(Pre-exposure Prophylaxis)

The Theory, Practice and Results

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What is PrEP?

• One pill once a day to reduce risk of contracting HIV
• > 90% protective against sexually acquiring HIV
• Reduces HIV acquisition risk in intravenous drug users (IVDU)
• Currently only two agents approved for PrEP
What are we trying to accomplish? A Case Study

Herman, a 54-year-old man (HIV-negative) comes into the hospital unable to talk normally. He is the longtime partner of Bill, a 35-year-old man who is HIV-positive, compliant with anti-retroviral therapy and whose HIV-1 RNA (viral loads) are nearly always non-detectable.

Bill was hospitalized for 10 for diabetes mellitus, neuropathy and renal failure. He came to clinic weeks later; his HIV-1 viral load was >3,000 copies of RNA.

Herman was hospitalized 1 month later slurring his speech and could move his tongue only to the right. The HIV-1 RNA was >1,000,000 copies and the platelets <30,000/dL.

Herman was treated with plasmapheresis and ART. He is doing well and compliant with ART.
Roger is a 56-year-old man (MSM) who has “come out” two months ago. He was an insurance executive with a good income and no sexual activity with women or men for years. In the past he occasionally had HIV tests and they were all negative. (The testing was done at his place of work.)

He had one male partner 3 weeks ago and was primarily the partner on the bottom. He now complains of fever, skin rash and a sore throat.

On physical examination he has oropharyngeal thrush, tender lymphadenopathy and a macular rash on the extremities and abdomen.

The HIV-1 RNA was >2,000,000 copies and the RPR was negative.

He was started on ART and has done well.
Truvada (FTC/TDF)

- Single pill containing two medications
  - Emtricitabine (FTC) 200 mg
  - Tenofovir disoproxil (TDF) 300 mg

- One tablet once a day
  - No more than 90-day prescription provided

- Can be taken with or without food

- Take missed doses as soon as remembered
  - If close to next dose, wait until then and take 1 tablet
Descovy
(FTC/TAF)

• Single pill containing two medications
  • Emtricitabine (FTC) 200 mg
  • Tenofovir alafenamide (TAF) 25 mg

• Same instructions for use as Truvada

• ONLY studied in MSM and transgender women
  • Not recommended for use in cisgender women or for IVDU
NRTIs
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

Indirectly inhibits enzyme required to copy viral RNA to DNA.
Side Effects of PrEP

- May experience nausea, bloating upon initiation
  Usually resolves within 2-3 weeks
- Headache
- Increased risk of decreased renal function
  Uncommon but known adverse effect from TDF
  Renal function usually returns to normal if PrEP stopped
- Increased risk of decreased bone mineral density
Tenofovir Disoproxil Drug Issues

Primarily known for its potential renal issues

Risk of renal dysfunction may be multifactorial
- Age
- Addition of other nephrotoxic agents

May also lead to decreased bone mineral density
- Possibly 1-3% greater loss with TDF
- Calcium/vitamin D supplementation may help
Same concerns as TDF but appears to be lower risk

- Improved renal/bone adverse effect profile

Not as well studied for PrEP

- Only recently approved
- Effects of missing doses less clear than with TDF regimen
Descovy for PrEP

• DISCOVER study looked at MSM and transgender women
  • Found to be equivalent to Truvada

• Major concerns again relate to female use
  • A previous PK study with TAF found poor tissue levels
    • 11-fold lower in cervicovaginal fluid

• Uncertain how important adherence is for use
When PrEP is NOT Recommended

• Do not begin Truvada if CrCl < 60 mL/min

• If CrCl declines to < 50 mL/min, stop Truvada
  • FTC and TDF have recommended dose adjustments
  • Renally-adjusted doses were not studied for PrEP

• Descovy should be stopped if CrCl < 30 mL/min
  • An option for PrEP in patients with mild-moderate CKD
### Table 11: PrEP Medication Drug Interactions

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>TDF</th>
<th>FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>No significant effect.</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>No dosage adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>No significant effect.</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>No dosage adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>No significant effect.</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>No dosage adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>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</td>
<td>Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related renal toxicities.</td>
<td>No data</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir</td>
<td>Serum concentrations of TDF may be increased. Monitor for toxicities.</td>
<td>No significant effect</td>
</tr>
</tbody>
</table>
PrEP (Descovy)

Drug Interactions

- Descovy more likely to have interactions than Truvada

- TAF more susceptible to p-glycoprotein effects
  - Efficacy may be compromised with select agents

- Avoid use with:
  - Barbiturates
  - Carbamazepine/oxcarbazepine
  - Phenytoin
  - Rifamycins
  - St John’s Wort
PrEP Activity

- Truvada deposits at varying rates into different tissues
- Estimate ~7 days for maximal rectal tissue levels
- Estimate ~20 days for maximal vaginal tissue/blood levels
- This data is not yet known for Descovy
On-Demand PrEP (Truvada)

- Recent evidence supports this potential approach
  - 2 tablets 2-24 hours before sexual encounter
  - 1 tablet 24 hours after sexual encounter
  - 1 tablet 48 hours after sexual encounter

- Missing doses here may not be as forgiving

- Reliant on anticipation of a sexual encounter

- Not officially recommended as of yet
Vaginal Exposures and Adherence

- Far less clear how levels are affected in this tissue
- DOES appear to be much more susceptible to missed doses
- Would avoid on-demand PrEP in this group
Indications - MSM

Box B1: Recommended Indications for PrEP Use by MSM

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- 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
- A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in past 6 months
Indications - Heterosexuals

**Box B2: Recommended Indications for PrEP Use by Heterosexually Active Men and Women**

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
- A **bacterial STI** (syphilis, gonorrhea in women or men) diagnosed or reported in past 6 months
**Box B3: Recommended Indications for PrEP Use by Persons Who Inject Drugs**

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)
Patient Visits

Typically PrEP patients are seen every 3 months

Visits should be focused around:

- Risk reduction counseling
- Assessment of HIV status/signs and symptoms of acute infection
- STI screening as recommended or needed
- Medication adherence counseling
Virtual Visits

Patients Access:
Telephone needed for phone consults
Smartphone or Computer with working camera needed for video consultations

Telemedicine Coordination:
- Confirm patient’s appointment type
- Coordinate necessary lab work and access to virtual consults
- Make sure patient has a clear understanding of follow up plan, provide in writing if possible
- Make sure patient has access to all necessary testing, including STI swabs
Baseline Testing

- HIV screening test
- Estimated creatinine clearance
- Hepatitis B serologies (HBsAb, HBcAb, HBsAg)
  - Follow up with HBV DNA if HBsAg is positive
- Hepatitis C screening
- Bacterial STI testing
Every 3 Month Monitoring

- HIV testing (preferably 4\textsuperscript{th} generation)
- Pregnancy testing for women who may become pregnant
- Bacterial STI testing if signs/symptoms present
- Bacterial STI testing for asymptomatic MSM patients
  - If history of STI or multiple partners
Every 6 Month Monitoring

Monitor estimated creatinine clearance

Bacterial STI testing for all sexually active patients
HIV 4\textsuperscript{th} Generation Screening Test

Preferred test, quickest identification on HIV

Can detect a new infection 10-14 days after exposure

May affect decision to initiate PrEP

- If unprotected encounter within 2-week period, may repeat test
PrEP Initiation by Race/Ethnicity

- **Phase 1**
  - Asian: 2
  - Black: 2
  - Multi Racial: 1
  - Other: 2
  - Pacific Islander: 0
- **Phase 2**
  - Hispanic: 31
  - White: 51

**Legend:**
- Pink: Phase 1
- Red: Phase 2
**PrEP Initiation by Age Category**

- **Phase 1**: 01/01/2014-09/30/2016
- **Phase 2**: 10/01/2016-12/31/2018

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>25-34</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>35-44</td>
<td>9</td>
<td>34</td>
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<tr>
<td>45-54</td>
<td>7</td>
<td>15</td>
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<tr>
<td>55-64</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>65+</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>
PrEP Initiators by Gender

Phase 1 – 01/01/2014-09/30/2016
Phase 2 – 10/01/2016-12/31/2018

- **Female**
  - Phase 1: 5
  - Phase 2: 3

- **Male**
  - Phase 1: 53
  - Phase 2: 87

- **Transgender/GNC**
  - Phase 1: 1
  - Phase 2: 3

**NUMBER OF PATIENTS**
Patient Snapshot by Sexual Orientation

PrEP Initiation by Sexual Orientation

Phase 1 – 01/01/2014-09/30/2016
Phase 2 – 10/01/2016-12/31/2018

<table>
<thead>
<tr>
<th>Sexual Orientation</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisexual</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Homosexual</td>
<td>51</td>
<td>81</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

NUMBER OF PATIENTS

Legend:
- Phase 1
- Phase 2
PrEP Initiators by Risk Group

Phase 1 vs Phase 2

- Bisexual Multi Partner: 0 Phase 1, 3 Phase 2
- Heterosexual HIV + Partner: 6 Phase 1, 5 Phase 2
- MSM HIV + Partner: 19 Phase 1, 25 Phase 2
- MSM Multi Partner: 33 Phase 1, 58 Phase 2
- Other: 1 Phase 1, 3 Phase 2

Phase 1: 01/01/2014-09/30/2016
Phase 2: 10/01/2016-12/31/2018
Clinical PrEP Cascade

INTERESTED: 193, 100%
LINKED: 176, 91.2%
INITIATED: 155, 88.1%
RETAINED (Q1): 111, 71.6%
ADHERENCE (Q4): 66, 42.6%

Retention Baseline

2014-2018 seroconversion prior to initiation: 5
STI Positivity Rate

STI Positivity Rate

- Gonorrhea / Chlamydia (urine), RPR
- Gonorrhea & Chlamydia Swabs

HIV Positivity Rate for those maintained in care: 0%

Initiation Q1 Q2 Q3 Q4
PERCENT POSITIVE
- STI Positivity Rate
  - Gonorrhea / Chlamydia (urine), RPR
  - Gonorrhea & Chlamydia Swabs
Increased Risk of STI Acquisition?

A recent meta-analysis suggests increased STIs with PrEP

Unclear association as even newer data refutes this

Arguably, STI rates have increased for all MSM despite PrEP

- However, PrEP clearly has reduced the rate of HIV acquisition
U=U: Need for PrEP?

Undetectable = Untransmittable

Recent CDC initiative to raise awareness

- If HIV RNA < 200 copies/mL, do not sexually transmit HIV

If patient in a monogamous, sero-discordant relationship:

- PrEP may not be warranted
- Discussion with patient regarding desire for use
Paying for PrEP

AWP per tablet = $70.32

If high copays:

- Gilead offers a copay card good for several thousand dollars/year

If insurance will not cover or a PA appeal is denied:

- Gilead may pay for medication
THANK YOU!