Advancing PrEP Delivery
An Update on Pre-Exposure Prophylaxis

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Disclosures

I have no actual or potential conflicts of interest in relation to this presentation.

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Overview

- A brief look at the NCATEC network
- Clinical case addressing questions we’ve gotten
- News since last year’s webinar
  - HIV epidemiology
  - Adolescents and PrEP
  - Resistance
  - Impact, uptake, and access
  - TAF, the “pipeline,” and local clinical trials
<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
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<tbody>
<tr>
<td>Sites statewide</td>
<td>55*</td>
</tr>
<tr>
<td>Responded to census</td>
<td>25</td>
</tr>
<tr>
<td>Patients on PrEP across 24 sites</td>
<td>536</td>
</tr>
<tr>
<td>Take uninsured patients</td>
<td>76%</td>
</tr>
<tr>
<td>Accept Medicaid</td>
<td>88%</td>
</tr>
<tr>
<td>Wanted to remain listed</td>
<td>100%</td>
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</tbody>
</table>
You’re seeing Brandon in clinic

• Healthy 18 year-old Black man

• Sexual exposure about 60 hours ago
  o New male partner of unknown status
  o Partner (top) wasn’t wearing condom

• Oral rapid test negative at home yesterday

• Still concerned – “I just want to get checked”
What tests do we need to obtain?

**Sexual health**
- Syphilis
- Gonorrhea NAAT*
- Chlamydia NAAT*
- Pregnancy

*from all exposed sites

**Viral hepatitis**
- HBV surface Ab
- HBV surface Ag
- HBV core Ab
- Hepatitis C Ab

**HIV testing**
- Ag/Ab combo
  - rapid test, if possible
- Too early for RNA

  § Ab-only is acceptable if Ag testing unavailable

**Notes:**
- baseline & 4-6 wks
- baseline & 6 mos
- baseline & 4-6 wks & 3 mos

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Timeline following infection

- RNA precedes p24 Ag by 5-7d
- Earliest Ab detection around 20-25d (IgM in 3rd – 5th gen)
- Earliest 2nd gen Ab detection at 35-40d (as IgG begins rising)
- Rapid tests with oral transudate may take **up to 90d** to convert (self-test implications)

Adapted from Branson BM, et al. Laboratory testing for the diagnosis of HIV infection: updated recommendations. (2014)
Ag/Ab combo allows very early detection

Fourth & fifth generation

3rd gen with simultaneous p24 Ag detection added

Monoclonal anti-p24 Ab

p24 antigen (from patient)

Enzyme-linked anti-p24 antibody

Detection reagent
Alere Determine HIV-1/2 Ag/Ab Combo

Fourth generation
Lateral flow “sandwich”

First FDA-approved 4\textsuperscript{th} gen \textbf{rapid}\textsuperscript{1}

Marketed for detection of early infections\textsuperscript{2}

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**Advantages**

- Ab sensitivity is \textbf{excellent} (99.4\%)\textsuperscript{3,4}
- Portable; 1 year shelf-life
- Results in 20 minutes

**Disadvantages**

- Multiple \textit{field} studies replicated poor sensitivity in p24 detection (ranging 0-50\%)\textsuperscript{3,5-7} [7 = meta-analysis]
- False (+) p24 in 1.7\% of HIV(−) \textsuperscript{3}

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Brandon, cont’d

- Rapid 2nd gen Ab test negative
  - Fingerstick specimen used, not oral swab
- Four months ago, prescribed 28 days of:
  - emtricitabine/tenofovir disoproxil fumarate
  - lopinavir/ritonavir
- Didn’t finish prior regimen due to adverse effects
- “Is there an alternative to what I took before?”
Is he a candidate for PEP?

**Substantial risk**
Mucosal, nonintact skin, or percutaneous contact
Blood, semen, rectal & genital secretions, or body fluid visibly contaminated with blood
Known HIV+ source

- **≤ 72 hours** since exposure
  - Source known to be HIV+
    - nPEP recommended
  - Source of unknown status
    - Case-by-case determination
- **> 72 hours** since exposure

**Negligible risk**
Mucosal, skin, or percutaneous contact
Urine, nasal secretions, saliva, sweat, tears (if not visibly contaminated with blood)
Regardless of HIV status of source

nPEP not recommended

Dominguez KL, et al. CDC nPEP Guidelines 2016. https://stacks.cdc.gov/view/cdc/38856  Fig 1 & Table 1
Which ARVs are recommended for PEP?

Adults with normal renal function \( (CrCl \geq 60 \text{ mL/min}) \)

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Alternative</th>
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<tbody>
<tr>
<td><strong>emtricitabine/tenofovir DF</strong></td>
<td><strong>daltegravir INI</strong></td>
</tr>
<tr>
<td>2 NRTIs</td>
<td>2 NRTIs</td>
</tr>
<tr>
<td>Truvada (Gilead)</td>
<td>Truvada (Gilead)</td>
</tr>
<tr>
<td>QD</td>
<td>QD</td>
</tr>
<tr>
<td><strong>BID</strong></td>
<td><strong>darunavir PI</strong></td>
</tr>
<tr>
<td>Isentress (Merck)</td>
<td>QD</td>
</tr>
<tr>
<td><strong>QD</strong></td>
<td>Prezista (Janssen)</td>
</tr>
<tr>
<td><strong>PrepSTED WITH</strong></td>
<td></td>
</tr>
<tr>
<td><strong>raltegravir INI</strong></td>
<td><strong>ritonavir PKE</strong></td>
</tr>
<tr>
<td>QD</td>
<td>QD</td>
</tr>
<tr>
<td>Tivicay (ViiV)</td>
<td>Norvir (AbbVie)</td>
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</table>

Brandon, cont’d

- Returns 6 months after starting PEP regimen
  - Was HIV uninfected at 3 months
  - HBV immune, HCV uninfected
  - All STI testing was negative

- No sex partners since episode prompting PEP

- “I’ve read some about PrEP online. Do you think it would be good for someone like me?”
Does he meet criteria for PrEP?

- HIV uninfected, plus:
  - Any HIV+ partner(s)
  - Condomless sex in past 6m
  - Any STI in past 6m
  - High number of sex partners
  - In high-prevalence area or sexual network
  - Commercial sex work
  - Shared injection equipment
  - Recent drug treatment & current relapse

USPHS PrEP Guidelines 2014
https://stacks.cdc.gov/view/cdc/23109
Does he meet criteria for PrEP?

“Persons who repeatedly seek nPEP should be evaluated for possible PrEP use after confirming they have not acquired HIV infection.

Because HIV infection has been reported in association with exposures soon after an nPEP course, daily PrEP may be more protective than repeated episodes of nPEP.”

USPHS PrEP Guidelines 2014
https://stacks.cdc.gov/view/cdc/23109
Does he meet criteria for PrEP?

Young, Black MSM were less likely to have an indication for PrEP

≥ 2 sex partners plus either bacterial STI or UAI in past 12 m

1 main HIV+ partner in past 12 m

Sexual behavior alone is insufficient to explain higher incidence among Black MSM

In high prevalence networks, fewer missteps needed to acquire HIV

See various papers by Greg Millett

Hoots et al. CID. 2016:63(5):672-7
Maulsby et al. AIDS Behav 2014:18(1):10-25
Brandon, cont’d

- Seeing him 6 months after he starts PrEP
  - Adherence good, feeling well
  - Interim rectal chlamydia, treated
  - Now in “monogamish” relationship

- Follow-up labs show stable SCr

- Transaminases were checked with today’s visit:
  - AST 70
  - ALT 92
What’s new since our last webinar?
Who should get PrEP?

Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition — United States, 2015

Dawn K. Smith, MD1; Michelle Van Handel, MPH1; Richard J. Wolitski, PhD1; Jo Ellen Stryker, PhD1; H. Irene Hall, PhD1; Joseph Prejean, PhD1; Linda J. Keenig, PhD1; Linda A. Vallesoy, PhD1

On November 24, 2015, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

Abstract

Background: In 2014, approximately 40,000 persons in the United States received a diagnosis of human immunodeficiency virus (HIV) infection. Preexposure prophylaxis (PrEP) with daily oral antiretroviral medication is a new, highly effective intervention that could reduce the number of new HIV infections.

Methods: CDC analyzed nationally representative data to estimate the percentages and numbers of persons in the United States, by transmission risk group, with indications for PrEP consistent with the 2014 U.S. Public Health Service’s PrEP clinical practice guideline.

Results: Approximately 24.7% of sexually active adult men who have sex with men (MSM) (492,000 [95% confidence interval [CI] = 212,000–772,000]), 18.5% of persons who inject drugs (115,000 [CI = 45,000–185,000]), and 0.4% of heterosexual active adults (624,000 [CI = 404,000–846,000]), had substantial risks for acquiring HIV consistent with PrEP indications.

Conclusions: Based on current guidelines, many MSM, persons who inject drugs, and heterosexual active adults have indications for PrEP. A higher percentage of MSM and persons who inject drugs have indications for PrEP than heterosexual active adults, consistent with distribution of new HIV diagnoses across these populations.

Implications for Public Health Practice: Clinical organizations, health departments, and community-based organizations should raise awareness of PrEP among persons with substantial risk for acquiring HIV infection and their health care providers. These data can be used to inform scale-up and evaluation of PrEP coverage. Increasing delivery of PrEP and other highly effective HIV prevention services could lower the number of new HIV infections occurring in the United States each year.

Introduction

In 2014, 40,000 persons in the United States were diagnosed with HIV infection. PrEP is a complementary strategy to other effective HIV prevention methods, including early diagnosis and treatment of HIV, and the use of antiretroviral suppression and consistent condom use.
Who should get PrEP?

- 1 in 4 sexually active MSM
- 1 in 5 persons who inject
- 1 in 200 heterosexually active adults

Smith DK et al. MMWR 2015 64(46):1291-1295
Who should get PrEP?

492,000
sexually active MSM

115,000
persons who inject

624,000
heterosexually active adults

Smith DK et al. MMWR 2015 64(46):1291-1295
Lifetime risk of acquiring HIV

Hess K et al. CROI 2016, abstract #52

Map from CDC website: http://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html
Hess K et al. CROI 2016, abstract #52

Map from CDC website: http://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html

Lifetime risk of acquiring HIV

1 in 93
North Carolinians

Highest – Lowest
Lifetime risk of acquiring HIV

If current diagnosis rates persist...

2 out of 100 Black women will become HIV+

Hess K et al. CROI 2016, abstract #52
Lifetime risk of acquiring HIV

If current diagnosis rates persist...

9 out of 100 White MSM will become HIV+

Hess K et al. CROI 2016, abstract #52
Lifetime risk of acquiring HIV

If current diagnosis rates persist...

25 out of 100 Hispanic MSM will become HIV+

Hess K et al. CROI 2016, abstract #52
Lifetime risk of acquiring HIV

50 out of 100 Black MSM will become HIV+

If current diagnosis rates persist...

Hess K et al. CROI 2016, abstract #52
Can addressing barriers improve adherence?

HIV Prevention Trials Network Study 073, 2013-15
Los Angeles, Washington DC, Raleigh-Durham-Chapel Hill
Client-centered care coordination plus offer of PrEP through study

225 Black MSM
40% under 25 y.o.
79% accepted PrEP
68% on PrEP at week 26

Can adolescents be prescribed PrEP?

- Truvada is FDA approved:
  - “with safer sex practices … to reduce the risk of sexually acquired HIV-1 in adults at high risk”
  - for “treatment of HIV-1 infection in adults and pediatric patients weighing at least 17 kg”

- USPHS/CDC PrEP guidelines:
  - safety, efficacy data insufficient for adolescents
  - weigh risks & benefits in context of local laws on autonomy in health care decision-making

What about bone health in young adults?

Project PrEPare 2 (ATN 110), 72 who stopped FTC/TDF

**Mulligan K, et al. 18th Int'l Workshop on Comorbidities and Adverse Drug Reactions in HIV. 12-13 Sept 2016. New York City, NY. Abstract 001.**
What about bone health in young adults?

Project PrEPare 2 (ATN 110), 15 who continued FTC/TDF

18-22 years old

What about adherence in young adults?

Project PrEPare 2 (ATN 110), Oct 2012 - Feb 2015

18-22 years old

Median TFV-DP Concentration

Follow-up Week

≥ 4 doses per week

What about adherence in young adults?

Project PrEPare 3 (ATN 113), Aug 2013 – Mar 2016

Minor’s capacity to consent for STI services

Can HIV break through PrEP?

Patient

• On PrEP for 24 months

• Likely fully adherent (based on DBS drug levels and Rx refill data)

Can HIV break through PrEP?

Patient
- Meets partner on barebacking hook-up site
- Tried following up afterward, but partner became unreachable

"Negative"
Can HIV break through PrEP?

Patient

• p24 antigen positive on routine quarterly testing
• No reported symptoms suggestive of acute HIV infection

Can HIV break through PrEP?

Patient

- p24 antigen positive on routine quarterly testing
- No reported symptoms suggestive of acute HIV infection

Resistance testing

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Can HIV break through PrEP?

Patient
- p24 antigen positive on routine quarterly testing
- No reported symptoms suggestive of acute HIV infection

Donor (inferred)
- Acquired (and/or transmitted) resistance
- Viremic with resistant HIV (off ARVs or failing)

Resistance testing

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Implications
- Special, unusual circumstances but could certainly happen again
- **Any condomless sex poses a risk; lower with PrEP, but never truly zero**

Acquired resistance is much more likely...

Hypothetical scenario

• Period of nonadherence
• Exposure event(s)
• Symptoms develop but aren’t reported
• Concern prompts resumption of PrEP
• Perfect adherence
• Resistance develops to emtricitabine ± tenofovir DF*

* Assuming still taking PrEP at time of HIV diagnosis and resistance testing

Can we use FTC/TAF for PrEP?

The jury is still out…

• CDC: TAF was protective against repeated low-dose rectal SHIV\textsubscript{162p3} challenges in 6 macaques

• UNC: after 1 dose TAF, human genital & rectal levels of active tenofovir were unexpectedly low

• FTC/TAF (Descovy) should NOT be used for PrEP until more comprehensively evaluated

Potential impact of interventions, 2015-2020

- **Scenario 1:** Projected new infections by 2020 at current testing and treatment rates
  - Total: 265,330

- **Scenario 2:** If PrEP use increases among high-risk populations at current testing and treatment rates
  - Total: 217,109
  - PrEP infections prevented: 48,221

- **Scenario 3:** If 85% of people diagnosed are linked to care, 60% achieve viral suppression, plus PrEP use
  - Total: 144,434
  - Testing and treatment: 88,908

- **Scenario 4:** Achieving NHAS goals – if 85% of people diagnosed are linked to care, 80% achieve viral suppression, plus PrEP use
  - Total: 80,270
  - Testing and treatment: 168,132

Legend:
- New infections
- HIV infections prevented due to expanded testing and treatment
- HIV infections prevented due to PrEP (assumes PrEP use among high-risk populations = 40% MSM; 10% PWID; 10% HET)

Yaylali E et al. CROI 2016, abstract #1051
Graphic from CDC
PrEP is taking off in the US…

738% increase

USPHS / CDC guidelines issued

Individuals starting FTC/TDF for PrEP

2012 2013 2014 2015

Rawlings K et al (McAllister presenting). IAC Durban 2016, abstract #TUAX0105LB
http://www.natap.org/2016/IAC/IAC_17.htm
PrEP is taking off in the US...

79,684 individuals

Individuals starting FTC/TDF for PrEP

Rawlings K et al (McAllister presenting). IAC Durban 2016, abstract #TUAX0105LB
http://www.natap.org/2016/IAC/IAC_17.htm
...but its distribution is uneven...

Rawlings K et al (McAllister presenting). IAC Durban 2016, abstract #TUAX0105LB
http://www.natap.org/2016/IAC/IAC_17.htm
...but its distribution is uneven...  
n=21,463  
(44% of all started)

Bush S et al. ASM / ICAAC 2016, abstract #2651
...and it’s not reaching those most at-risk

22% of all new infections in 2014 among 13-24 yo

18,812 women prescribed

28% < 25 yo

11% < 25 yo

60,872 men prescribed

Rawlings K et al (McAllister presenting). IAC Durban 2016, abstract #TUAX0105LB
http://www.natap.org/2016/IAC/IAC_17.htm
...and it’s not reaching those most at-risk

**US Population 2014**
- 62%
- 12%
- 18%

**PrEP Utilization Sept 2015**
- 74%
- 10%
- 12%

**New Infections 2014 (estimated)**
- 44%
- 27%
- 23%

Bush S et al. ASM / ICAAC 2016, abstract #2651
PrEP is now a matter of social justice
PrEP 2.0 is coming...

- FTC / TAF
- DISCOVER (Gilead)
- cabotegravir-LA INI
- TRIUMPH (HPTN 083)

- dapivirine NNRTI
- broadly neutralizing monoclonal antibodies (bnAbs)
- AMP Study (HPTN 085)
IGNORANCE = FEAR
SILENCE = DEATH
FIGHT AIDS
ACT UP

Questions?
Feel free to email me
churt@med.unc.edu
NCATEC online PrEP resources

• Visit us at www.med.unc.edu/ncatec for information & resources for:
  – Consumers
  – PrEP prescribers (protocols, etc.)
  – “PrEP curious” providers

• Need more training assistance related to HIV, STIs, hepatitis C, cultural competency?
  – Email Michele Bailey, NCATEC Program Manager at: michele.bailey@med.unc.edu