such as Medicare (apply to PAF or PAN Foundation).
   If the pharmacy doesn’t accept Gilead’s Co-pay Card, keep sales and pharmacy receipts. Call the number on the back of co-pay card. Submit paperwork for reimbursement for every refill.

2. Patient Advocate Foundation (PAF)
   https://www.copays.org/diseases/hiv-aids-and-prevention
   - $5,000 max/year, re-apply
   - Income < 400% FPL ($47,080)
   - Based on taxable income (1040 line 7, 1040 EZ line 1)
   - Must be insured (as listed under “YES” above)
   - Covers co-pays only
   - Proof of US residence (utility bill, etc.)
   - Case managers available to help resolve medical cost issues (800-532-5274)

3. Patient Access Network Foundation
   panfoundation.org/hiv-treatment-and-prevention
   866-316-7263
   - $4,000 max/year, re-apply
   - Income < 500% FPL ($58,850)
   - Based on taxable income (1040 line 7, 1040 EZ line 1)
   - Must be insured (as listed under “YES” above)
   - Covers co-pays, deductibles and co-insurance
   - Proof of US residence (utility bill, etc.)
   - Pharmacies can bill PAN Foundation directly
Open Arms Healthcare Center

• Located in Jackson, MS
• Opened in 2013
• LGBT friendly Healthcare
• Staff: 4 MDs, 1 NP, 1 Clinical Psychologist, 2 RN, 2 LPN, 1 PN, 3 Case Managers
• PrEP awareness
  • 2014: < 15%
  • 2015: 28%

MSM Tested for HIV 2014 (n=538)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>1</td>
</tr>
<tr>
<td>18-24</td>
<td>49</td>
</tr>
<tr>
<td>25-34</td>
<td>33</td>
</tr>
<tr>
<td>35+</td>
<td>17</td>
</tr>
<tr>
<td>Race/Ethnicity:</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>11.1</td>
</tr>
<tr>
<td>African-American</td>
<td>78.3</td>
</tr>
<tr>
<td>Other</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7.2</td>
</tr>
<tr>
<td>HIV-positive rate</td>
<td>12.9</td>
</tr>
</tbody>
</table>
AA MSM 18-29 years on PrEP OAHCC

- Received Prescription for PrEP: 100%
- Initiated PrEP: 69%
- Retained in Care at 3 Months: 56%
- Retained in Care at 6 Months: 35%
Case 1

• A 24 year old man is presenting to you for primary care establishment. He is currently sexually active with men, and has been active with multiple men within the last 3 months. He engages in oral and anal sex with inconsistent condom use. He has no medical history and no previous STI history.

• Vitals and physical examination are unremarkable.

• His pre-visit labs performed a week ago were negative for HIV and other STIs
Case 1

• Is this patient a candidate for PrEP?
  • A. Yes, start now
  • B. Not a candidate
Case 1

• According to the CDC, MSM who fulfill the following criteria are candidates:
  • Adult man
  • Without acute or established HIV infection
  • Any male sex partners in the past 6 months
  • Not in a monogamous partnership with a recently tested, HIV negative man

AND at least one of the following:
  • Any anal sex without condoms (receptive or insertive) in past 6 months
  • Any STI diagnosed or reported in past 6 months
  • Is in an ongoing relationship with an HIV-positive male partner
Who is “high risk?”

**MSM**
- Condomless anal sex
- Recent sexually-transmitted infection
- HIV-infected partner

**Heterosexual adults**
- Condomless sex with a partner who injects drugs or is a bisexual man
- HIV-infected partner

**Injection drug users**
- Use of shared injection equipment

---

Case 1

• Which tests must be sent before starting PrEP?
  A. HIV antibody, Hepatitis B surface antibody, urinalysis
  B. HIV antibody, Hepatitis B surface antigen, serum creatinine
  C. HIV RNA, hepatitis B surface antibody, urinalysis
  D. HIV RNA, hepatitis B surface antigen, serum creatinine
Case 1

• Which tests must be sent before starting PrEP?
  A. HIV antibody, Hepatitis B surface antibody, urinalysis
  B. HIV antibody, Hepatitis B surface antigen, serum creatinine
  C. HIV RNA, hepatitis B surface antibody, urinalysis
  D. HIV RNA, hepatitis B surface antigen, serum creatinine
What side effects should you counsel the patient on?

• Nausea may occur with initiation of TDF-FTC; it typically resolves over time

• Kidney injury rarely occurs (~2% in iPrex)
  • Periodic monitoring is obligatory and abnormalities usually resolve with drug discontinuation

• A small decrease in bone mineral density may occur; however this does not appear to be clinically significant at this time

• Antiretroviral resistance is unlikely but possible
How would you counsel him about...

• The length of time on PrEP before he is maximally protected?
  • About 7 days, when maximal levels are achieved in rectal tissue

• If stopping PrEP, how long should he take it beyond his last high-risk sexual encounter?
  • 4 weeks seems to be the answer

• Does PrEP protect against other STIs?
  • No! (although there does seem to be data for ↓ HSV risk)
Case 2

• A 27 year old MSM in generally good health presents for care establishment. He has had a cold with fever, sore throat, and swollen glands for 2 days. He is taking frequent ibuprofen. He notably had unprotected anal sex with 1 primary and 2 occasional male partners (most recently about 10 days ago). He is interested in PrEP.

• Labs reveal a negative HIV antibody and negative HBsAg; Cr is normal
Case 2

• What’s the next best step?
  A. Start PrEP today
  B. Wait until his cold has improved and he’s off ibuprofen; then start PrEP
  C. Start PEP, then transition to PEP after 28 days
  D. Send an HIV viral load and base the PrEP decision on the result
Case 2

• What’s the next best step?
  A. Start PrEP today
  B. Wait until his cold has improved and he’s off ibuprofen; then start PrEP
  C. Start PEP, then transition to PEP after 28 days
  D. Send an HIV viral load and base the PrEP decision on the result
Case 2, follow up

• His HIV viral load returns at 2.5 million copies/mL
• Acute HIV and PrEP
  • Remember that patients may be symptomatic from HIV but have negative serologic testing (i.e. in the “window period”)
  • In clinical trials of PrEP, drug resistant has been noted in those who were in the window period at enrollment
  • Use of the 4th generation antibody/antigen test decreases but does not eliminate the window period
  • If in doubt, SEND AN HIV RNA
Case 3

• A 48 year old man is presenting to clinic to establish care. He asks about obtaining PrEP as he is in a monogamous relationship with one male partner who is HIV-positive but virologically suppressed for over 5 years.

• Your patient’s physical examination is unremarkable

• HIV antibody/antigen and HBsAg negative; Creatinine is 1.09 mg/dL

• He asks if PrEP is worthwhile for him since his partner is undetectable
Case 3

**NO**

• HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small

**YES**

• Viral rebound may occur because of poor ART adherence or other reasons
• People may not be monogamous
• CDC guidelines support PrEP in this context.
Case 3

• ART substantially reduces HIV transmission
  • HPTN 052 study: HIV treatment reduced HIV transmission by 96% in serodiscordant couples
  • IAS 2018: Zero transmissions after the HIV-infected partner was stably suppressed on ART in PARTNERS1 (heterosexuals) and PARTNERS2 (MSM)
  • Opposites Attract study: 0 HIV transmissions in 152 serodiscordant MSM couples despite ~6,000 episodes of condomless anal sex

➢ Grulich AE, et al. HIV in male serodiscordant couples in Australia, Thailand, and Brazil. CROI, 2015. Abstract 1019LB.
Case 4

• A 36 year old female and her 39 year old husband present to discuss conception. He is HIV-positive and virologically suppressed, and she is HIV-negative. They wish to conceive a child, and cannot afford sperm washing. They ask if you would recommend PrEP for her and condomless sex in this situation.
Case 4

• Would you agree with this approach?
  A. Yes
  B. No
Case 4

• PrEP may be a part of a conception strategy
• There is no evidence for increased birth defects with TDF-FTC among women in the Antiretroviral Pregnancy Registry (ART report)
• Other reproductive strategies for such couples may be limited to non-existant
• Notably, modeling suggests that PrEP adds little if ART and other factors are optimized (Hoffman)

HIV PrEP: Future Directions

• More data is needed in women, adolescents, and youth (15-17 year olds currently being studies in ATN 113)

• Novel PrEP Agents are being evaluated
  • Tenofovir alafenamide (TAF) for PrEP (Pro-drug of TDF) has less effect on bone and mineral metabolism and renal function
  • Intramuscular injections of long-acting integrase inhibitors
  • Tenofovir vaginal ring
  • Long-acting TAF (GS-7340) subdermal implant

• Additional research is ongoing on different dosing regimens as well
Take Home Points

• Daily TDF-FTC substantially reduces the risk of HIV infection in individuals at high risk.

• Serious side effects are rare; renal function must be monitored periodically while on PrEP.

• Before starting PrEP, test for acute HIV if there are suggestive clinical signs of symptoms.

• There is no evidence of adverse pregnancy outcomes among women who conceive on TDF-FTC.
Questions?