HIV Preexposure Prophylaxis and Treatment as Prevention

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Division of Disease Control
Annual Infectious Disease Conference
November 15, 2017 at the Augusta Civic Center

Disclosures

Gilead Sciences - unrestricted research project support
Learning Objectives

1.) Describe the epidemiology of HIV in the US, including notable disparities.
2.) Define the evidence base for HIV PrEP.
3.) Identify patients for PrEP during routine primary care and apply CDC guidelines for prescribing PrEP using case-based scenarios.

Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2015—United States and 6 Dependent Areas

N = 39,920

- Male-to-male sexual contact: 67%
- Heterosexual contact—Female: 16%
- Heterosexual contact—Male: 8%
- Injection drug use (IDU)—Female: 2%
- Injection drug use—Male: 4%
- Male-to-male sexual contact and IDU: 3%

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. Data for the year 2015 are preliminary and based on 6 months reporting delay. Data have been statistically adjusted to account for missing transmission category. “Other” transmission category not displayed as it comprises less than 1% of cases.

* Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
Disparities in new HIV diagnoses exist in Massachusetts (and the U.S.)

Annual rate of HIV diagnosis among...

**MSM = 28x** that of non-MSM men

**Black women = 33x** that of white women

**Hispanic/Latina women = 12x** that of white women

**Non-US born individuals = 2x** that of those born in US or Puerto Rico

New HIV Diagnoses Among the Most-Affected U.S. Subpopulations, 2014

MMWR, 2017
## The New Paradigm: Treatment as Prevention

### HPTN 052: Treatment as Prevention
- **Public Health Benefit**: Begin treatment at any CD4+ T-cell count

### START and Temprano Studies: Early Treatment
- **Individual Health Benefit**

### Study Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Efficacy overall</th>
<th>Drug detected overall</th>
<th>Estimated Risk reduction with drug detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM and Transgender Women (iPrEx)</td>
<td>42%</td>
<td>~50%</td>
<td>92%</td>
</tr>
<tr>
<td>Heterosexual Serodiscordant Couples (Partners PrEP)</td>
<td>67-75%</td>
<td>82%</td>
<td>90% (FTC/TDF) 86% (TDF)</td>
</tr>
<tr>
<td>Heterosexual Men and Women (TDF2)</td>
<td>62%</td>
<td>80%</td>
<td>78%</td>
</tr>
<tr>
<td>Persons who Inject Drugs (Bangkok Tenofovir Study)</td>
<td>49%</td>
<td>N/A</td>
<td>74%</td>
</tr>
<tr>
<td>Young Women (Fem-PrEP)</td>
<td>No efficacy</td>
<td>26%</td>
<td>“adherence too low to assess efficacy”</td>
</tr>
<tr>
<td>Young Women (VOICE)</td>
<td>No efficacy</td>
<td>29%</td>
<td>“ ”</td>
</tr>
</tbody>
</table>
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Daily PrEP is highly effective in a "real-world" study of MSM in the UK (PROUD) (McCormack, Lancet 2015).

- N = 544
- Efficacy: 86%
- NNT for 1 year: 13

Bacterial STIs in PROUD Study

<table>
<thead>
<tr>
<th></th>
<th>Immediate</th>
<th>Deferred</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>57%</td>
<td>50%</td>
<td>0.74</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>39%</td>
<td>37%</td>
<td>0.46</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>30%</td>
<td>22%</td>
<td>0.27</td>
</tr>
<tr>
<td>Syphilis</td>
<td>11%</td>
<td>9%</td>
<td>0.39</td>
</tr>
<tr>
<td>Rectal gonorrhea or Chlamydia</td>
<td>36%</td>
<td>32%</td>
<td>0.99</td>
</tr>
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The state of STDs in the United States in 2016.

- 1.59 million cases of Chlamydia, 4.7% increase since 2015
- 468,514 cases of Gonorrhea, 18.5% increase since 2015
- 27,814 cases of Syphilis, 17.6% increase since 2015
**Preexposure Prophylaxis for HIV Prevention in a Large Integrated Health Care System**  
(J Marcus, JAIDS, 2017, CID 2017)

- 972 Kaiser pts, 850 py f/u
- Mean adherence 92%, no seroconversions on PrEP, 2 among those who discontinued
- Less adherence among pts who were Black, smokers, and/or had higher co-pays
- 22.5% discontinued
- Women, those with substance use disorders more likely to stop
- Only 5 discontinued b/c renal function
- STD rates continued to rise
- Update: ~5000 and no infections among adherent pts
Mild changes in renal function may occur with TDF/FTC as PrEP

PrEP associated with small decreases in bone mineral density that reverse after stopping PrEP

### Case Reports: HIV Infection with High Adherence to PrEP

<table>
<thead>
<tr>
<th>Pt</th>
<th>PrEP Adherence</th>
<th>Seroconversion</th>
<th>Likely Cause of PrEP Failure</th>
</tr>
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<tbody>
<tr>
<td>43-yr-old MSM[1]</td>
<td>24 mos, supported by pharmacy records, blood, and clinical history</td>
<td>Acquired MDR HIV infection</td>
<td>Exposure to PrEP-resistant, multiclass-resistant HIV strain</td>
</tr>
<tr>
<td>MSM in his 20s[2]</td>
<td>Excellent by self report, supported by blood and hair concentration analyses</td>
<td>Acquired MDR HIV condomless anal intercourse with 2 different partners within 11 weeks before diagnosis</td>
<td>Exposure to PrEP-resistant, multiclass-resistant HIV strain</td>
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<td>50-yr-old MSM[3]</td>
<td>Excellent by self report, supported by blood analyses</td>
<td>Acquired wild-type HIV infection after 2-5 median condomless anal sex partners per day in each month following PrEP initiation</td>
<td>Chronic rectal inflammation +/- trauma</td>
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### USPHS/CDC Guidelines on Prescribing PrEP

- **Determine Eligibility** (negative HIV test, at high-risk for HIV acquisition, renal function, screen/treat for STIs, screen/vaccinate for Hep B, HCV Ab; pregnancy test)
- **Prescribe** tenofovir-emtricitabine 1 tablet by mouth daily
- **Provide** condoms and risk-reduction counseling
- **Monitor closely** (q 2-3 mo: HIV test, risk assessment/counseling; q 6 mo: renal function, STI screen (q 3 months for some populations?))

Persons likely to benefit from using PrEP

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<td>Any use of injection drugs AND...</td>
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<tr>
<td>Ongoing relationship with HIV+ partner</td>
<td>Ongoing relationship with HIV+ partner</td>
<td>Any sharing of injection equipment (past 6 months)</td>
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<td>Condomless anal sex (past 6 months)</td>
<td>Man who is behaviorally bisexual</td>
<td>Been in methadone, suboxone, buprenorphine treatment program (past 6 months)</td>
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34F with HIV-infected male partner, stable relationship. He declines ART, VL 9,000. Vaginal sex 2-3x/week, do not use/wish to use condoms.

- 1. PrEP
- 2. No PrEP
- 3. Other
34F with HIV-infected male partner, stable relationship. He uses ART, VL < 20. Vaginal sex 2-3x/week, do not use/wish to use condoms.

- 1. PrEP
- 2. No PrEP
- 3. Other

PrEP if serodiscordant partner has a suppressed viral load?

PARTNER study
- 888 HIV discordant couples
- HIV+ partner VL < 200
- 39% MSM couples
- ~36,000 condomless sex acts
- No transmissions when HIV+ pts' PVL BLD

Opposites Attract
- 358 HIV discordant MSM couples
- >12,000 condomless anal acts
- No HIV transmissions when HIV+ pt. PVL BLD
- 3 pts infected by outside partner

Rodger JAMA 2016; Bavington IAS 2017
Same couple, would like to have children.

• 1. Sperm washing
• 2. ART for him
• 3. Periconception PrEP for her
• 4. ART plus periconception PrEP
• 5. Timed condomless sex to peak fertility
• 6. Screen and treat for STIs
• 7. Other

1.2 million Americans are likely to benefit from using HIV pre-exposure prophylaxis (PrEP)

1 in 4 sexually active MSM...........492,000
1 in 5 persons who inject drugs...115,000
1 in 200 heterosexual adults........624,000

~100,000 have been prescribed PrEP so far

Smith MMWR 2015; McCallister IAS 2016
PrEP Utilization in the US

PrEP Use (2016)

- Black: 4.0%
- White: 13.0%
- Hispanic: 10.0%
- Asian: 73.0%

New HIV Infections (2015)

- Black: 2.0%
- White: 26.0%
- Hispanic: 24.0%
- Asian: 44.0%

PrEP Use Among Blacks and Hispanics Was Low Relative to Rate of New HIV Infections


16y adolescent male has sex with men. Receptive anal sex without condoms with multiple partners. Heard about PrEP and would like to try it.

• 1. Prescribe
• 2. Decline
• 3. Other
ATN 110/113

- Young MSM 15 to 22 y.o.
- PrEP plus individual versus group intervention to ↑ risk reduction in YMSM
- HIV incidence: 3.3% in 18-22; 6.4% in 15-17 y.o. (better than < 30 y.o. in HPTN 061)
- Black MSM least adherent
- Youth were more adherent during first 3 months of the study, with monthly visits → whether more frequent contact would enhance adherence?

Answers to FAQ

- Financial issues
  - Gilead patient assistance program: [https://start.truvada.com/hcp/prep-cost](https://start.truvada.com/hcp/prep-cost)

- Time to protection: 7-21 days?
- Duration after last exposure: 28 days?
28y MSM presents for PEP. Syphilis 6 months ago, condomless anal sex with 4 partners since then.

- 1. No PrEP
- 2. PEP, wait for negative HIV Ab/Ag, then PrEP
- 3. PEP to PrEP, no break
- 4. Other

How to improve chemoprophylaxis effectiveness?

New oral PrEP drugs and dosing strategies

Vaginal & Rectal Microbicides (Tenofovir, other ARVs)

Intravaginal rings (Dapivirine, Tenofovir) +/- Contraception

Novel adherence strategies

Injectables: ARVs and mAbs (Cabotegravir, VRC01)

Alternative delivery systems and formulations
23y MSM has sex every few months with anonymous partners in NYC. Would like on demand PrEP.

- 1. Prescribe on demand PrEP
- 2. Recommend daily PrEP, but prescribe on demand if he insists
- 3. Recommend daily PrEP, do not prescribe on demand
- 4. Recommend daily PrEP or PEP as needed
- 5. Other

Ipergay Trial Open-Label Extension Study

- Median follow-up: 18.4 months
- Single incident HIV infection
  - Subject had not used PrEP in 40 months
  - Neither emtricitabine nor tenofovir were detectable at time of HIV diagnosis
- Estimated efficacy
  - 97% relative reduction in HIV transmission versus placebo

MyChoices (Biello/Mayer), also Lynx (Liu/Scott)

- Create an HIV testing plan with built-in reminders
  - Find testing locations
  - Order home test kits & condoms
- Assess if PrEP might be appropriate
  - Info about local PrEP providers
  - FAQs, PEP, STIs, Insurance

Other approach PrEP@home
Using EHR data to identify PrEP candidates: patients with incident HIV (cases) and patients without HIV (controls)

Demographics
- Age
- Race
- Sex
- Home language
- No. of Encounters Per Year
- No. of Gonorrhea tests per year
- Rectal Gonorrhea tests per year
- Positive rectal Gonorrhea tests per year
- Positive pharyngeal Gonorrhea tests per year
- No. of Chlamydia tests per year
- Positive Chlamydia tests per year
- Rectal Chlamydia tests per year
- Positive rectal Chlamydia tests per year
- Pharyngeal Chlamydia tests per year
- Positive pharyngeal Chlamydia tests per year
- No. of syphilis tests per year
- Syphilis diagnosis per ESP
- LGV testing
- Anal cytology testing

Laboratory Results
- No. of HCV antibody tests
- No. of HCV RNA tests
- HCV antibody or RNA tests positive
- Acute Hepatitis C per ESP
- No. of HBV DNA tests per year
- HBsAg or HBV DNA positive
- Acute Hepatitis B per ESP
- No. of HIV ELISA tests per year
- No. of HIV Western Blots per year
- No. of HIV RNA tests per year
- HIV status per ESP
- HIV new diagnosis
- History of HIV meds
- HIV negative with HIV RNA tests
- Abnormal anal cytology
- Dx for Syphilis
- Dx for Anogenital warts
- Dx for Gonococcal pharyngitis
- Dx for Chlamydia infection of anus
- Dx for Chlamydia pharyngitis
- Dx for LGV
- Dx for Chancroid
- Dx for Granuloma inguinale
- Dx for non-gonococcal urethritis

Diagnoses
- Dx for HSV with complications
- Dx for Genital Herpes
- Dx for Anogenital warts
- Dx for Anorectal ulcers
- Dx for PID
- Dx for Contact / exposure to STD
- Dx for High risk sexual behavior
- Dx for HIV counseling
- Dx for Anorexia nervosa
- Dx for Bulimia nervosa
- Dx for Eating disorders
- Dx for Counseling for childhood sex abuse
- Dx for Alcohol dependence
- Dx for Opioid dependence
- Dx for Sedative, hypnotic, or anxiolytic dependence
- Dx for Cocaine dependence
- Dx for Amphetamine dependence
- Rx for bicillin
- Rx for azithromycin 1g
- Rx for ceftriaxone 125mg or 250mg
- Rx for methadone
- Rx for Suboxone
- Rx for sildenafil or tadalafil or vardenafil

Prescriptions

Using EHR data to identify PrEP candidates: patients with incident HIV (cases) and patients without HIV (controls)
8,414 (1.1%) of patients in the HMO population had HIV prediction scores above an inflection point in the distribution of scores (D Krakower, ID Week, 2016)

Atrius Health
~800,000 patients
885 HIV-infected patients
249 currently receiving PrEP

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“Getting (close) to zero” new infections is a realistic goal

- PrEP works if taken, and is generally safe
- Uptake is increasing in some centers, but disparities exist
- STIs are at an all time high in the US; screen and counsel
- New PrEP modalities under development
- Combination of prevention strategies most effective way to control epidemic
Thank You

Ken Mayer
Katie Biello
Connie Celum
Demetre Daskalakis
Sheldon Fields
Marcy Gelman
Chris Grasso
Sybil Hosek
Ken Levine
Sheena McCormack
Kevin Maloney
Matthew Mimiaga

Amy Nunn
Steve Safren
Aaron Siegler
Patrick Sullivan
Darrell Wheeler
Mike Klopmas
Ben Kruskal
Susan Gruber
JT Menchaca
Ira Wilson

NIAID, NIMH, Mass DPH, Gilead