PrEP:
Pre Exposure Prophylaxis

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ANAC
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Faculty Disclosure

Lyn Stevens

No relationships to disclose

The Association of Nurses in AIDS Care (ANAC) endorses the standards and guidelines of the Virginia Nurses Association Continuing Education Committee that the sponsors and speakers at these activities disclose significant relationships with commercial companies.

Faculty Disclosure

My presentation will include discussion of "off-label" use of the following:

Tenofovir (TDF)
Emtricitabine (FTC)
Tenofovir and Emtricitabine (TDF/FTC)
(brand name Truvada)
Maraviroc (MVC)

Objectives

- Define PrEP
- Discuss current research studies
- List populations that would benefit from PrEP
- Describe the benefits and challenges
- Identify the elements of a 'PrEP package'
- Discuss the nurses role in PrEP implementation

HIV/ AIDS Prevention Tool Kit

Prior to Exposure	Point of Transmission	After Infection
•Education & Behavioral Change	•Male and female condoms	•Antiretroviral therapy
•Male circumcision	•Anti-retroviral therapy (mother-to-child)	•Care
•Prevention Vaccines		•Education & Behavioral change
•Pre-Exposure Prophylaxis	•Post-Exposure prophylaxis (PEP)	•Therapeutic Vaccines
•HSV-2 suppression	•Topical (vaginal and rectal) microbicides	

Adapted AVAC

What is PrEP?

- Bio-medical prevention strategy that would use antiretrovirals (ARV's) to protect HIV-negative people from HIV infection
- Consists of taking a single drug or combination of drugs before exposure to lower risk of infection
- Daily dosing or intermittent dosing

Adapted AVAC

Ideal PrEP Product Criteria

- Safety Profile – use for years in healthy individuals
- Ease of Use – once daily, weekly, intermittent, missed dose
- Good drug penetration – at the viral ports of entry (rectum and genital tract)
- High effectiveness – in real world situations
- High barrier for resistance – requirement for multiple mutations to cause virologic failure
- Limited impact on therapy – low or no level of cross resistance
- Cost effective and accessible

Adapted AVAC – Derdelinckx et al PLosMedicine 2006

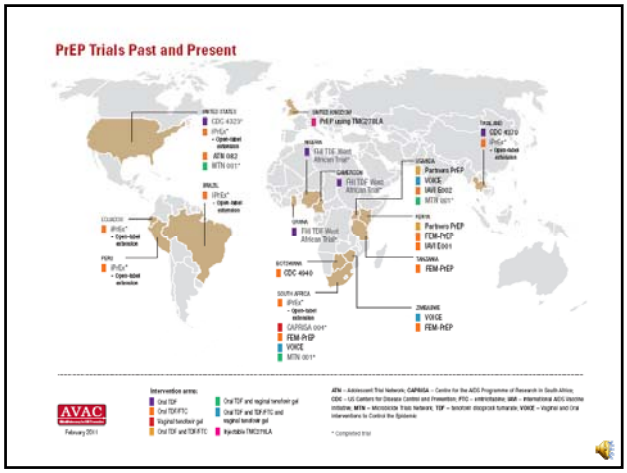
Why TDF and TDF/FTC?

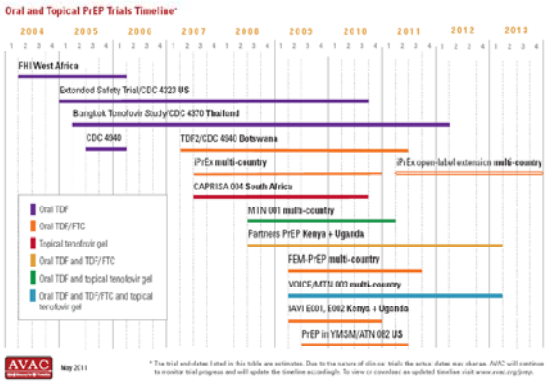
- Limited side effects
- Strong safety profile as therapy among HIV positive people
- Relatively long duration of action in the body (product 'half life')
- Less likelihood of promoting drug resistance compared to other ARVs

TDF = Tenofovir FTC = Emtricitabine Adapted AVAC

Who are the Potential Users?

- Most Vulnerable
  - Sex workers
  - MSM
  - IDU
- Serodiscordant couples
- Concurrent relationship
- For all over a certain age?





Pre - Exposure Prophylaxis (PrEP)

Topical Agents
Microbicides

Highlights of AIDS 2010
clinicaloptions.com/hiv

CAPRISA 004: 1% Tenofovir Microbicide Gel for Prevention of HIV in Women

- Randomized, placebo-controlled, double-blind, proof-of-concept study conducted at 2 sites in South Africa

HIV-uninfected women, at high risk of HIV, ≥ 2 vaginal sex acts within 30 days of screening (N = 889)*

→ 1% Tenofovir Gel† (n = 445)

→ Placebo Gel† (n = 444)

→ *Study continued until 92 HIV infections observed*

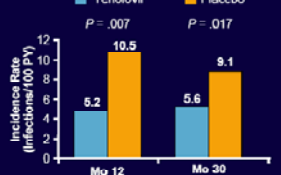
*N = 889 enrolled and eligible subjects from screened population of 2160 subjects. Common causes of exclusion included HIV infection (n = 536), failure to return for further evaluation (n = 142), no sexual activity (n = 132), coenrollment in a separate study (n = 135), pregnancy (n = 51).
†Gel applied using "BAT 24" regimen: 1 gel dose up to 12 hrs before sex, 1 gel dose as soon after sex as possible within 12 hrs after sex; maximum of 2 doses to be used within 24-hr period.

Abdool Karim Q, et al. Science DOI: 10.1126/science.1193748.
Abdool Karim Q, et al. AIDS 2010. Abstract TUSS0202.

Highlights of AIDS 2010
clinicaloptions.com/hiv

CAPRISA: Reduced HIV Incidence With Tenofovir vs Placebo Gel

- Tenofovir gel associated with decrease in HIV incidence[1]
  - 50% decrease at 12 mos
  - 39% decrease at 30 mos



Tenofovir Efficacy vs Levels of Adherence

Adherence Level, %	n	No. of Infections	Efficacy, %
> 80	336	36	54
50-80	181	20	38
< 50	367	41	28

- ↑ cervicovaginal fluid tenofovir concentrations associated with ↓ HIV seroconversion[2]
- No HIV resistance to tenofovir in patients infected while using gel
- Use of tenofovir gel also associated with 51% decrease in HSV-2 infection[3]

1. Abdool Karim Q, et al. Science DOI: 10.1126/science.1193748. 2. Kashuba A, et al. AIDS 2010. Abstract TUSS0203. 3. Abdool Karim S, et al. AIDS 2010. Abstract TUSS0204.

Pre - Exposure Prophylaxis (PrEP)

Oral Agents

iPrEX Study
(Pre-exposure Prophylaxis Initiative Trial)

- Purpose: evaluate safety and efficacy
- 2499 'high risk' HIV-negative men or transgendered women
- Double blind placebo controlled
- Emtricitabine and Tenofovir (FTC-TDF) or placebo once daily
- All subjects received HIV testing, risk reduction counseling, condoms, and management of STIs

"Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men" Grant, nejm.org, November 23, 2010

iPrEX Results

- Followed 1.2 – 2.8 years
- 100 became infected during follow-up
  - 36 in FTC-TDF group
  - 64 in placebo group
- 44% reduction in the incidence of HIV
- Nausea reported more frequently in FTC-TDF group
- Two groups had similar adverse events
- If drug levels measurable, 92% reduction in risk

FEM-PrEP Trial

- Heterosexual women
- 2,000 high risk women
- 3 African nations
- Once-daily pill (tenofovir and emtricitabine)
- Could not demonstrate efficacy

CDC – TDF-2

- Double blind, placebo-controlled study in Botswana
- 18-39 year old, heterosexual, sexually-active
- 1200 followed over time (45% women)

	TDF/FTC	Placebo	
N	601	599	
Lost to f/u	9%	10%	
New HIV infections	9	24	Protective efficacy 63% (21%, 83%) p=0.0133

- No safety differences
- No differences by sex

Thigpen, abstract WELBC01

Partners PREP

- 4758 serodiscordant couples in Kenya and Uganda
- HIV- 38% women, 62% men; 98% married
- 95% retention; 97% adherence
- unprotected sex 27% at baseline and ↓ during

	TDF	TDF/FTC	placebo	
N	1584	1579	1584	
HIV infections	18	13	47	
Protective efficacy (vs. placebo)	62% (34%, 78%) p=0.0003	73% (49%, 85%) p=<0.0001		P=0.18 TDF vs. TDF/FTC

- No difference in AE, lab abnormalities, deaths

Baeten, abstract MOAX0106

Maraviroc for PREP: Advantages

- Entry inhibitor
- MVC safety profile X 5 years
- MVC achieves high tissue levels
  - 3X higher in vaginal secretions Dumond JAIDS 2009
  - 8-26X higher in rectal tissue Brown JID 2011
- MVC prevented HIV infections in animal model Neff PLoS One 2010;5:e15257
- MVC drug resistance is uncommon
- MVC used uncommonly for HIV treatment
- MVC once-daily dosing possible
  Rosario Brit J Clin Pharm 2008

HPTN 069: NEXT-PREP

- Design: Phase II, 4-arm, multisite, study
- Study population (N=400)
  - At-risk HIV-negative gay men in 12 U.S. cities
- Study Treatment:
  - MVC monotherapy
  - MVC + FTC
  - MVC + TDF
  - TDF + FTC (control)
- Duration: 48 weeks
- Primary endpoint: Grade ≥3 toxicities; time to study treatment discontinuation

The Argument for PrEP

- If proven effective in trials and well implemented
  - Opportunity to provide ongoing periodic risk reduction counseling and HIV testing
  - Opportunity to improve links to preventive care
  - Can as readily be used by women as by men
  - Can be used without negotiation with partner
  - Not dependent on anticipating risk events
  - May work for more than one type of exposure
  - Can be stopped during low risk periods

The Challenges of PrEP

- ARV related
  - Off label use
  - Drug Resistance
  - Side effects & Long term effects
  - Effect on other viral infections (Hep B/C)
  - Interactions with other drugs (inc. recreational)
- Ethics
  - Prioritization of available ARV
  - PrEP vs other prevention options
  - Treating uninfected people

The Challenges of PrEP

- Requires regular HIV Testing
- Behavior changes/ Disinhibition/ Condom migration
- Impact on Public Health
  - Cost (resources & drugs)
  - Implementation and Monitoring

Cost of PrEP

- Mathematical Model
- Over 5 years
- 25% of high risk MSM in NYC could prevent 780 (4%) – 4510 (23%) of 19510 HIV infections
- Result: HIV Chemoprophylaxis among high risk MSM in a major US city could prevent a significant number of HIV infections and be cost effective

- *Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost effectiveness*
  Kamal Desai, et al AIDS, 2008

Cost of PrEP

- $523 - $900 per month
- Providing 100,000 most at-risk people in US could exceed $1 billion per year
- Exceeds the CDC's current HIV prevention budget
- Costs
  - ARV
  - Infrastructure
  - Training clinical providers
  - Outreach
  - Community education
  - Monitoring and surveillance
  - Safety screening
  - Long term HIV testing
  - Supportive behavioral interventions
  - Ongoing research

What Guidance is Available for Providers?

- CDC issues Fact Sheet (11/23/10)
- Fenway Institute issues physician guidelines (12/21/10)
- CDC issues interim guidance (1/28/11)

CDC Interim Guidance MSM: **Before initiating PrEP**

- *Determine eligibility*
- Document negative HIV antibody test(s) immediately before starting PrEP medication.
- Test for acute HIV infection if patient has symptoms consistent with acute HIV infection.
- Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
- Confirm that calculated creatinine clearance is ≥60 mL per minute (via Cockcroft-Gault formula).

CDC Interim Guidance MSM: *Other recommended actions*

- Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision about prescribing PrEP.
- Screen and treat as needed for STIs.

CDC Interim Guidance MSM:
Beginning PrEP medication regimen

- Prescribe 1 tablet of Truvada* (TDF [300 mg] plus FTC [200 mg]) daily.
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.
- If active hepatitis B infection is diagnosed, consider using TDF/FTC for both treatment of active hepatitis B infection and HIV prevention.
- Provide risk-reduction and PrEP medication adherence counseling and condoms.

CDC Interim Guidance MSM:
Follow-up while PrEP medication is being taken

- Every 2--3 months, perform an HIV antibody test; document negative result.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
- Every 2--3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STI as needed.
- Every 6 months, test for STI even if patient is asymptomatic, and treat as needed.
- 3 months after initiation, then yearly while on PrEP medication, check blood urea nitrogen and serum creatinine.

CDC Interim Guidance MSM:
On discontinuing PrEP

- **(at patient request, for safety concerns, or if HIV infection is acquired)**
- Perform HIV test(s) to confirm whether HIV infection has occurred.
- If HIV positive, order and document results of resistance testing and establish linkage to HIV care.
- If HIV negative, establish linkage to risk-reduction support services as indicated.
- If active hepatitis B is diagnosed at initiation of PrEP, consider appropriate medication for continued treatment of hepatitis B.

Nursing Implications:
Assess for risk

- Man > 18 yo
- Without acute HIV or established HIV
- Any male sexual partner in last year
- Not in a monogamous relationship

AND

- Inconsistent condom use in past year
- STI diagnosis
- Ongoing sex with HIV positive male

Nursing Implications:
Educate about opportunity for PrEP

- Who?
  - Colleagues
  - Consumers
- What?
  - PrEP
  - Availability in your community
  - Follow up care
  - Behavioral counseling
  - Adherence counseling

Nursing Implications:
Implementing PrEP program

- Testing
  - HIV, Hepatitis, STI
- Risk reduction
  - Condoms,
- Medication
  - Adherence, side effect management
- Linkage to prevention and treatment services as needed
- Vaccination
  - HBV

Treatment as a Form of Prevention

- HPTN 052
- First randomized clinical trial
- 2005
- 1,763 couples
- 13 sites around the world
- 28 linked infections – 27 in group not treated immediately with ART
- 96% reduction in HIV transmission to the HIV uninfected partner

http://www.niaid.nih.gov/news/newsreleases/2011/Pages/HPTN052.aspx

Summary

- PrEP presents a potentially powerful new prevention tool
- Prioritization, engagement of individuals for PrEP present practical and ethical challenges
- Uncertain whether long-term daily dosing is feasible
- Potential for accelerating health disparities
- Costs and reimbursement structures of PrEP and support systems may be untenable

Kevin Cranston, Director,Massachusetts DPH

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See you in Baltimore!