Women and HIV prevention

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Overview

- Risk of HIV among U.S. women
- Preventing acquisition of HIV infection in women with PrEP
- Implementation of pre-exposure prophylaxis (PrEP)
- Research needed to support PrEP implementation
HIV infection among women in the United States
New HIV infections in most affected subpopulations, United States 2010

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of HIV Infections</th>
</tr>
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<tbody>
<tr>
<td>White MSM</td>
<td>11,200</td>
</tr>
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<td>Black male IDU</td>
<td>1,100</td>
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Number of HIV infections

New HIV infections in most affected subpopulations, United States 2010

HIV Surveillance Supplemental Report 2012
New HIV infections in most affected subpopulations, United States 2010

Number of HIV infections

- White MSM: 11,200
- Black MSM: 10,600
- Hispanic MSM: 6,700
- Black heterosexual women: 5,300
- Black heterosexual men: 2,700
- White heterosexual women: 1,300
- Hispanic heterosexual women: 1,200
- Black male IDU: 1,100
HIV diagnoses among adult and adolescent females by race and ethnicity, 2013

Diagnoses of HIV Infection
N=9,278

- 17% American Indian/Alaska Native
- 15% Hispanic/Latino a
- 63% Black/African American
- 2% Asian
- 2% Native Hawaiian/other Pacific Islander
- <1% Multiple races

Female Population
N = 134,687,181

- 65% White
- 13% Hispanic/Latino a
- 15% Black/African American
- 1% Asian
- 2% Native Hawaiian/other Pacific Islander
- <1% Multiple races
HIV diagnoses among adult and adolescent females by race and ethnicity and region, 2013

HIV Surveillance Report 2013

**Region of residence**

- **Northeast**
  - Black/African American: 39.8
  - Hispanic/Latino: 16.8
  - White: 1.8
  - N = 1,917

- **Midwest**
  - Black/African American: 22.6
  - Hispanic/Latino: 4.8
  - White: 1.1
  - N = 1,000

- **South**
  - Black/African American: 38.9
  - Hispanic/Latino: 7.7
  - White: 2.5
  - N = 5,109

- **West**
  - Black/African American: 21.8
  - Hispanic/Latino: 3.4
  - White: 1.6
  - N = 839
Why are women at risk of HIV infection?

- Social/sexual networks
- Unaware of their male partner’s HIV risk status
- Sexual behaviors
- Lack of control/negotiation to protect themselves
- Sexually transmitted infections
Network of black MSM in North Carolina

Hurt et al. 2012
Behavioral risk increase by men and women in HIV discordant couples

Sex with HIV+ partner

![Graph showing average monthly frequency of unprotected sex per person for reported and predicted frequencies over time.]

Sex with outside partner

![Graph showing average monthly frequency of unprotected sex per person for reported and predicted frequencies over time.]
Estimated per-act probability of acquiring HIV from an infected source, by exposure act

<table>
<thead>
<tr>
<th>Type of Exposure</th>
<th>Risk per 10,000 Exposures</th>
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<tbody>
<tr>
<td><strong>Parenteral</strong></td>
<td></td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>9,000</td>
</tr>
<tr>
<td>Needle-sharing during injection drug use</td>
<td>67</td>
</tr>
<tr>
<td>Percutaneous (needle-stick)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Sexual</strong></td>
<td></td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>50</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>10</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>6.5</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>5</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>low</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>low</td>
</tr>
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</table>

Sexual behavior with opposite-sex partners among females aged 15–44 years, United States 2006–2008

Chandra et al. 2011
Barriers to condom use
Sexually transmitted infections

*Treponema pallidum*

*Neisseria gonorrhoeae*
Sexually transmitted infections

- HIV seroconversion higher among women with STIs
  - Syphilis: 598/100,000 person-years
  - Gonorrhea: 171/100,000 person-years
  - Chlamydia: 66/100,000 person-years
  - No STI: 30/100,000 persons-years

- Women with STIs with were only a small fraction of all HIV diagnoses
  - 2,118 HIV diagnoses among women with an STI
  - 19,531 HIV diagnoses among women without an STI

Peterman et al. 2015
Preventing acquisition of HIV infection in women
Oral PrEP

- FDA approved Truvada (tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC)) for PrEP indication in July 2012

- CDC published PrEP recommendations in May 2014
Several drugs are marketed for treatment of HIV-1 infection in the United States

TDF/FTC is a good choice for PrEP

- Co-formulated as single once-daily pill marketed as Truvada
- Long half-lives
  - Plasma: 10 to 17 hours
  - Intracellular: 40 to ≥60 hours
- Forgiving of imperfect daily use
- Higher penetration in vaginal and rectal tissues
## PrEP Efficacy Trials

<table>
<thead>
<tr>
<th>Trial (Sponsor)</th>
<th>Intervention vs. placebo</th>
<th>Population</th>
<th>Outcome (TDF detected in blood)</th>
</tr>
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<tr>
<td><strong>iPrEx</strong> (NIH, Gates) <em>n=2499</em></td>
<td>Oral TDF/FTC</td>
<td>MSM, transgender women</td>
<td>0.92 (0.40 – 0.99)</td>
</tr>
<tr>
<td><strong>Partners PrEP</strong> (Gates) <em>n=4747 couples</em></td>
<td>Oral TDF/FTC Oral TDF</td>
<td>Heterosexual serodiscordant couples</td>
<td>0.90 (0.58 - 0.98) 0.86 (0.67 – 0.94)</td>
</tr>
<tr>
<td><strong>TDF2</strong> (CDC) <em>n=1200</em></td>
<td>Oral TDF/FTC</td>
<td>Sexually active adults</td>
<td>Drug detected: 50% among HIV infected 80% among not infected</td>
</tr>
<tr>
<td><strong>Bangkok Tenofovir</strong> (CDC) <em>n=2413</em></td>
<td>Oral TDF</td>
<td>Injection drug users</td>
<td>0.74 (0.17– 0.94)</td>
</tr>
<tr>
<td><strong>FEM-PrEP</strong> (USAID, Gates, FHI 360) <em>n=1951</em></td>
<td>Oral TDF/FTC</td>
<td>Heterosexual women</td>
<td>Drug detected: &lt;40% among participants</td>
</tr>
<tr>
<td><strong>VOICE</strong> (MTN-003) <em>n=5029</em></td>
<td>Oral TDF/FTC Oral TDF 1% tenofovir gel</td>
<td>Heterosexual women</td>
<td>Drug detected: &lt;30% among participants</td>
</tr>
</tbody>
</table>

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Grant et al. NEJM 2010; 363 :2587 - 2599  
Baeten et al NEJM 2012;367:399-410;CROI 2014: Abstract 43  
Thigpen, et al. NEJM 2012;367:423-34  
Marrazzo et al. CROI 2013: Abstract 26LB
Indications for prescribing PrEP

- Heterosexually active men and women who are at substantial risk of HIV acquisition
  - History of inconsistent or no condom use
  - HIV-positive sexual partner
    - Including women who are or intend to become pregnant
  - Recent bacterial STD
  - High number sexual partners
  - Commercial sex work
  - In high prevalence area or network

- Injection drug users
  - HIV-positive injecting partner
  - Sharing injection equipment
  - Recent addiction treatment (but currently injecting)
Continuum of HIV prevention with PrEP among uninfected women

Perform HIV test*
Assess HIV risk
Prescribe PrEP
Support adherence
Test for HIV and STIs

* Use of 4th generation HIV testing recommended
Recommended care for patients receiving PrEP

- **Initiation**
  - Negative HIV test (preferably 4th generation test)
  - No symptoms or signs of acute HIV infection
  - Normal renal function
  - No contraindicated medications
  - Hepatitis B virus infection and vaccination status

- **Follow-up visits**
  - Every 3 months
    - HIV test
    - Pregnancy test
    - STD testing (syphilis, chlamydia, gonorrhea)
  - At 3 months, then every 6 months
    - Renal function
HIV Resistance and PrEP

- Viral resistance occurs when mutations arise in genetic material of HIV that help it to survive in presence of an antiretroviral drug.

- Resistance means that a drug no longer works optimally, or at all, to suppress HIV.

- Resistance to one antiretroviral drug can result in cross-resistance to others that have never been taken.

- Persons who acquire HIV while taking TDF/FTC, or who have HIV before taking TDF/FTC for PrEP, are at risk for viral resistance that may limit treatment options.
HIV prevention for serodiscordant couples who are trying to conceive

- **HIV-positive woman/HIV-negative man**
  - Anti retroviral treatment (ART) for infected partner
  - Limited conception attempts
  - Intrauterine insemination (IUI)
  - Intravaginal insemination (IVI)
  - STI testing and treatment
  - Male circumcision
  - PrEP

- **HIV-negative woman/HIV-positive man**
  - ART for infected partner
  - Limited conception attempts
  - Sperm washing with IUI, IVI, or intracytoplasmic sperm injection (ICSI)
  - STI testing and treatment
  - PrEP
PrEPception

- PrEP protects uninfected partners during conception and pregnancy who might be exposed to HIV during conception attempts
  - Uninfected female who is trying to conceive with an HIV-infected male partner
  - Uninfected pregnant female to help her remain uninfected if she has an HIV-infected male partner
  - Uninfected male partners whose HIV-infected female partner is trying to conceive

- Truvada is safe and effective in pregnancy
  - Women became pregnant in clinical trials
  - Used as part of some pregnancy ARV regimens
  - ARV use in Pregnancy Registry
Non-pregnant women

- **Who should be evaluated for PrEP?**
  - Women who are concerned about HIV acquisition
  - Women with an HIV-positive partner
  - Women in a relationship that is not mutually monogamous
  - Women in a community or network with high HIV prevalence
    - Black women
  - Women with STIs, especially syphilis or gonorrhea
    - Biomarker for risk
    - Co-factor for HIV transmission
  - Women with history of high risk behavior (e.g., anal sex)
Topical PrEP

- **Vaginal microbicides**
  - CAPRISA 004
    - HIV acquisition: 39% reduction
    - HSV-2 acquisition: 51% reduction
  - VOICE
    - HIV acquisition: no reduction, poor adherence
  - FACTS 001
    - HIV acquisition: no reduction, poor adherence

- **Rectal microbicides**
  - MTN 017
    - Ongoing
Future PrEP delivery methods

- Non-oral and non-topical
  - Vaginal ring
  - Long lasting injectables
  - Subdermal implants

- Possible to combine with contraception
Implementation of PrEP
PrEP use in the United States is low but increasing

- **Commercial pharmacy database with 55% of U.S. prescriptions**
  - Prescriptions rose 8.5-fold
    - 150 in 2011
    - 1274 in 2012

- **PrEP prescribed for**
  - <25 years of age: 14%
  - Women: 48%

PrEP uptake among persons with commercial health insurance, 2010-2013

*Weighted for national representativeness

2013
Male: 87.9%
Mean age: 43.6 years
Urban: 97.7%

Wu et al. 2015 unpublished data
Implementation of PrEP for at-risk women

- **Clinical venues of care for women**
  - Ob/gyn clinics
  - Family planning clinics
  - Primary care clinics
  - Federally Qualified Health Centers (FQHCs)
  - STI clinics

- **Prepare healthcare providers**
  - Training
  - Toolkits
  - Academic detailing

- **Create demand among women**
  - Educate women about PrEP for HIV prevention
  - Social marketing
A roadmap for PrEP implementation

**Needs**
- Documented efficacy and safety
- Consensus on PH use
- Provider support
- User acceptability
- Advocates for access
- Policy/regulatory support
- Evaluation framework

**Activities**
- Trials
- Consultations
- Targeted evaluations

**Outputs**
- Guidelines
- Policy development
- Training materials
- Educational materials
- Tool creation
- Media campaigns

**Immediate Outcomes**
- Providers trained
- Risk ppn recruited
- Funding available
- Counseling available
- Practice-based evidence

**Intermediate Outcomes**
- PrEP provided to risk ppn
- Adherence high
- Little risk compensation

**Objective**
- Reduced HIV incidence

**CDC sphere of control**
- Identified needed improvements

**CDC sphere of influence**
- Smith et al. 2013
Barriers to implementation

- **Women**
  - Unaware of PrEP
  - Mistrust of medical institution
  - Concern about medication side effects
  - Potential stigma about taking HIV medications
  - Lack of access/health insurance
  - High co-payments

- **Health care provider**
  - Unaware of PrEP
  - Inexperience with HIV medication
  - Concern about risk compensation
  - Challenging to conduct sexual risk history

Auerbach et al. 2015
Research needed to support PrEP implementation
CDC health services research priorities

- Operational research to understand PrEP service models
  - Develop, pilot, and evaluate PrEP models for various healthcare settings

- Implementation research to scale up effective PrEP service models

- Disseminate best practices for PrEP delivery

- Monitor access, utilization, and quality of PrEP healthcare services
Ongoing studies – oral PrEP

- HPTN 067: Phase II, Randomized, Open-Label, Pharmacokinetic and Behavioral Study of the Use of Intermittent Oral Emtricitabine/Tenofovir Disoproxil Fumarate PrEP

- HPTN 069: Phase II Randomized, Double-Blind, Study of the Safety and Tolerability of Maraviroc (MVC), Maraviroc + Emtricitabine (MVC+FTC), Maraviroc + Tenofovir disoproxil fumarate (MVC+TDF), or Tenofovir disoproxil fumarate + Emtricitabine (TDF+FTC) for PrEP to Prevent HIV Transmission in At-Risk MSM and in At-Risk Women
Ongoing studies – long acting injectable PrEP

- HPTN 076: Phase II Safety and Acceptability of an Investigational Injectable Product, TMC278 LA, for PrEP

- HPTN 077: Phase IIa Safety, Tolerability, and Acceptability Study of an Investigational Injectable HIV Integrase Inhibitor, GSK1265744, for PrEP in HIV Uninfected Men and Women
Ongoing studies – vaginal ring PrEP

- MTN 020: Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase 3 Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women (ASPIRE Trial)

- IPM 027: Safety and Efficacy Trial of a Dapivirine Vaginal Matrix Ring in Healthy HIV-Negative Women (The RING Study)
Ongoing studies – rectal microbicides

- MTN 017: Phase II Safety and Acceptability Study of Tenofovir Gel Reformulated for Rectal Use
Ongoing studies - implementation

- **Sustainable Healthcenter Implementation PrEP Pilot (SHIPP) Study**
  - FQHCs in 4 cities: Chicago, Newark, Philadelphia, Washington
  - Recruiting at-risk men and women
    - Evaluation of healthcare service provision of persons prescribed PrEP
    - Sub-study to monitor adherence to PrEP medication

- **Context Matter companion study**
  - Surveys of patients, healthcare providers, and community stakeholders in SHIPP cities
Thank you!

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For more information please contact Centers for Disease Control and Prevention

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