HIV Pre-Exposure Prophylaxis (PrEP): Challenges and Opportunities

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Disclosures

Grant funding to institution from Gilead Sciences
Objectives

1. Provide brief overview of PrEP
2. Describe some common challenges with PrEP management and implementation
3. Describe opportunities for PrEP access and scale-up
Introductions

Familiar with PrEP before today’s talk?

Referred patients for PrEP?

Prescribed PrEP?
What is PrEP?

PrEP (pre-exposure prophylaxis)

• Strategy of administering antiretrovirals to HIV-uninfected, at-risk individuals in order to prevent HIV infection

• Similar strategies: malaria prophylaxis, oral contraceptives

Tenofovir-emtricitabine (TDF/FTC or Truvada) was approved for HIV PrEP by the FDA in July 2012
Why do we need PrEP?

Why do we need PrEP?

Ending the HIV Epidemic: A Plan for America

- **Diagnose** all people with HIV as early as possible after infection.
- **Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- **Protect** people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.
- **Respond** rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.

**HIV HealthForce** will establish local teams committed to the success of the Initiative in each jurisdiction.
Why do we need PrEP?

An HIV provider’s perspective…
How effective is PrEP?
## PrEP Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Category</th>
<th>Intervention</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOICE</td>
<td>Heterosexual Women</td>
<td>TDF</td>
<td>-49%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FTC/TDF</td>
<td>-4%</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td></td>
<td>FTC/TDF</td>
<td>6%</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>Heterosexual Men</td>
<td>TDF</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FTC/TDF</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td>Heterosexual Men</td>
<td>TDF</td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FTC/TDF</td>
<td>84%</td>
</tr>
<tr>
<td>IPrEx</td>
<td>MSM/TGW</td>
<td>FTC/TDF</td>
<td>44% (92%)</td>
</tr>
<tr>
<td>IPERGAY</td>
<td>MSM/TGW</td>
<td>FTC/TDF</td>
<td>86% (On Demand)</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study</td>
<td>IVDU</td>
<td>TDF</td>
<td>49%</td>
</tr>
</tbody>
</table>

Adherence

PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention

- CAPRISA 004 (tenofovir gel, BAT-24 dosing)
- FEM-PrEP
- IPERGAY (TDF/FTC)
- iPrEx
- Partners PrEP (TDF)
- Partners PrEP (TDF/FTC)
- PROUD (TDF/FTC)
- TDF2
- VOICE (TDF)
- VOICE (TDF/FTC)
- VOICE (tenofovir gel, daily dosing)

Who Should be Considered for PrEP?

1. IV Drug Use (IVDU)
2. Condomless sex
3. Multiple partners
4. History of STI
5. Previous need for HIV post-exposure prophylaxis
6. Illicit drug use (party drugs)
7. Commercial sex work
8. Sex with known HIV infected partner(s)?
# PrEP Management

<table>
<thead>
<tr>
<th>Clinical Measure</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV 1/2 antigen/antibody</td>
<td>Every 3 months</td>
</tr>
<tr>
<td>Basic Metabolic Panel</td>
<td>Baseline, 3 months, then every 6 months</td>
</tr>
<tr>
<td>HBV s antigen/s antibody</td>
<td>Baseline</td>
</tr>
<tr>
<td>HCV antibody</td>
<td>Baseline, then yearly in IVDU/MSM</td>
</tr>
<tr>
<td>Syphilis antibody</td>
<td>Baseline, then every 6 months</td>
</tr>
<tr>
<td>Chlamydia/Gonorrhea (all exposed sites)</td>
<td>Baseline, then every 3-6 months</td>
</tr>
<tr>
<td>Urine, pregnancy</td>
<td>Every 3 months</td>
</tr>
</tbody>
</table>
POC HIV Testing

Abstracted from: Government of Canada Public Health Agency of Canada, HIV Services
Alere Determine

Read the results at 20mins to 30mins maximum.

<table>
<thead>
<tr>
<th>Line</th>
<th>Positive</th>
<th>Negative</th>
<th>Invalid</th>
</tr>
</thead>
</table>

The control line should appear for all results. If it does not appear, the result is invalid.

# PrEP Cost

**Truvada®** (emtricitabine/tenofovir DF) = \(~$2,350\) (WAC)

<table>
<thead>
<tr>
<th>Lab</th>
<th>Frequency</th>
<th>Cost</th>
<th>PrEP Annual Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC HIV Test</td>
<td>Baseline &amp; Q3 Months</td>
<td>$25</td>
<td>$100</td>
</tr>
<tr>
<td>Metabolic Panel</td>
<td>Baseline, 3 Months, Q6 Months</td>
<td>$200</td>
<td>$600</td>
</tr>
<tr>
<td>HBV s antigen</td>
<td>Baseline</td>
<td>$125</td>
<td>$125</td>
</tr>
<tr>
<td>HBV s antibody</td>
<td>Baseline</td>
<td>$125</td>
<td>$125</td>
</tr>
<tr>
<td>HCV antibody</td>
<td>Baseline, Annually (IDU, MSM)</td>
<td>$125</td>
<td>$125</td>
</tr>
<tr>
<td>Syphilis antibody</td>
<td>Baseline, Q6 Months</td>
<td>$75</td>
<td>$150</td>
</tr>
<tr>
<td>Chlamydia/Gonorrhea</td>
<td>Baseline, Q3-6 Months</td>
<td>$300</td>
<td>$2,700</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Total Annual PrEP Lab Cost (Gross)</strong></th>
<th><strong>$3,925</strong></th>
</tr>
</thead>
</table>
PrEP Cost

<table>
<thead>
<tr>
<th>Total Annual PrEP Costs (Gross)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual Lab Costs</td>
</tr>
<tr>
<td>Annual Drug Costs</td>
</tr>
<tr>
<td>Annual PrEP Costs</td>
</tr>
</tbody>
</table>

• There should rarely be a cost for FTC/TDF
  • High deductible plans
  • Copay cards
  • PAF, PANF grants

• Lab follow-up is always the cost factor
  • Sliding scale fee
  • Patient assistance
# Nebraska HIV Disparities

<table>
<thead>
<tr>
<th></th>
<th>% of Total Population</th>
<th>% Living w/HIV</th>
<th>% New HIV Diagnosis (2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Races</strong></td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td>85.4%</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>African American</strong></td>
<td>4%</td>
<td>28%</td>
<td>19%</td>
</tr>
<tr>
<td><strong>Hispanic</strong></td>
<td>7.2%</td>
<td>14.9%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Asian</strong></td>
<td>1.8%</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>American Indian</strong></td>
<td>0.7%</td>
<td>1.6%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>0.1%</td>
<td>1.4%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Multiracial</strong></td>
<td>0.9%</td>
<td>0.1%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Adapted from Nebraska DHHS HIV Surveillance Report, 2016
Chlamydia Rates by ZIP Code
Both Sexes, 15 to 24 Age Group
Douglas County, Nebraska - Five Year Average

* Populations for 2011-2016 are based on 2010 US Decennial Census.
Based on Date of Report

Rates per 100,000*
- 3000 & Greater
- 2000 to 3000
- 1000 to 2000
- 1000 to 2000
- Less than 1000

Douglas County Health Department 02/02/2017
PrEP Providers

Omaha (pop. ~500,000)

October 2018

May 2019

Preplocator.org
PrEP Providers

Miami (pop. ~500,000)  Oakland (pop. ~500,000)

Preplocator.org
PrEP Travel

Pharmacist-Led PrEP

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Mean (Range or N %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34 (20-61)</td>
</tr>
<tr>
<td>Male</td>
<td>57 (95%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>50 (83%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Hispanic or Latino/a</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>48 (80%)</td>
</tr>
<tr>
<td>Medicare</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>11 (18.3%)</td>
</tr>
<tr>
<td>HIV Risk Factor at Screening</td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>53 (88%)</td>
</tr>
<tr>
<td>Partner with HIV</td>
<td>17 (28%)</td>
</tr>
<tr>
<td>Transgender and High-Risk Sex</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Transactional Sex</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Stimulants and High-Risk Sex</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Anogenital STI in Last Year</td>
<td>19 (32%)</td>
</tr>
</tbody>
</table>

Retention in P-PrEP Program

- Received Prescription for PrEP
- Initiated PrEP
- Retained in P-PrEP Program at 3 months
- Retained in P-PrEP program at 6 months

Bares S, et al. IDWeek 2018
# Telehealth PrEP

## Pre-Visit
- **Tell Us About Yourself**
  - Full name
  - Address
  - Phone number
  - Email address
  - Birthdate
  - Communication preferences
- **Insurance & Paying for PrEP**
  - No insurance? That’s ok!
    - We’ll help you find insurance or low cost options for PrEP
  - High deductible plan?
    - We’ll keep out-of-pocket costs low for you
  - All insurance accepted
  - Send us a current picture of your insurance card
- **Decide where to get labs drawn**
- **Vaccinations**
  - Have you been vaccinated for:
    - Hepatitis B?
    - Hepatitis A?
    - HPV (Gardasil)?

## Labs
- **What to expect at the lab**
  - Blood draw*
  - Swab**
  - Urine sample
  - *some labs may be done by finger stick
  - **Chlamydia & gonorrhea testing
- **Labs**
  - HIV test
  - Kidney function (creatinine)
  - STI testing*
    - Syphilis
    - Gonorrhea
    - Chlamydia
  - Hepatitis C
  - Hepatitis B
    - To assess immunity & ensure there is no underlying infection
  - Hepatitis A
    - To assess immunity
  - *Iowa law requires labs and healthcare providers to report all positive lab results to the Iowa Department of Public Health
  - **Urine test, throat swab, rectal swab, vaginal swab

## Visit
- **Telemedicine visit**
  - You can be at home or wherever you like
  - You will receive an email with a link to the visit
  - Click on the link to download the app and also to join the visit
  - Plan for the 1st visit to be ~ 30 minutes

## Medication
- **Pharmacy**
  - Medication mailed to you from Iowa City
  - OR
  - Pick up the medication from a pharmacy of your choice*
  - *some insurance plans will require you to use a specific pharmacy
- **Paying for Truvada**
  - Insurance will cover a portion or all of the cost of medication
  - If insurance doesn’t cover the full cost, other options include:
    - Gilead CoPay card
      https://www.gileadvancingaccess.com/copay-coupon-card
    - Gilead Advancing Access Program (full medication coverage)
    - Other copay assistance programs
      https://pfi.foundation
      http://www.patientadvocate.org

[https://www.prepiowa.org/what-to-expect](https://www.prepiowa.org/what-to-expect)
PrEP concerns

- Is it safe?
- Will it lead to resistance?
- Will it lead to riskier behavior?
Is PrEP Safe?

Start-up syndrome
• Nausea, vomiting, +/- dizziness occurred in <10% and primarily during first month

Renal safety
• 0.2% grade 2-4 elevations in creatinine among 5469 participants randomized to TDF/FTC

Bone safety
• ~1% loss of BMD
• Return to baseline with withdrawal
• Not associated with increased fracture risk

Marrazzo JM et al. NEJM 2015.
Resistance

- Resistance rare in clinical trials of PrEP

- Analysis of drug resistance mutations among participants who acquired HIV in IPERGAY trial found that NONE of the participants had resistance mutations to TDF or FTC

- Most people who acquired HIV were probably not taking their PrEP and, when individuals don’t take the antiretroviral they also don’t develop resistance

Risk Compensation

Notion that PrEP use will lead to increase in high risk sexual activity due to perceived protection from PrEP

Concerns not unfounded
- PrEP does not protect against non-HIV STIs
- 42% of patients initiating PrEP in Kaiser health care system were diagnosed with STI during first year of use
- High STI rates may be attributable to increased screening or may reflect higher rates of condomless sex

BUT…
- Risk compensation hasn’t led to higher rates of HIV acquisition
- Routine follow-up enables prompt detection and treatment of STIs
- Modeling study suggests STI testing and treatment as part of PrEP care will reduce bacterial STIs

Case 1

DY, 28 y/o trans-female, presents for initial primary care establishment. She is in a relationship with an HIV infected man who is “undetectable.”

How would you counsel DY on her HIV risk?

1. Condoms are needed to fully protect DY from HIV infection
2. Condoms are only needed when DY is on “bottom”
3. No condoms are needed with any sexual activity
4. PrEP and condoms are needed to prevent HIV
TaSP – Treatment as Prevention

Sexual Transmission
- HPTN 052: 1763 heterosexual discordant couples
- Partner: 900 serodiscordant couples, no condoms
- Partner2: 77K sexual events in MSM serodiscordant couples

Zero Transmissions
Case 2

Jim, 52 y/o, MSM, on Truvada for PrEP for 1 year presents for f/u. Reports 5 partners in past 3 months w/ intermittent condom use. No STI or acute viral syndrome s/s.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC HIV 1/2 Ag/Ab Test</td>
<td>Non-reactive</td>
</tr>
<tr>
<td>HBV serology</td>
<td>Immune</td>
</tr>
<tr>
<td>HCV Antibody</td>
<td>Non-reactive</td>
</tr>
<tr>
<td>CMP</td>
<td>Creatinine 1.49; CrCl 58 mL/min</td>
</tr>
<tr>
<td>STI screenings</td>
<td>Positive Rectal Chlamydia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Today</th>
<th>3 mo ago</th>
<th>6 mo ago</th>
<th>9 mo ago</th>
<th>1 yr ago</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>1.49</td>
<td>1.34</td>
<td>1.26</td>
<td>1.15</td>
<td>1.28</td>
</tr>
</tbody>
</table>
Case 2

Jim, 52 yo, MSM, on PrEP with rising creatinine (creatinine clearance of 58 mL/min)

How would you manage this case?

1. Take off PrEP
2. Take PrEP less often
3. Work up renal dysfunction
4. Refer to ID
5. Change to different medicine
On-Demand PrEP

IPERGAY : Sex-Driven iPrEP

- 2 tablets 2-24 hours before sex
- 1 tablet 24 hours later
- 1 tablet 48 hours after first intake

86% Efficacious vs. Placebo

4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse
Discover Trial

DISCOVER Primary Endpoint Analysis: HIV Incidence

22 HIV infections in 8756 PY of follow-up

HIV Incidence

- 7 infections in 4370 PY
  - F/TAF: n=2694
  - Incidence Rate: 0.16
- 15 infections in 4386 PY
  - F/TDF: n=2693
  - Incidence Rate: 0.34

Incidence Rate Ratio [95% CI]

- Favors F/TAF
- Favors F/TDF
- Noninferiority

F/TAF is noninferior to F/TDF for HIV prevention

Cl, confidence interval; RR, rate ratio.

Hare, CROI 2019
Discover Trial

DISCOVER Adherence and Resistance Analyses of HIV Infections

- 7 F/TAF infections: 1 suspected baseline infection, 5 low levels of TFV-DP in DBS, 1 medium level
- 15 F/TDF infections: 4 suspected baseline infections, 10 low levels of TFV-DP in DBS, 1 high level
- In a sensitivity analysis that excluded suspected baseline infections, noninferiority was maintained (0.55 [0.20, 1.48])

<table>
<thead>
<tr>
<th>n</th>
<th>F/TAF n=7</th>
<th>F/TDF n=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance genotyped*</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Resistance to study drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTC</td>
<td>0</td>
<td>4†</td>
</tr>
<tr>
<td>TFV</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*3 samples could not be amplified; †All 4 participants with resistance were suspected baseline infections.

Hare, CROI 2019
Case 3

Corey, 48 y/o, MSM presenting for initial PrEP evaluation. 1 reported partner within the past year without condoms. Diagnosed with Strep pharyngitis after development of fevers/chills, night sweats and prescribed amoxicillin/clavulanate. Developed rash after 3 days that worsened after antibiotic discontinuation. He was hospitalized and a drug allergy was diagnosed. HIV test in hospital was non-reactive.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>POC HIV 1/2 Ag/Ab Test</td>
<td>Reactive Ab; p24 Ag faintly reactive</td>
</tr>
<tr>
<td>CMP</td>
<td>ALT 71; all others normal</td>
</tr>
<tr>
<td>HBV s Ag/Ab, c Ab</td>
<td>All non-reactive</td>
</tr>
<tr>
<td>HCV Ab</td>
<td>Non-reactive</td>
</tr>
<tr>
<td>STI screenings (G/C, Syphilis)</td>
<td>All Negative</td>
</tr>
</tbody>
</table>
Case 3

Corey, 48 y/o, MSM, with acute viral symptoms, 1 partner, no condoms, reactive HIV Ab, faintly reactive HIV Ag, CMP unremarkable, non-reactive HBV/HCV serology's, negative STI screenings

What is the most appropriate next step for Corey based on his history and labs?

1. Collect baseline HIV labs
2. Collect baseline HIV labs and start bicitgravir/emtricitabine/tenofovir AF
3. Collect HIV confirmatory testing and HIV RNA
4. Start emtricitabine/tenofovir DF
5. Have Corey return in 4 weeks for a repeat POC HIV test
Is That Real?

False Positive Reasons:
• Auto-antibodies
• Vaccinations
• Viral infection

Ambiguous Results:
1. Continue PrEP
2. Add additional antiretroviral agent
3. Discontinue PrEP

Smith et al, Open Forum Infect Dis, 2018
Case 4

TK, 19 y/o male, presents to clinic asking for nPEP. TK reports anal intercourse and the condom broke. TK is an established patient and is in good health.

What baseline labs would you get prior to starting nPEP?

1. Blood chemistries
2. HIV screening test
3. Hepatitis B serologies
4. STI screening
5. All of the above
Case 4

TK, 19 y/o male, presents back to clinic 1 month later for nPEP follow-up. TK reports 20 partners with minimal condom usage in the past 6 months. Most partners are random that he meets off Grindr and he sometimes uses meth and poppers during sexual encounters.

What should be offered to TK? *Select all that apply*

1. Continuation of nPEP for 4 weeks
2. Valacyclovir for genital herpes prophylaxis
3. PrEP
4. Strict risk reduction counseling
5. HPV vaccination series
6. Substance use treatment
Summary

1. PrEP works
2. It is relatively easy to incorporate and manage
3. Access to PrEP in the Midwest is limited
4. Challenges still arise with implementation and scale up
5. Many opportunities exist
ENDING the AIDS epidemic by 2030 is possible—with your help
Resources

Local:
• Sara Bares, MD sara.bares@unmc.edu
• Josh Havens, PharmD jhavens@unmc.edu

National:
• PrEPline Phone Consultations through UCSF Clinical Consultation Center
  • (855) HIV-PREP; Mon-Fri 9am-8pm EST