Prevention-Effective Adherence in a Demonstration Project of PrEP among HIV Serodiscordant Couples in East Africa

Jessica E. Haberer, Lara Kidoguchi, Renee Heffron, Nelly Mugo, Elizabeth Bukusi, Elly Katabira, Stephen Asiimwe, Connie Celum, and Jared M. Baeten on behalf on the Partners Demonstration Project Team
Declarations

• Funding:
  – NIH
  – Bill and Melinda Gates Foundation
  – USAID

• Consultation:
  – NIH
  – WHO
  – IAVI
  – FHI 360
  – Natera (stock)
Adherence and efficacy in PrEP trials

- **iPrEx**: 51% adherence / 44% efficacy
- **Bangkok**: 67% adherence / 49% efficacy
- **TDF2**: 79% adherence / 62% efficacy
- **Partners PrEP**: 81% adherence / 75% efficacy
- **FEM-PrEP and VOICE**: ≤30% adherence / No efficacy

(with permission from J. Baeten)
Adherence has been high in demonstration projects to date

<table>
<thead>
<tr>
<th></th>
<th>Partners Demonstration Project</th>
<th>The Demo Project</th>
<th>Project ADEPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Serodiscordant couples (East Africa)</td>
<td>MSM (US)</td>
<td>Young women (South Africa)</td>
</tr>
<tr>
<td>Adherence</td>
<td>85% by TFV</td>
<td>80-86% of TFV consistent with 4+ doses/week</td>
<td>79%</td>
</tr>
<tr>
<td>HIV incidence</td>
<td>0.2</td>
<td>0.4</td>
<td>--</td>
</tr>
<tr>
<td>(per 100 person years)</td>
<td></td>
<td></td>
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</tbody>
</table>

(Baeten et al, CROI 2015; Liu et al, JAMA IM 2016; Bekker et al, CROI 2015)
Prevention-effective adherence

(a) **Paradigm for ART and clinical trials**: Success is achieved through 100% adherence.

- Adherence behavior
- Time on drug

(b) **Prevention-effective adherence paradigm**: Success is achieved because PrEP is used during all episodes of HIV exposure. Adherence to PrEP may be periodic and mapped to periods of risk.

- Adherence behavior:
  - PREP
  - PREP

- HIV exposure over time:
  - No risk
  - No risk

*(Haberer et al, AIDS 2015)*
Understanding prevention-effective adherence requires knowledge of dynamic risk behaviors and concurrent use of multiple prevention strategies.
Partners Demonstration Project

• Open-label study of integrated PrEP and ART among 1,013 high-risk (>5% estimated incidence) serodiscordant couples in 4 sites in East Africa
• HIV-uninfected partner encouraged to take PrEP until HIV-infected partner had taken ART for 6 months ("bridge strategy")
• 24 months follow-up with quarterly visits
Methods

• Analysis reflects 12 months of follow-up per participant

• Adherence measured with MEMS
  – Based on PrEP as dispensed
    • Per participant preference
    • Per protocol (i.e., study holds)
  – Data censored if adherence >120% (N=9)
  – Average doses/week in month prior to a study visit
Definitions of risk

- HIV-infected partner on ART <6 months
- Reported sex with HIV-infected partner
- Reported <100% condom use

HIGH RISK
Definitions of risk

HIV-infected partner on ART <6 months

Reported sex with HIV-infected partner

PROBABLE RISK
Definitions of risk

HIV-infected partner on ART <6 months
Definitions of sufficient adherence

• **4+ doses/week** for MSM  *(Anderson et al, Sci Tran Med, 2012)*

• **6+ doses/week** for women  *(Cottrell et al, JID, 2016)*

• Unclear what is needed for heterosexual men
Analysis

• Prevention-effective adherence defined descriptively
• Predictors of prevention-effective adherence assessed by multivariable repeated measures regression
  – Socio-demographics
  – Reported risk
  – Concerns/beliefs about PrEP
  – Relationship characteristics
  – Sexual activity
• A priori gender interactions
• Variables assessed for collinearity
## Participant characteristics  
(at enrollment)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%) or median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>656 (67%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>29 (26-36)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>8 (6-12)</td>
</tr>
<tr>
<td>Number of children with study partner</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>Unprotected sex with study partner in past month</td>
<td>638 (67%)</td>
</tr>
<tr>
<td>Unprotected sex with non-study partner in past month</td>
<td>60 (6%)</td>
</tr>
<tr>
<td>CD4 count of HIV-infected partner</td>
<td>437 (271-640)</td>
</tr>
<tr>
<td>HIV RNA of HIV-infected partner (log$_{10}$)</td>
<td>4.6 (3.9-5.0)</td>
</tr>
</tbody>
</table>
High overall PrEP initiation and adherence

- PrEP initiation: 985 of 1,013 (97%) participants
  - 960 at enrollment
  - 20 at Month 1
  - 5 at Month 3+

- Overall MEMS adherence
  - Median = 88% (IQR 65-98%)
  - Mean = 78% (SD 27%)
Study months with prevention-effective adherence

Total N= 3,156 study months

<table>
<thead>
<tr>
<th>Sufficient adherence (doses/week)</th>
<th>Total visits</th>
<th>Risk of HIV acquisition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>N visits</td>
<td>% high risk visits</td>
</tr>
<tr>
<td>4+</td>
<td>2,556</td>
<td>475</td>
</tr>
<tr>
<td>6+</td>
<td>2,120</td>
<td>392</td>
</tr>
</tbody>
</table>

- People know how to adhere when they are at risk
- Achieving sufficient adherence is easier with a lower threshold
Predictors of prevention-effective adherence
(sufficient adherence = 4+ doses/week)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>RR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No concerns about daily PrEP</td>
<td>1.24</td>
<td>1.12 - 1.39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pregnancy intentions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not pregnant, not trying</td>
<td>ref</td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>Not pregnant, trying</td>
<td>1.05</td>
<td>1.00 - 1.11</td>
<td></td>
</tr>
<tr>
<td>Current partnership pregnancy</td>
<td>1.05</td>
<td>1.00 - 1.10</td>
<td></td>
</tr>
<tr>
<td>Partner on ART &gt;6 months</td>
<td>0.94</td>
<td>0.88 – 1.00</td>
<td>0.038</td>
</tr>
<tr>
<td>No longer in couple w/ study partner</td>
<td>0.76</td>
<td>0.64 - 0.91</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- Non-significant: age 25+ years*, study month enrollment, any condom use, any sex, sex with or without condoms, social support, want relationship to succeed
- 155 study-months (<5%) excluded due to missing data *p=0.055
Predictors of prevention-effective adherence
(sufficient adherence = 6+ doses/week)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>RR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex risk with study partner in past 30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sex with study partner</td>
<td>ref</td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Had sex w/ study partner, all protected</td>
<td>1.44</td>
<td>1.07 - 1.95</td>
<td></td>
</tr>
<tr>
<td>Had sex w/ study partner, any unprotected</td>
<td>1.52</td>
<td>1.12 - 2.05</td>
<td></td>
</tr>
<tr>
<td>No concerns about daily PrEP</td>
<td>1.34</td>
<td>1.16 - 1.55</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Want desperately/very much for relationship to succeed</td>
<td>1.17</td>
<td>1.04 - 1.33</td>
<td>0.007</td>
</tr>
<tr>
<td>Age 25+ (years)</td>
<td>1.13</td>
<td>1.03 - 1.24</td>
<td>0.008</td>
</tr>
<tr>
<td>Female</td>
<td>1.08</td>
<td>1.01 - 1.16</td>
<td>0.023</td>
</tr>
<tr>
<td>Has problem alcohol use</td>
<td>0.88</td>
<td>0.81 - 0.96</td>
<td>0.003</td>
</tr>
<tr>
<td>In follow up &gt;6 study months</td>
<td>0.87</td>
<td>0.81 - 0.93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No longer in couple w/ study partner</td>
<td>0.63</td>
<td>0.49 - 0.81</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

- Not significant: study month enrollment, married to study partner, any condom use, any sex, any sex, abuse in partnership, CD4 count
- No significant gender interaction terms in either model
Conclusions

- PrEP adherence is different than ART adherence
- Most people are achieving prevention-effective adherence
- Adherence is higher in those at higher risk
- Achieving prevention-effective adherence is more challenging when the threshold for protection is higher
Implications

• Predictors may help identify PrEP candidates
  – No concerns about taking a daily pill
  – Aware of risk (e.g., being sexually active in a serodiscordant couple)
  – Commitment to something that may be achieved through PrEP (e.g., relationship)

• Predictors may be helpful in targeting support
  – Enabling factors above
  – E.g., problem alcohol use, age <25 years
Partners Demonstration Project Team

Investigators

- University of Washington Coordinating Center: Jared Baeten (protocol chair), Connie Celum (protocol co-chair), Deborah Donnell (protocol statistician), Renee Heffron (project director), Ruanne Barnabas, Bettina Shell-Duncan, ICRC Operations, Data and Administration teams
- Kabwohe, Uganda (KCRC): Elioda Tumwesigye, Steven Asiimwe, Edna Tindimwebwa
- Kampala, Uganda (Makerere University): Elly Katabira, Nulu Bulya
- Kisumu, Kenya (KEMRI): Elizabeth Bukusi, Josephine Odoyo
- Thika, Kenya (Kenyatta National Hospital, UW): Nelly Mugo, Kenneth Ngure
- MGH/Harvard: David Bangsberg, Jessica Haberer, Norma Ware
- Johns Hopkins: Craig Hendrix
- Fred Hutchinson Cancer Research Center: Dara Lehman
- DF/Net Research (data management)

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Research participants
Thank you!

jhaberer@mgh.harvard.edu