PrEP for Indian Country: Moving HIV Acquisition to Zero

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University of North Carolina

Introduction by Jonathan Iralu, MD
IHS ID Chief Clinical Consultant
Greg

26 yo man who has sex with men who presents to primary care for skin rash

• Waiting tables and going to night school for accounting
• Social History:
  – Not in a stable relationship currently
  – Uses condoms with some partners, but not all
  – Versatile for anal sex
• Past History:
  – Rectal gonorrhea 2014, NGU 2011
  – Currently on no daily medications
• Uninsured
• Physical Exam:
  – Reveals lesions c/w secondary syphilis
    • Confirmed with blood testing
Questions to Discuss

• Is Greg a good candidate for PrEP?
• What should the condom messaging be?
• What tests/assessments are needed before starting PrEP?
• Who will pay for all this?
PrEP: The Issues

• New HIV infections in the US continue
• Vast majority of infections are sexually acquired
• Condoms work but are not loved by all
• TDF/FTC PrEP has been demonstrated to be effective
• TDF/FTC PrEP is a reality
• How do we get PrEP to those who want it and can benefit from it
A Snapshot of HIV/AIDS in the United States

- Number of people living with HIV: 1.2 million
- Number of new infections: ~ 50,000 per year
- Percent of people who are infected and unaware: 14%

HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome.
AIDSVu (www.aidsvu.org). Emory University, Rollins School of Public Health. Accessed 2/26/15;

Rates of persons living with an HIV diagnosis by county, 2010
New Cases of HIV, USA, AI/AN
(CDC surveillance, 2010-2014)

- Approximately 44,000 new cases/year in the USA

- HIV incidence among AI/AN patients has increased from 174 cases (7.9/100,000) in 2010 to 222 in 2014 (9.5/100,000)

- In 2014, an estimated 84% of new HIV cases were transmitted via sexual contact among Men Who Have Sex with Men (MSM)

Main Transmission routes, Indian Country

- **Males (N-170)**
  - Male-to-Male Sexual Contact (142) 84%
  - Heterosexual Contact (10) 6%
  - Male-to-Male Sexual Contact/IDU (7) 4%
  - IDU (11) 6%

- **Females (N-49)**
  - Heterosexual Contact (36) 73%
  - IDU (13) 27%
Multiple, proven prevention strategies
Evidence-Based HIV Prevention Strategies

- Condom access and distribution
- Health education and risk reduction counseling
- Needle and syringe exchange
- STI screening and testing
- HIV testing
- ART for prevention
- Post-exposure prophylaxis (PEP)
- Pre-exposure prophylaxis (PrEP)
What is PrEP?

Pre-exposure prophylaxis

Use of anti-HIV medications **before** an exposure, to reduce the risk of becoming infected

**Tenofovir** is the most studied agent for PrEP
- Pharmacokinetics allow infrequent dosing
- Few drug-drug interactions
- Safe and well tolerated
- Resistance less likely
Fixed-dose TDF/FTC is the recommended PrEP regimen* for MSM, heterosexually active men and women, and IDU who meet prescribing criteria:

- FDA approved indication
- Dosed as a single pill (300/200 mg) once daily

*MSM, heterosexually active men and women, and IDU who meet PrEP prescribing criteria.

Concept rooted in 4 lines of evidence

Prophylactic use of anti-infectives
Concept rooted in 4 lines of evidence

Prevention of mother-to-child transmission
Concept rooted in 4 lines of evidence

Studies in animal models (macaques)
Concept rooted in 4 lines of evidence

Post-exposure prophylaxis (PEP)
Five major studies demonstrated PrEP’s preventive efficacy across risk groups

<table>
<thead>
<tr>
<th>Study</th>
<th>ARV Used</th>
<th>Frequency</th>
<th>Group</th>
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<tbody>
<tr>
<td>CAPRISA 004</td>
<td>Tenofovir vaginal gel</td>
<td>Before &amp; after sex</td>
<td>Heterosexual women</td>
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<tr>
<td>iPrEx</td>
<td>Truvada oral</td>
<td>Daily</td>
<td>MSM &amp; transwomen</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>Tenofovir &amp; Truvada oral</td>
<td>Daily</td>
<td>Heterosexual discordant couples</td>
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<tr>
<td>TDF2</td>
<td>Tenofovir &amp; Truvada oral</td>
<td>Daily</td>
<td>Heterosexual men &amp; women</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study</td>
<td>Tenofovir oral</td>
<td>Daily</td>
<td>Injection drug users</td>
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Two major studies demonstrated a lack of efficacy among heterosexual women.

<table>
<thead>
<tr>
<th>Study</th>
<th>ARV Used</th>
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<tbody>
<tr>
<td>FEM-PrEP</td>
<td>Truvada oral</td>
<td>Daily</td>
<td>Heterosexual women</td>
</tr>
<tr>
<td>VOICE (MTN-003)</td>
<td>Tenofovir gel, tenofovir oral, Truvada oral</td>
<td>Daily</td>
<td>Heterosexual women</td>
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Adherence is critical

Protective efficacy (%)

<table>
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<tr>
<th>All participants</th>
<th>High adherers</th>
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<tbody>
<tr>
<td>44</td>
<td>92</td>
</tr>
<tr>
<td>62-73</td>
<td>~95</td>
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iPrEx OLE confirmed prior estimates

Key points

Daily dosing affords greatest protection

Occasional missed dose probably OK

Nonadherence creates opportunities for infection
July 2012- February 2015: 1,045 referrals for PrEP, of which 835 (80%) led to an in-person evaluation.

Of the 801 participants, 657 (82%) opted to start PrEP. 144 people (18%) decided not to do so.

No new HIV diagnoses occurred among PrEP users during 388 person-years of follow-up.

After 6m: 30% of diagnosed with any STI, 18% rectal STI, 17% chlamydia, 15% gonorrhea, and 3.3% syphilis;

After 12 months, the corresponding percentages were 50%, 33%, 33%, 28%, and 5.5%, respectively.

Among the 143 PrEP users after 6m on PrEP, 56% said condom use unchanged, 41% reported a decrease, and 3% reported an increase; 74% said their number of sexual partners stayed the same, 15% reported a decrease, and 11% reported an increase.
FDA Approves First Medication to Reduce HIV Risk

People diagnosed with HIV—the human immunodeficiency virus that without treatment develops into AIDS—take antiviral medications to control the infection that attacks their immune system.

Now, for the first time, adults who do not have HIV but are at risk of becoming infected can take a medication to reduce the risk of sexual transmission of the virus.

The Food and Drug Administration (FDA) has approved the new use of Truvada—a drug already used in combination with other medications to treat HIV-infected adults and children over 12 years old.

In the 80s and early 90s, HIV was viewed as a life-threatening disease in some parts of the world and still is. Medical advances, along with the availability of inexpensive individual HIV drugs, have enabled us to treat it as a chronic disease most of the time,” Birnbaum says.

“But it is still better to prevent HIV than to treat a life-long infection of HIV,” she says.

Birnbaum stresses that Truvada is meant to be used as part of a comprehensive HIV prevention plan that includes consistent and correct condom use, risk reduction counseling, regular HIV testing, and treatment of any other sexually transmitted infections. Truvada is not a substitute for safer sex practices, she says.

U.S. Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE
MSM Risk Behavior During ANRS IPERGAY Trial

(a) Median number of sexual intercourses (previous 4 weeks)
(b) Median number of sexual partners (previous 2 months)
(c) Percentage of condomless last anal intercourse
(d) Percentage of condomless last receptive anal intercourse

Sagaon-Teyssier, L. AIDS Care 2016;28:48-55
CDC PrEP Guidance:
For Whom Is PrEP Recommended?

Daily oral PrEP is recommended for adults at substantial risk of acquiring HIV infection:

- Sexually active MSM
- Heterosexually active men and women
- Injection drug users

<table>
<thead>
<tr>
<th>Detecting substantial risk of acquiring HIV infection</th>
<th>MSM</th>
<th>Heterosexual Women and Men</th>
<th>IDUs</th>
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<tbody>
<tr>
<td>• HIV-positive sexual partner</td>
<td></td>
<td>• HIV-positive sexual partner</td>
<td></td>
</tr>
<tr>
<td>• Recent bacterial STI</td>
<td></td>
<td>• Recent bacterial STI</td>
<td></td>
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<tr>
<td>• High number of sex partners</td>
<td></td>
<td>• High number of sex partners</td>
<td></td>
</tr>
<tr>
<td>• History of inconsistent or no condom use</td>
<td></td>
<td>• History of inconsistent or no condom use</td>
<td></td>
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<tr>
<td>• Commercial sex work</td>
<td></td>
<td>• Commercial sex work</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• In high-prevalence area or network</td>
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Step 1: Assess need

Open a dialogue about sexual health

• Get to know your patient and her/his risk(s)
• Ask *lots* of embarrassing questions!
• Educate about signs & symptoms of STIs
• Don’t forget about drug use around sex
• Don’t forget about shared drug paraphernalia
Step 1: Assess need

Tips for talking about sex with patients

- Avoid preface statements before inquiring
- Make sure definition of “sexually active” is clear
- It’s OK to use colloquial terminology
- My standard brief history:
  - “Do you have sex with men, women, or both?”
  - For MSM: “Do you top, bottom, or both?”
  - “Are you in a relationship with anyone?”
  - “Do you have sex with anyone (else)?”
  - “How often do you use condoms for…?”
Step 2: Determine clinical eligibility

HIV status

- Ag/Ab (4th gen)
- Rapid (blood)
- ELISA / EIA

Must be HIV(–)

→ Maybe RNA, too?

Step 2: Determine clinical eligibility

- **Viral hepatitis**
  - HBsAg
  - HBsAb
  - HCV Ab
  
  **CAUTION if active HBV!**

- **Renal function**
  - Creatinine
  - eCrCl
  
  eCrCl must be ≥ 60 mL/min

- **HIV status**
  - Ag/Ab (4th gen)
  - Rapid (blood)
  - ELISA / EIA
  
  Must be HIV(−)
  → Maybe RNA, too?

Step 2: Determine clinical eligibility

Screen for symptoms of acute HIV

- Must be free of these, within prior 4 weeks:
  - Fever (75%)
  - Fatigue (68%)
  - Skin rash (48%)
  - Pharyngitis (40%)
  - Cervical adenopathy (39%)

- Suspect acute HIV? Send HIV RNA (viral load)
Step 3: Screen for STIs

If not already done in prior 3-6 months:

- RPR for syphilis
- Gonorrhea and chlamydia
  - NAA testing preferred
  - Extragynital sites too!
Step 3: Screen for STIs
Don’t forget the triple dip
Step 4: Counsel the patient

Establish ground rules

- Ongoing relationship – quarterly visits
- No HIV test? No prescription!

“Startup syndrome”

- Flatulence, nausea / GI upset, headache
- Symptoms resolve within first 30d, for most
Sign a Contract

Patient Section

It has been explained to me that:

- Taking a dose of PrEP medication every day lowers my risk of getting HIV infection
- If I miss doses of my PrEP medications, I am less protected against HIV infection
- This medication does not completely eliminate my risk of getting HIV infection
- This medication does not protect me from other sexually transmitted infections
- This medication may cause side effects, so I should contact my PrEP provider for advice if I have any health problems I think might be related to my medications
- It is important for my health to find out quickly if I get HIV infection while I'm taking this medication, so I will contact my PrEP provider right away if I have symptoms of possible HIV infection (fever, sore throat, rash, headache, or swollen glands)
- My PrEP provider will not prescribe me any medication unless I attend my scheduled appointments and have a negative HIV test at least once every 3 months
- I need to have a primary care provider for my general medical needs

Therefore, I will:

- Try my best to take my medication at about the same time every day
- Talk to my PrEP provider about any problems I have taking my medication every day
- Not share my medication with any other person
- Attend all scheduled appointments with my PrEP provider
- Call our clinic within 48 hours prior to any appointments I cannot attend, and ask to be rescheduled
- Not receive a prescription for any medication without first seeing my PrEP provider in the clinic and getting tested for HIV
- Work with my PrEP provider to identify a primary care provider for my general medical needs, if I do not already have one
- Not hold my provider responsible for any negative issues or outcomes resulting from my failure to abide with the terms of this agreement

____________________  ____________________
Patient Signature       Date

____________________  ____________________
Provider Signature      Date
Step 4: Counsel the patient

Adherence strategies

- Pair pill-taking with daily task (even weekends!)
  - Plugging cell phone in before bedtime
- Set an alarm (clock, watch, or phone)
- Use a pill box
- Keep a dose on / near you
Step 5: Prescribe & follow-up

First Rx: Thirty days, NO refills

Return to clinic in 30 days

- Adherence?
- Side effects?
- Risk behaviors?

2nd Rx: Thirty days, 2 refills
Step 6: Maintenance & reassessment

**At least every 3 months**
- Assess adherence, side effects, risk behavior
- Repeat HIV testing
- Prescription renewal

**At least every 6 months**
- Check creatinine and eCrCl
- Screen for STIs, if not already done
- Determine need – “seasons of risk”
Frequently asked questions
Won’t PrEP encourage riskier sex?

Risk compensation

- Repeatedly examined in multiple trials
  - Indices of risk **stable or reduced**
    - Condomless sex
    - Number of partners
    - Bacterial STIs

How long before I’m protected?

Time to Maximum Intracellular Concentration of Tenofovir Diphosphate (TFV-DP)

- Rectal: 7
- Blood (PBMC): 20
- Cervicovaginal: 20

Consecutive Days of Oral Dosing

Won’t it be less effective in practice?

Effectiveness is often lower than efficacy
- Condoms (97% → 70-80%)
- Oral contraceptive pills (99% → 90%)

PROUD Study
- 545 MSM, transwomen in English GUM clinics
- Half got PrEP immediately, half waited 1 year
- Stopped early due to strong positive effect
- **Protective effectiveness 86%** (IRR; 95%CI 58, 96)

Can my patient afford PrEP?

Cost to PrEP users

- Out-of-pocket (uninsured) = around $1300/mo.
- Insurance covers (even Medicaid) – **pre-authorizations**
- Access programs and co-pay assistance
- Potentially free from Gilead if income <$58K

- See NCATEC’s “For PrEP prescribers” page
Managing Side Effects

• Side effects reported in clinical trials
  • Uncommon and usually resolved within the first month of taking PrEP
    – iPrEx: significant increase in nausea and weight loss
    – Mild decrease in CrCl that was reversible

• Signs/symptoms that require urgent evaluation (renal injury, acute HIV infection)

• Inform about potential for drug-resistant HIV infection if PrEP taken inconsistently and HIV infection occurs

iPrEX = pre-exposure prophylaxis initiative.

What prevents PrEP from being adopted?

• Awareness/Education
  – Provider
  – Patients

• Resistance to departure from condom-centric prevention counseling

• Integration into primary care and STI treatment settings

• Cost
What prevents PrEP from being adopted?

• Identification of at Risk Populations
  (History, Biologic markers, Self Identified)
• Access to screening and monitoring tests
  (extra-genital NAT, serum Cr, CBC, etc.)
• Fear of Sex....... Need to reframe to Sexual Health Message
• Should IHS make PrEP a covered service?
The Arizona Experience

Paul Bloomquist, MD, AAHIVS
The HIV Center of Excellence for American Indians/Alaska Natives
Phoenix Indian Medical Center
Estimate of PrEP Eligible Individuals

- 90,000 active user population
- 45,000 males
- 33,750 adult males
Estimate of PrEP Eligible Individuals

- 2.9% of adult men describe male sexual contact in last 12 months - 979 people (1)
- 4.5% of adult men identify as “gay” – 1516 people (2)
- CDC estimates that 24.7% of all MSM meet criteria for indication of PrEP (3)

Estimate of PrEP Eligible Individuals

• 241-375 MSM are eligible for PrEP
• This does not include IDU or high risk heterosexual people

• $750 / month/individual-wholesale
• $2.17-3.38 M expense for medication
NCATEC has lots of resources

http://www.med.unc.edu/ncaidstraining/prep

For PrEP Prescribers

These resources are intended to help you initiate and manage PrEP.

On this page, we have condensed the 2014 US Public Health Service supplement into a step-by-step guide for providers managing PrEP.

If after reviewing the information here you still have a specific question, please contact us at the UNC Infectious Diseases Clinic's working group on PrEP meeting, which sets some "ground rules" at baseline.

Step-by-Step Guidance

To download this information in checklist form, click here.

The UNC Infectious Diseases Clinic's working group on PrEP meets regularly to discuss PrEP issues, update guidelines, and present data.

Step 1: Assess Need for PrEP
Step 2: Determine Clinical Eligibility
Step 3: Consider STI Screening
Step 4: Counsel the Patient
Step 5: Initiate PrEP
Step 6: Follow-Up

Clinician Contacts for Help with PrEP

- Call PrEPline, a service of the Clinician Consultation Center: 855-448-7737 (11 AM and 6 PM EST)
- Contact a UNC Infectious Diseases clinical fellow or attend 862-6264. Between 8 AM and 5 PM on weekdays, you'll see a UNC doctor from 11 AM to 4 PM.

Consumers Interested in or Currently Taking PrEP

Pre-exposure prophylaxis (PrEP) is a new way of protecting yourself from becoming infected with HIV. We have put these resources together to help you learn more about PrEP and to find a local provider who can prescribe PrEP and help you maintain your sexual health.

To the left is a short video from My PrEP Experience about PrEP basics.

Below, you'll find a list of frequently asked questions (FAQs) about PrEP, provided by the San Francisco AIDS Foundation. If you don't find an answer to a question you have here, feel free to check out their website, PrEPfacts.org, for more information. They have separate FAQ pages for women and for men (along with transwomen).

Map of North Carolina PrEP Providers

There is a search bar in the lower right-hand section of the map. You can search by zip code or city.
Acknowledgements

HIS
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