**PrEP**: Pre Exposure Prophylaxis

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**Faculty Disclosure**

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No relationships to disclose

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**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

**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

**HIV/ AIDS Prevention Tool Kit**

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

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


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

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
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 transgndered 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

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)

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<thead>
<tr>
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<th>TDF/FTC</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>N</td>
<td>601</td>
<td>599</td>
</tr>
<tr>
<td>Lost to f/u</td>
<td>9%</td>
<td>10%</td>
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<tr>
<td>New HIV infections</td>
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</table>

- 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 study

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<thead>
<tr>
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<th>TDF</th>
<th>TDF/FTC</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>N</td>
<td>1584</td>
<td>1579</td>
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<tr>
<td>HIV infections</td>
<td>18</td>
<td>13</td>
<td>47</td>
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</table>

- 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 preventative 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

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

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.

CDC Interim Guidance MSM: 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

[Link to NIAID news release](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

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Thank you to...

- **Dawn Smith, MD, MS, MPH**
  Biomedical Interventions Implementation Officer
  DHAP/SOHSTP/CDC
- **Trip Gulick, MD, MPH**
  Chief of the Division of Infectious Diseases
  Weill Medical College of Cornell University
- **Kevin Cranston, MDiv**
  Director, Bureau of Infectious Disease
  Massachusetts Department of Health
- **AVAC: Global Advocacy for HIV Prevention**
  For permission to use their slides

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  Akron, Ohio 44333
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See you in Baltimore!