PrEP in young African women: Rationale & lessons from HPTN 082 (and other studies)

Connie Celum MD MPH
Departments of Global Health and Medicine
University of Washington
Disproportionate Success in Epidemic Control by Age Group

New HIV Infections by Population and Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Pediatric (0-14 yrs)</th>
<th>15 - 24 yrs</th>
<th>25 yrs +</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020**</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Projected

Sources: * UNAIDS AIDS info Online Database, 2016; ** 15-24 yrs age group projected based on Africa Development Forum / World Bank 2015, “Africa’s Demographic Transition: Dividend or Disaster?”
Young African Women at Risk

1 out of 3 new HIV infections are in youth in SSA (15-24yr)

2 out of 3 new HIV infections are in sub-Saharan Africa

HIV Incidence among Young Women
More than 1/3 New HIV Infections Globally Occur among Young Women in Africa

Estimated number of new HIV infections per week among young women aged 15-24 years in East and Southern Africa, 2012
Data source: UNAIDS 2013

Over 7,000 new HIV infections every week among young women globally
Youth Bulge in Zambia

At the beginning of the Epidemic

- Young Men Population: 781,000
- Young Men PLHIV: 38,000
- Young Women Population: 772,000
- Young Women PLHIV: 66,000

Today

- Young Men Population: 1.6 million
- Young Men PLHIV: 48,000
- Young Women Population: 1.6 million
- Young Women PLHIV: 77,000

What factors increase young women’s vulnerability to HIV?

- Poverty & transactional sex:
  - Young girls have sex with older men to access resources.

- Limited livelihood opportunities:
  - Women’s economic dependence on partner, labor migration, separation of families

- Gender inequality & violence:
  - Women have difficulty negotiating sex or condom use when economically dependent on partner &/or fear violence

- Stigma & discrimination:
  - Prevents those most vulnerable to HIV from accessing HIV testing & services

- Risk-taking & self-efficacy in adolescence

- Limited availability of youth-friendly services
World Bank Estimate of Income Inequalities

Gini index in 148 countries & territories
Trials of PrEP

Trials where only a minority were adherent did not demonstrate HIV protection.

FEM-PrEP and VOICE
≤30% adherence / No efficacy
Does PrEP work in young women?

• Yes, if taken; PrEP efficacy ≈70% in all subgroups of women in Partners PrEP
  – Age <30, high risk, high plasma viral load in partner
  – Adherence ≈ 80% based on drug levels

(Murnane, et al, AIDS 2013)

• No efficacy with low uptake in VOICE & FEM-PrEP
  – <30% with drug detected
  – Disconnect between low perceived risk and high STI incidence in FEM-PrEP (Van Damme NEJM 2012)
  – Low uptake due to low risk perception, low motivation for prevention, need for social support and/or challenges with daily pill-taking (remembering, product storage)?
Studies to understand PrEP uptake & adherence among young African women

- HPTN 067 ADAPT (Bekker)
- Plus Pills in Cape Town (Bekker)
- HPTN 082/HERS: Uptake & adherence to PrEP (Celum & Delany-Moretiwe)
- 3P: Uptake of PrEP & role of conditional incentives on motivating adherence in Cape Town (Bekker & Celum)
- POWER: Prevention Options Research for Women (Baeten & Celum)
Primary Objectives of HPTN 082

• To assess the proportion and characteristics of young HIV-uninfected women who accept versus decline PrEP.

• To assess the difference in PrEP adherence in young women randomized to enhanced adherence support (using drug level feedback) versus standard of care adherence support.
HPTN 082: Metrics of Success

• Reaching those who need PrEP
  • Measures of vulnerability at enrollment

• PrEP uptake
  • Among women with greater vulnerability & who think PrEP will benefit them

• PrEP adherence
  • Goal: >50% detectable tenofovir at weeks 4 & 8
  • Goal: Adherence levels during periods of higher risk
  • Testing effect of drug level feedback on subsequent adherence
HPTN 082: Design & PrEP uptake

HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population

- Uninfected women
  - Ages 16-25 yrs

- Johannesburg & Cape Town, South Africa
- Harare, Zimbabwe

Target Enrollment

- 400 women who accept PrEP at enrollment
- ≤ 200 women who decline PrEP at enrollment

Primary objectives:
- Assess the proportion and characteristics of women who accept versus decline PrEP
- Assess PrEP adherence using drug levels in young women

Figure 1: PrEP uptake overall and by site

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Harare</th>
<th>Cape Town</th>
<th>Johannesburg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrEP accepted</td>
<td>95%</td>
<td>97%</td>
<td>99%</td>
<td>88%</td>
</tr>
</tbody>
</table>

Population

Uninfected women
- Ages 16-25 yrs
- Johannesburg & Cape Town, South Africa
- Harare, Zimbabwe
Get PrEPed!

Educational video

- Explains PrEP using youth-friendly graphics
- Filmed and edited by Umuzi (South Africa)
- Script, graphics and film developed in collaboration with and evaluated by youth in South Africa and Zimbabwe

https://www.youtube.com/watch?v=tt-O4ZORrYQ

Young women screening for HPTN 082 shared the video with peers on social media

Young women have less questions about how PrEP works after viewing the video in the waiting room
### Demographics of PrEP ‘acceptors’

<table>
<thead>
<tr>
<th></th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PrEP Accepted at Baseline</strong></td>
<td>412</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>21 (19,22)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>Completed secondary school or higher*</td>
<td>404 (98%)</td>
</tr>
<tr>
<td>Ever dropped out of school*</td>
<td>122 (30%)</td>
</tr>
<tr>
<td><strong>Age difference ≥5 years with primary partner</strong></td>
<td>139 (44%)</td>
</tr>
<tr>
<td><strong>HIV status of main partner</strong></td>
<td></td>
</tr>
<tr>
<td>HIV negative</td>
<td>204 (59%)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>He doesn’t know his status</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>She doesn’t know his status</td>
<td>58 (17%)</td>
</tr>
<tr>
<td><strong>Any transactional sex in past month</strong></td>
<td>95 (23%)</td>
</tr>
<tr>
<td><strong>Vaginal sex acts past month</strong> (median, IQR)</td>
<td>4 (2,8)</td>
</tr>
<tr>
<td><strong>Condom use with vaginal sex, past month</strong></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>65 (20%)</td>
</tr>
<tr>
<td>Rarely</td>
<td>48 (15%)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>104 (33%)</td>
</tr>
<tr>
<td>Often</td>
<td>37 (12%)</td>
</tr>
<tr>
<td>Always</td>
<td>65 (20%)</td>
</tr>
</tbody>
</table>
## STIs, risk, risk perception, IPV & depression

<table>
<thead>
<tr>
<th>Enrollment characteristics</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curable STI</td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>161 (39%)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>33 (8%)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>120 (29%)</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>9 (2%)</td>
</tr>
<tr>
<td></td>
<td>27 (7%)</td>
</tr>
<tr>
<td>VOICE risk score* (median, IQR)</td>
<td>7 (6,8)</td>
</tr>
<tr>
<td>Chances of getting HIV in next year</td>
<td></td>
</tr>
<tr>
<td>No risk at all</td>
<td>193 (47%)</td>
</tr>
<tr>
<td>Small chance</td>
<td>127 (31%)</td>
</tr>
<tr>
<td>Moderate chance</td>
<td>33 (8%)</td>
</tr>
<tr>
<td>Great chance</td>
<td>33 (8%)</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>CES-D score &gt; =11</td>
<td>171 (42%)</td>
</tr>
<tr>
<td>&gt; 1 episode of intimate partner violence, past year</td>
<td>200 (49%)</td>
</tr>
</tbody>
</table>

* Maximum VOICE risk score of 10
(score > 5 associated with 6-8% in prior HIV prevention trials among young African women)
Insights from qualitative research: Narrative sexual histories

Khosa & Scorgie, Unpublished data
HPTN 082: Preliminary Conclusions

• High uptake (95%) of PrEP
  • Despite reported low perceived risk of HIV

• Risk behavior is high; we are reaching women at risk
  • Median score on the VOICE risk score was 7

• Half had symptoms of depression and IPV in past year

• High prevalence (39%) of curable STIs (& incidence)
  • Need etiologic diagnoses (rather than) syndromic management & effective interventions for young African women.

• High demand for PrEP among women at risk for HIV
  • Adherence data will indicate proportion with effective use
  • Randomization will assess effect of drug level feedback at wks 8 and 13
HPTN 082: Metrics of Success

✓ Reaching those who need PrEP
  • Measures of vulnerability at enrollment

✓ PrEP uptake
  • Among women with greater vulnerability & who think PrEP will benefit them

☐ PrEP adherence
  • Goal: >50% detectable tenofovir at weeks 4 & 8
  • Goal: Adherence levels during periods of higher risk
  • Testing effect of drug level feedback on subsequent adherence
What about adherence in HPTN 082?

Adherence Support

1. Counselling
2. Weekly SMS
3. Adherence clubs
4. Drug Level Feedback at 8 & 13 wks
Counseling Categories

4 or more doses per week (>500 fmol/punch at wk 4 and >700 fmol/punch at wk 8)

Key message: You are doing great! Keep up the good work and remember that taking one PrEP pill every day is needed for strong protection against HIV.

~1-3 doses per week (between detectable – 499 fmol/punch at wk 4 and detectable to 699 fmol/punch at wk 8)

Key message: It looks like you are trying to take the PrEP medication, but are having some difficulties. Remember that taking one pill every day is needed for strong protection against HIV. How can we help you do even better?

No TFV-DP detected (confirm BLQ level)

Key message: It looks like you haven’t been able to take the PrEP medication. Is PrEP something that you are still interested in? If yes, how can we help you?
Discrete, non-medial product storage
Pill cases & carrying bags
HPTN 082 closing thoughts

- Young African women are a priority population for PrEP
- Young women face challenges but also have “agency”
- High uptake (95%) of PrEP in HPTN 082/HERS
  - Key role of peers & social influencers
  - Risk behavior, depression, and IPV are high in HPTN 082
  - Innovative qualitative methods can help us understand their lived experiences & perspectives about ‘risk’
  - Women at risk are accepting PrEP
- High prevalence & incidence of curable STIs
- Oral PrEP isn’t for everyone
  - Important to learn about messaging & delivery of a proven method
  - Increasing options will increase uptake, adherence & persistence
Next Steps: Evaluation of PrEP decision support tool
Celum & Delany-Morelwe, R01MH114544

WHAT YOU NEED TO KNOW ABOUT PrEP

THE GOOD STUFF:
- Very safe.
- Keeps you healthy by preventing HIV.
- Private method that you control.
- Increases confidence and decreases fear of getting HIV.
- Safe with all types of family planning.
- Safe to use while pregnant and breastfeeding.

THE ANNOYING STUFF:
- A few people have mild side effects like headache or nausea that go away quickly (in a few weeks).
- PrEP does not protect against other sexually transmitted infections. Only condoms prevent against HIV and other infections.
- PrEP does not prevent pregnancy. PrEP is safe to take with all forms of family planning, though!

STUFF TO NOT WORRY ABOUT:
- You don’t have to take PrEP for your whole life! You can use PrEP for as long as you need it. We suggest talking to your provider before stopping PrEP.

Shared decision-making approach to counseling
Women ages 18-25 who want to continue PrEP after 1 month run-in (N=350)

2 way SMS + counseling at PrEP refill visits*

At 4 months, assess adherence: desire to continue PrEP, challenges and drug levels (TDF-DP <700 fmol/punch)

Responder → Continue WhatsApp groups & counseling at quarterly visits
Non-responder → Drug level feedback (DBS TFV levels at M4, M7, M10)
Monthly visits until M10

Primary outcome, 10 months
Adherence (TDF-DP on DBS and plasma TFV; analyzed as continuous variable)

Responder → Continue 2 way SMS & counseling at quarterly visits
Non-responder → Drug level feedback (DBS TFV levels at M4, M7, M10)
Monthly visits until M10

Next steps:
SMART design of scalable PrEP adherence strategies
Celum & Delany-Morelwe, R01MH114544
ACKNOWLEDGEMENTS

• The youth CABs for their ideas and feedback
• The young women who are participating in HPTN082/HERS
• The HERS team with special thanks to the site teams at Ema, Spilhaus and Ward 21
ACKNOWLEDGEMENTS

- Sinead Delany-Moretlwe
- Bonnie Dye
- Jared Baeten
- Linda-Gail Bekker
- Sybil Hosek
- HPTN 067/ADAPT, Plus Pills, HPTN 082/HERS, 3P, & POWER study teams
- Funders: NIH (HPTN 082, ADAPT, 3P), BMGF (3P demand creation & enumeration, USAID (POWER)
ACKNOWLEDGEMENTS

The HIV Prevention Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068619, UM1AI068613, UM1AI1068617), with co-funding from the National Institute of Mental Health, and the National Institute on Drug Abuse, all components of the U.S. National Institutes of Health.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.