ACTHIV
THE AMERICAN CONFERENCE FOR THE TREATMENT OF HIV

ACTHIV 2017: A State-of-the-Science Conference for Frontline Health Professionals
Getting to know PrEP/PEP: A Case-based Approach
Learning Objectives

- Review the current usage of PrEP in the US in order to identify areas of ongoing need
- Illustrate the progression of PrEP research
- Obtain experience with complex day-to-day challenges when prescribing PrEP
- Discuss opportunities to expand the reach and effectiveness of PrEP
Disclosures

Received research grant funding from Gilead Sciences

Advisory Board Member, Gilead Sciences

Promotional Speaker's Bureau, Gilead Sciences
Outline

- PrEP: Who’s eligible, and who’s on it?
- Transition from RCTs to real-world PrEP
- PrEP Cases & Conundrums
- PrEP Possibilities

The best way to predict the future is to invent it – Alan Kay
**Unique Individuals Starting FTC/TDF for PrEP in US, 2012 to 2015 (by quarter)**

- **79,684** unique individuals started FTC/TDF for PrEP:
  - (1,671 in Q4 2012 → 14,000 in Q4 2015)

CDC estimates **1,231,000** eligible for PrEP in US

738% increase

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>0</td>
<td>200</td>
<td>600</td>
<td>1,400</td>
</tr>
<tr>
<td>Q2</td>
<td>400</td>
<td>600</td>
<td>1,200</td>
<td>3,000</td>
</tr>
<tr>
<td>Q3</td>
<td>1,200</td>
<td>1,600</td>
<td>1,800</td>
<td>3,600</td>
</tr>
<tr>
<td>Q4</td>
<td>1,400</td>
<td>1,800</td>
<td>2,000</td>
<td>4,000</td>
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</table>

Mayer IAS2016, Durban
# Region and State Use of FTC/TDF for PrEP 2012-2015

<table>
<thead>
<tr>
<th>South</th>
<th>Northeast</th>
<th>Midwest</th>
<th>West</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TX</strong> 6.8%</td>
<td><strong>NY</strong> 15.9%</td>
<td><strong>IL</strong> 5.4%</td>
<td><strong>CA</strong> 16.7%</td>
</tr>
<tr>
<td><strong>FL</strong> 5.7%</td>
<td><strong>MA</strong> 5.1%</td>
<td><strong>MN</strong> 2.5%</td>
<td><strong>WA</strong> 3.5%</td>
</tr>
<tr>
<td><strong>GA</strong> 3.7%</td>
<td><strong>PA</strong> 4.7%</td>
<td><strong>OH</strong> 2.1%</td>
<td><strong>AZ</strong> 1.8%</td>
</tr>
<tr>
<td><strong>DC</strong> 3.3%</td>
<td><strong>NJ</strong> 2.5%</td>
<td><strong>MO</strong> 1.2%</td>
<td><strong>CO</strong> 1.5%</td>
</tr>
<tr>
<td><strong>NC</strong> 1.7%</td>
<td><strong>CT</strong> 0.8%</td>
<td><strong>MI</strong> 1.2%</td>
<td><strong>OR</strong> 1.2%</td>
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<tr>
<td><strong>MD</strong> 1.5%</td>
<td><strong>RI</strong> 0.5%</td>
<td><strong>IN</strong> 1.0%</td>
<td><strong>NV</strong> 0.6%</td>
</tr>
<tr>
<td><strong>VA</strong> 1.2%</td>
<td><strong>NH</strong> 0.2%</td>
<td><strong>WI</strong> 0.6%</td>
<td><strong>UT</strong> 0.5%</td>
</tr>
<tr>
<td><strong>TN</strong> 1.0%</td>
<td><strong>ME</strong> 0.2%</td>
<td><strong>KS</strong> 0.5%</td>
<td><strong>NM</strong> 0.4%</td>
</tr>
<tr>
<td><strong>LA</strong> 0.9%</td>
<td><strong>VT</strong> 0.1%</td>
<td><strong>IA</strong> 0.3%</td>
<td><strong>HI</strong> 0.2%</td>
</tr>
<tr>
<td><strong>AL</strong> 0.5%</td>
<td><strong>NE</strong> 0.2%</td>
<td><strong>ID</strong> 0.2%</td>
<td></td>
</tr>
<tr>
<td><strong>SC</strong> 0.4%</td>
<td><strong>ND</strong> 0.1%</td>
<td><strong>MT</strong> 0.1%</td>
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<tr>
<td><strong>KY</strong> 0.4%</td>
<td><strong>SD</strong> 0.0%</td>
<td><strong>WY</strong> 0.1%</td>
<td></td>
</tr>
<tr>
<td><strong>OK</strong> 0.4%</td>
<td></td>
<td><strong>AK</strong> 0.0%</td>
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<tr>
<td><strong>MS</strong> 0.3%</td>
<td></td>
<td></td>
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<tr>
<td><strong>DE</strong> 0.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AR</strong> 0.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>WV</strong> 0.1%</td>
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</tbody>
</table>

CA, NY, TX, FL, & IL = 50.5% unique individuals starting FTC/TDF for PrEP

Mayer IAS2016, Durban
FTC/TDF for PrEP Utilization Compared With Population and New HIV Infections

Estimated Population Distribution by Race/Ethnicity, 2014, US\textsuperscript{a}

- AA: 12%
- White: 62%
- Hispanics: 18%
- Asians: 3%
- Multiracial/Other: 2%

Total FTC/TDF for PrEP Utilization by Race/Ethnicity, Sept 2015, US\textsuperscript{b}

- AA: 10%
- White: 74%
- Hispanics: 12%
- Asians: 4%
- Multiracial/Other: 3%

Estimated New HIV Infections, 2014, US\textsuperscript{c}

- AA: 27%
- White: 44%
- Hispanics: 23%
- Asians: 3%
- Multiracial/Other: 2%

PrEP use among AA/Hispanics is low relative to the rate of new HIV infections

Mayer IAS2016, Durban
Bush S, et al. ASM/ICAAC 2016; Boston, MA. #2651
Outline

- PrEP: Who’s eligible, and who’s on it?
- Transition from RCTs to real-world PrEP
- PrEP Cases & Conundrums
- PrEP Possibilities

You miss 100% of the shots you don’t take – Wayne Gretsky
From Clinical Trials to Clinics

- RCTs
- “Real world” studies
- Demonstration projects
However, if we isolate the study participants with *detectable* drug levels that reflect consistent use of PrEP, we see much higher rates of PrEP efficacy:

- iPrex: 92%
- Partners PrEP: 90%
PROUD: PrEP now or PrEP later?

MSM reporting UAI in last 90 days
18+, from 1 of 13 sexual health clinics in UK, willing to take a daily pill

Randomize HIV negative MSM
Median Age 35, Mostly white (80%, 82%), university grad (59%, 60%), employed (70%, 73%)

TDF/FTC NOW (n = 267)

TDF/FTC AFTER 12M (n = 256)

Follow every 3 months for up to 24 months

Endpoints:
1) Recruitment and retention
2) HIV infection in first 12 months

“Real world” studies
We found that our concerns about PrEP being less effective in the real world were completely unfounded. In fact, the opposite turned out to be the case.

- Sheena McCormack

McCormack S et al, 22nd CROI; Seattle, WA 2015. Abst 22LB.
Kaiser Permanente study 2012-2015

Updated Data:

- 972 patients on PrEP
- 92% self-reported adherence
  - Low adherence associated with black race, higher copays, smoking
- STI rates increased for rectal CT and urethral GC
- No HIV infections on PrEP
- 2 HIV seroconversions in individuals who stopped PrEP after losing insurance coverage

SFDPH: STRUT Program

Services for Gay, Bi, Trans, or Queer Men

- No new HIV infections among > 1200 men on PrEP in nurse-led intervention over nearly 1.5 years
- 82 new infections among men not enrolled in PrEP program
Outline

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*If you cannot do great things, do small things in a great way – Napoleon Hill*
Clinical case #1

44 year old man with HTN who comes to see you for a hospital discharge visit, and asks you at the end of the visit if you would write him a prescription for PrEP

- Reports being sexually active with women exclusively, is married to a (cisgender) female who is HIV-negative, and has no other partners
- He has a remote history of STIs, asymptomatic now
- His labs from last week show a negative HIV test and normal kidney function
Clinical case #1

Would you prescribe PrEP?

1) No, this patient is not “high-risk” enough
2) I am not comfortable prescribing PrEP in general
3) Yes
4) I’m not sure
PrEP is a “demand-driven” intervention, meaning that “the indication for PrEP is that someone asks for it.” This implies that people are good at determining their own risk and that overly tight criteria for offering PrEP are unnecessary because people will self-regulate in terms of use and uptake.

- Robert Grant of UCSF

Clinical case #1

Your 44 year old PrEP patient comes back for follow-up. He is doing well, now confides that he is occasionally sexually active with additional male and female partners, does not always use condoms, and does not want to put his wife at risk of HIV.
Need to improve communication about sexual risk behaviors and PrEP in primary care

- Survey of 1,394 MSM using partner-seeking website
- 42% were uncomfortable discussing male-male sex with their PCP
- Even when comfortable, few MSM had discussed PrEP with their PCP
- Most MSM perceived that PCPs would be unwilling to prescribe PrEP

**Versus other healthcare provider, the Internet, or other source**
A majority of HIV specialists would prescribe PrEP; only 1 in 3 has done so.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Consider part of clinical role</th>
<th>Have done in practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counseling about PrEP</td>
<td>87%</td>
<td>59%</td>
</tr>
<tr>
<td>Visits for HIV-neg partner</td>
<td>71%</td>
<td>41%</td>
</tr>
<tr>
<td>Prescribing PrEP</td>
<td>68%</td>
<td>32%</td>
</tr>
<tr>
<td>None of the above</td>
<td>7%</td>
<td>11%</td>
</tr>
<tr>
<td>No answer</td>
<td>3%</td>
<td>25%</td>
</tr>
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National survey of ID physicians (n=415) from IDSA’s Emerging Infections Network

Clinical case #1

You decide to prescribe PrEP for your 44 year old patient. Can he take PrEP just around the time of sex so he does not have to take it daily?

1) Yes the current data support on-demand PrEP
2) Yes a reasonable option despite supporting data
3) No, there are not enough data supporting this
4) It depends / not sure
IPERGAY: Sex-Driven iPrEP

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

4 pills of TDF/FTC taken over 3 days to cover one sexual encounter

14 HIV infections in placebo arm, 2 HIV infections in active arm
86% relative reduction in incidence of HIV-1; NNT = 18

Molina J et al, 22nd CROI; Seattle, WA 2/2015. Abst. 23LB.
Ipergay Open Label Extension (OLE)

- On-demand PrEP still effective
  - 1 new HIV infection in OLE
    - 1.3 months in OLE, no detectable drug since entering OLE
    - No RT resistant mutations
  - New STIs during OLE (33%)
  - 97% relative reduction in HIV incidence relative to placebo
  - Only 50% of subjects reported using iPrEP optimally

Summary

- On-demand PrEP safe and effective for rectal exposure
- Low condom use in the open-label phase did not undermine efficacy
- No significant change in number of partners or sex acts
- High rate of STIs needs to be addressed
- PrEP improved pleasure and removed fear during sex
- Results of this study led to PrEP approval in France with full reimbursement
- Caveat: Average of 18 pills taken/month
Potential for < Daily PrEP depends on Population/Location

% of patients at 30 wks who reported sex in last 7d with protective TFV plasma levels

Depends on his adherence as well as how often he is sexually active

Daily = daily TDF/FTC
Time = 2/wk + post-coital
Event = before and after intercourse

Clinical case #1

What if he only has sex with other partners once/year during Gay Pride?

Patients take daily PrEP during vacation and for 1 week before/after the trip.

Prescribe vacation PrEP, but with appropriate counseling about how long to take PrEP beforehand.
How quickly does PrEP work?

PrEP is extremely effective when taken daily. However it does need time to build up in blood and tissues.

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Time to Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal/Anal</td>
<td>7 days</td>
</tr>
<tr>
<td>Blood</td>
<td>21 days</td>
</tr>
<tr>
<td>Vaginal</td>
<td>21 days</td>
</tr>
<tr>
<td>Neo-Vaginal*</td>
<td>???</td>
</tr>
</tbody>
</table>

*still a lot of clinical research/education to be done to provide equitable care to our trans communities
Clinical case #1

Your 44 year old PrEP patient comes in for a second follow-up visit 3 months later. He reports he has been taking his PrEP “most of the days of the week,” averaging 3-4 doses per week, last dose 3 days ago. He had UAI with a male partner of unknown HIV status several times this week, last 2 days ago. How would you manage your patient?

1) Continue PrEP alone
2) Stop PrEP, send serum HIV test, follow up in 3-5 days
3) Start PEP
PrEP: Varying Concentration in Tissues

Open-label, 14-day pharmacokinetic study in HIV-negative female (n=7) and male (n=8) volunteers. Entry criteria included: 18-50 years of age; BMI 18-30 kg/m²; weight >50 kg; no HCV or HBV; nonpregnant women who were premenopausal and had regular menstrual cycles.

Clinical case #2

An 18 yo male reports unprotected anal intercourse with men and transwomen and is being evaluated for PrEP. His rapid HIV test is negative today, and labs have been sent (4th gen HIV test, CMP). Can he start PrEP today?

1) Yes, I would prescribe a 1-week starter pack
2) Yes, I would prescribe a 30-day starter pack
3) No, I would wait until his 4th gen HIV test and CMP are back and start in a few days
Diagnoses of HIV Infection among Adolescents and Young Adults 13–24 Years, by Race/Ethnicity, 2010–2014
United States and 6 Dependent Areas

Starting ART on the same day of HIV diagnosis results in higher treatment uptake and more rapid VL suppression. Patients are eligible for same-day PrEP start if they have a negative HIV rapid test and meet ≥ 1 of the following criteria:

- At high risk of exposure to HIV during the period from the PrEP screening visit (lab work, etc.) and initiation visit
- Diagnosed with STI (RPR or rectal gonorrhea) at current or last visit
- Partnered with an HIV positive individual with detectable or unknown HIV viral loads, or history of inconsistent engagement in care or adherence to ARV medications
- Not PEP eligible

Pilcher et al, IAS 2015
Clinical case #2

An 18 yo male reports unprotected anal intercourse with men and transwomen and is being evaluated for PrEP. His rapid HIV test is negative today, and labs have been sent (4\textsuperscript{th} gen HIV test, CMP).

How should he be monitored for STIs?
STIs are Common Among PrEP Users

- CDC recommendation:
  - Screen for STIs q6months
  - No specific requirement for pharyngeal or rectal screening

- Abstract by Cohen et al:
  - Treatment would have been delayed for 35% of STIs if screening was q6months
  - Q3 month screening prevented 3 exposures/STI case
  - 82.9% GC and 75.7% CT infections would have been missed if extra-urethral screening had not been conducted

Q3m triple-screen (GC/CT), RPR, +/- trich, annual HCAb

Cohen S et al, CROI 2016
Clinical case #2

For your 18-year old PrEP patient, how often should he be seen?

1) Every 6 months
2) Every 3 months
3) Every month
ATN 110 (yMSM age 18-22): Median TFV-DP by Race/Ethnicity

Hosek et al, IAS, Vancouver, Canada 7/2015.
ATN 113 (yMSM age 15-17): Adherence

- Drop off in TFV-DP levels between Wk 12 and Wk 24 corresponded to reduced frequency of scheduled study visits (from every 4 wks to every 12 wks)


Slide credit: clinicaloptions.com
FIGHT 48 week observational trial

- PrEP administered to 50 yMSM and TWc for 48 wks
- Needs-based dispensation schedule
  - Weekly, every other week, monthly depending on need
- Conclusions:
  - 70% program retention at 48 weeks
  - High acceptability of frequent monitoring
  - High adherence to PrEP over time using urine TFV

Adherence measured by urine TFV

Urine TFV Concentrations remain high in the majority of subjects over 48 wks

- **Fully Protected**: >1000ng/mL
- **Somewhat Protected**: >10ng/mL - >100ng/mL
- **Not Protected**: <10ng/mL

Clinical case #3

A 28 yo woman reports unprotected vaginal and anal intercourse with multiple male partners of unknown status. She took Plan B two times for unintended pregnancies before starting injectable medroxyprogesterone, and has had chlamydia 3 times. She would like to start PrEP but hates pills.

What are her options?
Dapivirine Vaginal Ring

- Vaginal ring with NNRTI dapivirine replaced q4 weeks
- MTN-020/ASPIRE: Malawi, S. Africa, Uganda, Zimbabwe (2629)
  - 27% reduction in HIV incidence ($p = 0.046$)
  - 56% reduction in women > 21 years
  - No decrease in infection rate in women < 21 years
- IMP 027: S. Africa, Uganda (1959)
  - 31% reduction in HIV incidence
  - 37.5% reduction in women > 25 years
  - No decrease in infection rate in women < 21 years
- Could be protective in cis-women with vaginal-only exposure
- Higher adherence associated with greater risk reduction

HPTN 083

- Cabotegravir: potent INSTI formulated as LA IM injection
- Randomized, double-blind phase IIb/III trial, results expected 2021

HPTN 084 will test cabotegravir as PrEP in cis-women, still in protocol development

Clinical case #3

A 28 yo woman reports unprotected vaginal and anal intercourse with multiple male partners of unknown status. She took Plan B two times for unintended pregnancies before starting injectable medroxyprogesterone, and has had chlamydia 3 times. She would like to start PrEP but hates pills.

• What are her options? Male/female condoms, learning about TasP, partner testing & disclosure, revisiting why she doesn’t like pills
The most important conversation to have when you start PrEP is how to stop

PrEP is different from other medications we prescribe in that we should expect PrEP use to stop
Outline

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All our dreams can come true, if you have the courage to pursue – Walt Disney
PrEP Possibilities

- Personalized PrEP
- Stop checking renal function
- De-medicalization of PrEP
- Ending the Epidemic

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