Disclosures

I have no financial relationships to disclose.
Objectives

- Provide an update on the current state of HIV in Maryland and the United States
- Define Biomedical HIV Prevention
- Describe newer Biomedical approaches to HIV prevention and supporting evidence for these interventions, including:
  - Treatment as Prevention (TasP)
  - Pre-Exposure Prophylaxis (PrEP)
  - Post-Exposure Prophylaxis (PEP)
  - non-occupational Post Exposure Prophylaxis (nPEP)
HIV and Epidemiology Definitions

HIV = Human Immunodeficiency Virus; attacks the immune system, binds to T-Cells / CD4 Cells, turning those cells into HIV replicators and ultimately destroying them

AIDS = Acquired Immune Deficiency Syndrome; when the immune system has become so weakened by the destruction of CD4 Cells that a person is more vulnerable to illness
- Classified by CD4/T-Cell Count <200 OR CD4% <14% OR Diagnosed Opportunistic Infection

PLWHA = People Living with HIV / AIDS, replacing HIV+ as a less stigmatizing term

Biomedical Prevention = umbrella-term for prevention that utilizes medical, clinical or public health approaches or interventions

Prevalence = the proportion of existing cases of an illness or condition in a population

Incidence = the rate of new infections or cases of an illness or condition in a population
Classes of HIV Treatment

HIV treatment inhibits the progress of HIV’s assault on the immune system cells

Classes of HIV medications include:

• Fusion Inhibitors & Entry Inhibitors / Chemokine Receptor Antagonists (CCR5 Antagonists)
• Reverse Transcriptase Inhibitors (NRTIs, NNRTIs)
• Integration Inhibitors (INSTIs)
• Protease Inhibitors (PIs)
HIV Replication Cycle

Entry Inhibitors:
enfurvitide maraviroc

RT Inhibitors:
NRTIs, NNRTIs

Protease Inhibitors

Integrase Inhibitors
Maryland’s HIV Epidemic

Figure 3 – Trends in Adult/Adolescent Reported HIV Diagnoses by Sex at Birth, 1985-2015, Reported through 6/30/2016

Percent by Sex at Birth of Adult/Adolescent Reported HIV Cases, Age 13+ at HIV Diagnosis, with or without an AIDS Diagnosis (Adult/Adolescent Reported HIV Diagnoses) by Year of HIV Diagnosis from 1985 through 2015, as Reported through 6/30/2016
Maryland’s HIV Epidemic

Figure 4 – Trends in Adult/Adolescent Reported HIV Diagnoses by Race/Ethnicity, 1985-2015, Reported through 6/30/2016

Percent by Race/Ethnicity of Adult/Adolescent Reported HIV Cases, Age 13+ at HIV Diagnosis, with or without an AIDS Diagnosis (Adult/Adolescent Reported HIV Diagnoses) by Year of HIV Diagnosis from 1985 through 2015, as Reported through 6/30/2016
Maryland’s HIV Epidemic

Figure 5 – Trends in Adult/Adolescent Reported HIV Diagnoses by Age at Diagnosis, 1985-2015, Reported through 6/30/2016

Percent by Age at HIV Diagnosis of Adult/Adolescent Reported HIV Cases, Age 13+ at HIV Diagnosis, with or without an AIDS Diagnosis (Adult/Adolescent Reported HIV Diagnoses) by Year of HIV Diagnosis from 1985 through 2015, as Reported through 6/30/2016
Maryland’s HIV Epidemic

Figure 6 – Trends in Adult/Adolescent Reported HIV Diagnoses by Exposure Category, 1985-2015, Reported through 6/30/2016

Percent by Exposure Category of Adult/Adolescent Reported HIV Cases, Age 13+ at HIV Diagnosis, with or without an AIDS Diagnosis (Adult/Adolescent Reported HIV Diagnoses) and with Reported Exposure Category by Year of HIV Diagnosis from 1985 through 2015, as Reported through 6/30/2016

Other Exposure Category not shown
2015 HIV Diagnoses by Jurisdiction

Rate per 100,000
- 2.4 - 4.7
- 4.8 - 8.7
- 8.8 - 20.4
- 20.5 - 36.7
- 36.8 - 67.5

State Rate = 26.5 per 100,000

Using data as reported through 6/30/2016
United States HIV Inequities

*Lifetime Risk of HIV Diagnosis by Transmission Group*

- **MSM**: 1 in 6
- **Women Who Inject Drugs**: 1 in 23
- **Men Who Inject Drugs**: 1 in 36
- **Heterosexual Women**: 1 in 241
- **Heterosexual Men**: 1 in 473

Source: Centers for Disease Control and Prevention
United States HIV Inequities

Lifetime Risk of HIV Diagnosis among MSM by Race/Ethnicity

- African American MSM: 1 in 2
- Hispanic MSM: 1 in 4
- White MSM: 1 in 11

Source: Centers for Disease Control and Prevention
United States HIV Inequities

**Lifetime Risk of HIV Diagnosis by Race/Ethnicity**

- **African American Men**: 1 in 20
- **African American Women**: 1 in 48
- **Hispanic Men**: 1 in 48
- **Hispanic Women**: 1 in 227
- **White Men**: 1 in 132
- **White Women**: 1 in 880

*Source: Centers for Disease Control and Prevention*
HIV Treatment Improvements

Expected impact of HIV treatment in survival of a 20 years old person living with HIV in a high income setting (different periods)
UNAIDS 90-90-90 Targets for 2020

90% diagnosed
90% on treatment
90% virally suppressed
UNAIDS 90-90-90 Targets for 2020

90% of all people living with HIV will know their HIV status.

90% of all people diagnosed with HIV will receive sustained antiretroviral therapy.

90% of all people receiving antiretroviral therapy will have durable suppression.
The Result

73% of all people living with HIV will be virally suppressed

= a three-fold increase over 2014 estimates
HPTN 052 Trial - Treatment as Prevention

Immediate vs. Delayed ART in Sero-Discordant Couples

- HR = 96.3% reduction in transmission
- No difference whether index patient was Male or Female

HPTN 052 – Clinical Benefits of Early ART

**Number of subjects experiencing ≥1 event**

<table>
<thead>
<tr>
<th>Event</th>
<th>Delayed</th>
<th>Immediate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis</strong></td>
<td>34 (4%)</td>
<td>17 (2%)</td>
</tr>
<tr>
<td><strong>Serious bacterial infection</strong></td>
<td>13 (1%)</td>
<td>20 (2%)</td>
</tr>
<tr>
<td><strong>WHO Stage 4 event</strong></td>
<td>19 (2%)</td>
<td>9 (1%)</td>
</tr>
<tr>
<td>Oesophageal candidiasis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cervical carcinoma</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HIV-related encephalopathy</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Herpes simplex, chronic</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CNS Lymphoma</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Septicemia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HIV Wasting</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: Grinsztejn B, et al, Lancet Infectious Diseases, 4 March 2014
1,166 sero-different couples enrolled, including both heterosexual and gay male couples at 75 clinical sites in 14 European countries

Study analysis showed no cases where someone with a viral load under 200 copies/ml (defined as undetectable) transmitted HIV to their partner

• Total of approximately 58,000 condomless acts among couples
  *some HIV diagnoses occurred, but individuals were infected with a different HIV strain than that of their primary partner

Results virtually the same for gay and heterosexual couples

HIV Transmission Risk by Sexual Behavior

Rate of Couple Transmission
(per 100 Couple-Years Follow-Up)

Heterosexual (Male)
- Vaginal sex with ejaculation (192 CYFU)

Heterosexual (Female)
- Vaginal sex (272 CYFU)

MSM
- Receptive anal sex:
  - With ejaculation (93 CYFU)
  - Without ejaculation (157 CYFU)
- Insertive anal sex (262 CYFU)

Overall risk = Zero through condomless sex with a partner on ART (HIV RNA <200 copies/mL)

HIV treatment: The most effective biomedical intervention for the prevention of HIV transmission

<table>
<thead>
<tr>
<th>Immediate antiretroviral therapy for HIV-positive partner</th>
<th>HPTN 052 ¹</th>
<th>2011</th>
<th>n=1783</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical male circumcision</td>
<td>ANRS1265 ²</td>
<td>2005</td>
<td>n=3274</td>
</tr>
<tr>
<td></td>
<td>Rakai ³</td>
<td>2007</td>
<td>n=4996</td>
</tr>
<tr>
<td></td>
<td>Kisumu ⁴</td>
<td>2007</td>
<td>n=2784</td>
</tr>
<tr>
<td>Tenofovir/emtricitabine oral pre-exposure prophylaxis</td>
<td>Partners PrEP ⁵</td>
<td>2011</td>
<td>n=1579</td>
</tr>
<tr>
<td></td>
<td>Partners PrEP (tenofovir only) ⁵</td>
<td>2011</td>
<td>n=1584</td>
</tr>
<tr>
<td></td>
<td>TDF² ⁶</td>
<td>2011</td>
<td>n=1219</td>
</tr>
<tr>
<td></td>
<td>iPrEx ⁷</td>
<td>2010</td>
<td>n=2499</td>
</tr>
<tr>
<td></td>
<td>FEM-PrEP ⁸</td>
<td>2012</td>
<td>n=2120</td>
</tr>
<tr>
<td></td>
<td>Voice ⁹</td>
<td>2013</td>
<td>n=1003</td>
</tr>
<tr>
<td></td>
<td>Voice (tenofovir only) ⁹</td>
<td>2013</td>
<td>n=1007</td>
</tr>
</tbody>
</table>
Global ART coverage

37%

Adults and children

Source: UNAIDS 2014
Effect of Increased ART Coverage

HIV incidence vs. ART coverage in 51 countries, weighted by epidemic size (2012 data)

AIDS-related death rates vs. ART coverage in 51 countries, weighted by epidemic size (2012 data)

HIV Prevention Strategies

Routine HIV Testing / knowing your status
Routine STI Testing / Treatment
Treatment as Prevention (TasP)
Latex condoms with water or silicone-based lubricant
Serosorting*
Pursuing recovery
Pre-Exposure Prophylaxis
Post-Exposure Prophylaxis

*Falling out of favor
Truvada as PrEP

Tenofovir (TDF) + Emtricitabine (FTC) = Truvada

Truvada is the only medication currently FDA approved for PrEP
HIV Pre-Exposure Prophylaxis

www.whatisprep.org
HIV Pre-Exposure Prophylaxis

When people are adherent, PrEP reduces risk of acquiring HIV by up to 99%

Recommended for persons

- In ongoing relationships with PLWHA*
  *who have not achieved viral suppression
- Sharing injection drug use equipment
- With a recent STI
- Having unprotected sex with persons of unknown status
Differences in Protection

It takes about 20 days of daily adherence to PrEP to achieve optimal protection in the vagina or in the blood.

It takes about 7 days of daily adherence to PrEP to achieve optimal protection in the rectum.
Differences in Protection - Modeling Study

SOURCE:
Mackenzie L. Cottrell, et al; A Translational Pharmacology Approach to Predicting Outcomes of PrEP Against HIV in Men and Women Using Tenofovir Disoproxil Fumarate With or Without Emtricitabine. The Journal of Infectious Diseases, Vol. 214, Iss. 1, 1 July 2016, Pgs 55-64, Acc. 8/23/17 https://doi.org/10.1093/infdis/jiw077
HIV Incidence and Drug Concentration

Participants in randomized placebo-controlled iPrEx, ATN 089, or US PrEP Safety trials were enrolled in the 72-week open label extension (iPrEx OLE).

<table>
<thead>
<tr>
<th>Drug Concentration</th>
<th>HIV Incidence per 100 PY (95%CI)</th>
<th>Risk Reduction (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>4.7 (2.99-7.76)</td>
<td>44% (-31-77)</td>
</tr>
<tr>
<td>&lt;2 pills/week</td>
<td>2.25 (1.19-4.79)</td>
<td>84% (21-99)</td>
</tr>
<tr>
<td>2-3 pills/week</td>
<td>0.56 (0.00-2.50)</td>
<td>100% (86-100)</td>
</tr>
<tr>
<td>≥4 pills/week</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7 pills/week</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

No infections in those with drug levels equal to ≥4 tabs/wk.
PrEP Effectiveness = Adherence!

Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Calculations based on analyses involving a subset of total trial participants.

PrEP Steps

Client is at risk for HIV and learns about PrEP
HIV test is done & provider discusses the window period
  • Based on type of HIV test and recent behavior, client re-tests to verify HIV negative status

Provider educates that PrEP doesn’t protect against other STIs or pregnancy; efficacy is dependent on adherence; PrEP may have side effects or adverse events like gas, stomach upset, impairment of renal function or loss of bone mineral density
  • Side effects are more common but tend to go away after some weeks of PrEP use; adverse events are very rare and usually reversible when PrEP is stopped
PrEP Steps - Continued

Prior to initiating PrEP, provider tests for:
• HIV infection
• Kidney function (creatinine clearance)
• Pregnancy
• Other STIs including Hepatitis B

Provider offers:
• Hepatitis A & B vaccinations (if negative, not already protected)
• HPV vaccination if eligible
• Condoms
PrEP Steps - Continued

Considerations when prescribing PrEP:

• Truvada is generally considered safe during pregnancy/breastfeeding, but most providers discuss possible risks and benefits with pregnant patients and allow patient to choose whether to continue or stop
  o If continuing PrEP, providers encourage registration on the ARV Pregnancy Registry – www.apregistry.com

• Truvada is a treatment for Hepatitis B, so if Hep B +, rigorous adherence counseling is provided and patient is informed of risks re: poor or non-adherence
PrEP Maryland
You may be able to protect yourself with a once a day pill

If you are HIV-negative
At risk for HIV
Recently been exposed to HIV or another STD
PrEP Locator on PrEPMaryland.org

Where to get PrEP and PEP

* Also offers Post Exposure Prophylaxis (PEP)
*** Only Post Exposure Prophylaxis (PEP) is available (no PrEP)

To start, this list is ordered alphabetically. To order from a specific address enter the street address and city.

975 Indian Landing Rd, Millerville, MD

Click Apply to submit search address.

Apply

4.4 miles
Chase Brexton - Anne Arundel County Center *
200 Hospital Drive
Suite 300
Glen Burnie, MD 21061
Map It
Telephone: 410-837-2050
Hours: Monday through Friday: 8:30 am to 5:00 pm

14.0 miles
Donal Walsh, MD, Anthony & Banerjee MD
900 S. Canton Avenue
Baltimore, MD 21220
Map It
Telephone: 410-225-8404
Hours: Tuesday 12:30-4:30, Wednesday, Thursday and Friday 8:00-12:00
Insurance Accepted: Medicare, Medical Assistance, Blue Cross, Blue Choice. All MCO’s, All PPO Programs, Champus, Kaiser, and Humana
PrEPme by emocha App

Learn about PrEP. Chat with a navigator. Get an appointment.

Dig into the research & take a survey find out if PrEP is a good fit for you

Chat with a navigator who can schedule you an appointment

Or view a location-based list of providers to schedule your own appointment

For iOS and Android
Post-exposure prophylaxis (PEP)

**Post**
→ After

**Exposure**
→ When a fluid containing (or potentially containing) HIV comes into contact with mucous membranes or non-intact skin

**Prophylaxis**
→ An action taken to prevent infection or disease
HIV PEP and nPEP

The use of a combination of antiretrovirals by HIV-negative individuals for a short period of time after a suspected or known exposure to HIV

- Must be started as soon as possible but within 48-72 hours after the exposure (data supports that earlier use = higher efficacy)
- Must be taken everyday for 28 days
- Must avoid additional exposures while taking PEP

Types of exposures
- Occupational
- Non-occupational (nPEP)
Occupational vs. non-occupational PEP

Occupational - “Standard of care”
• Work-related exposures to HIV
  ▪ Needle-stick injuries
  ▪ Sharp objects

Non-occupational (nPEP) - Not “standard of care”
• Exposures outside of the workplace
  ▪ Sex with increased risk for HIV (no or broken condom)
  ▪ Needle sharing
  ▪ Sexual assault
How well does PEP work?

We don’t know exactly how protective PEP is

We know it is not 100% protective
People have become infected despite using PEP

Protection likely depends on:
Starting PEP quickly
Being adherent
The risk of transmission from the exposure
Avoiding additional exposures
The number and type of antiretrovirals used
Occupational PEP Efficacy

Study Details
712 healthcare workers exposed to HIV-infected blood

Study findings
• 256 did use PEP
  ▪ 9 became infected
• 456 did not use PEP
  ▪ 24 became infected

PEP reduced the risk of HIV transmission by 81%

nPEP Efficacy

Study details
200 gay men in Brazil given a 4-day starter-pack of PEP, prescribed 24 days when needed
Followed for over 2 years

Study findings
- 68 men did use PEP after a high risk exposure
  - 1 became infected
- 86 men did not use PEP after a high risk exposure
  - 10 became infected

Study did not calculate effectiveness of nPEP

Does nPEP work?

Registries from 4 countries (Australia, France, Switzerland, and United States) documented about 2,000 nPEP cases with no seroconversions

• About 350 of these cases were nPEP use after a known exposure to HIV

SOURCE: CDC https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm
nPEP Failure is Rare

<table>
<thead>
<tr>
<th></th>
<th># People who used nPEP</th>
<th># HIV infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsterdam</td>
<td>261</td>
<td>5</td>
</tr>
<tr>
<td>France</td>
<td>776</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>374</td>
<td>1</td>
</tr>
<tr>
<td>Australia</td>
<td>1552</td>
<td>0</td>
</tr>
<tr>
<td>Switzerland</td>
<td>710</td>
<td>0</td>
</tr>
<tr>
<td>San Francisco</td>
<td>702</td>
<td>6</td>
</tr>
<tr>
<td>Montreal</td>
<td>~900</td>
<td>6</td>
</tr>
</tbody>
</table>

It is difficult to interpret how protective PEP is...
Would people have remained uninfected without using PEP?
Among those who became infected, was PEP used correctly?

Source: CATIE, Catie.ca
nPEP Steps

1. Assessment
   • Was the exposure within the last 72 hours?
   • Is the exposed person HIV-negative?
   • Was the exposure high-risk?
   • What activity led to the exposure?
   • What was the HIV status of the source person?

2. Counseling
   • What are the risks and benefits of starting PEP?
   • Is the exposed person ready to start PEP?
   • Adherence and risk-reduction counseling

3. Prescription
   • What antiretrovirals? How many?
   • Starter-packs

4. Follow-up
   • Ongoing risk-reduction and adherence counseling
   • Monitoring/management of side-effects and toxicity
   • HIV testing
Guidelines for non-occupational PEP

When is PEP recommended?

- Example, CDC nPEP guidelines
  - Is there a *substantial risk* from the activity?
    - No → PEP not recommended
  - If *yes*, was the exposure to someone who was HIV-positive?
    - No → PEP not recommended
    - Unknown → Case-by-case basis
    - Yes → PEP recommended
# Guidelines for non-occupational PEP

<table>
<thead>
<tr>
<th></th>
<th>USA</th>
<th>Australia</th>
<th>WHO</th>
<th>UK</th>
<th>Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing of PEP</strong></td>
<td></td>
<td></td>
<td>Within 72 hours</td>
<td></td>
<td>Within 48 hours</td>
</tr>
<tr>
<td><strong>Number of antiretrovirals</strong></td>
<td></td>
<td></td>
<td>2 or 3</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td><strong>What antiretrovirals?</strong></td>
<td>Two NRTIs</td>
<td>Two NRTIs + PI/NNRTI</td>
<td>Two NRTIs + PI</td>
<td>Truvada + Kaletra</td>
<td></td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td></td>
<td>Two NRTIs + tenofovir</td>
<td></td>
<td>28 days</td>
<td></td>
</tr>
</tbody>
</table>

NRTI = nucleoside reverse transcriptase inhibitor  
NNRTI = non-nucleoside reverse transcriptase inhibitor  
PI = protease inhibitor  
Truvada = tenofovir + emtricitabine  
Kaletra = Lopinavir  
Barber and Benn 2010
Barriers to Increased nPEP & PrEP Use

• Concerns about Feasibility, Medical Knowledge
  • Research suggests that nPEP and PrEP programs are widely feasible, but challenges exist
  • Providers falsely believe that Infectious Disease specialists need to be the ones prescribing these [HIV] medications

• Cost-effectiveness
  • Research suggests that targeted nPEP and PrEP programs are cost-effective

• Risk compensation
  • Research shows that there is little evidence of risk compensation
MDH Support for PrEP

- Provider awareness and education
- Awards for PrEP Navigation and Services
- Partnering with Johns Hopkins University AIDS Education and Training Center
- Social marketing campaigns will be staged to follow establishment of PrEP capacity
MDH PrEP Program Reach

Key:
- MDH-Funded PrEP Program
- CDC-Funded PrEP Program
- Program Application in Development or Under Review by MDH
Questions?

You can ask me anything you want, ask me anything.
Thank You!

Paul W. Foster
PrEP Program Coordinator
Center for HIV/STI Integration and Capacity
Maryland Department of Health
410.767.5287
paul.foster@maryland.gov