Psychosocial Issues in ART and HIV Prevention

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1. Why is behavioral science important when using ART as prevention?

2. How can we address the psychosocial context when looking at HIV risk and self-care? - Examples from successful ART for prevention trials.
The Effects of “Syndemics” on HIV Risk in MSM

- Cross sectional household telephone survey of MSM in Chicago, LA, New York, and SF (N = 2881)
- High occurrence and interconnectedness of depression, poly drug use, childhood sexual abuse, and partner violence
- Additive effects: Odds ratios increased as did number of these psychosocial health problems

<table>
<thead>
<tr>
<th></th>
<th>1 problem</th>
<th>2 problems</th>
<th>3 and 4 problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk sex (P &lt; .01)</td>
<td>1.6</td>
<td>2.4</td>
<td>3.5</td>
</tr>
<tr>
<td>HIV prevalence (P &lt; .001)</td>
<td>1.8</td>
<td>2.7</td>
<td>3.6</td>
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Example frequent set of Syndemics:

Mental ill-health

Instability → Homelessness

Substance Use

Incarceration
### Mental health problems when considering optimizing secondary prevention

<table>
<thead>
<tr>
<th>Condition</th>
<th>% Screening Positive (95% CI)*</th>
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<tbody>
<tr>
<td></td>
<td>HCSUS (N=2864)</td>
</tr>
<tr>
<td></td>
<td>HIV-infected</td>
</tr>
<tr>
<td>Major Depression</td>
<td>36.0 (33.6-38.3)</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>26.5 (23.5-29.5)</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder</td>
<td>15.8 (14.0-17.7)</td>
</tr>
<tr>
<td>Panic Attack</td>
<td>10.5 (8.0-13.0)</td>
</tr>
<tr>
<td>No drug use</td>
<td>49.9 (46.0-53.71)</td>
</tr>
<tr>
<td>Marijuana use only/ no dependence</td>
<td>12.1 (10.2-14.8)</td>
</tr>
<tr>
<td>Other drug use/ no dependence</td>
<td>25.6 (22.1-29.1)</td>
</tr>
<tr>
<td>Drug dependence</td>
<td>12.5 (10.2-14.8)</td>
</tr>
</tbody>
</table>

*Bing et al., 2001; Archives of General Psychiatry*
• 95 independent samples
• Depression significantly associated with non-adherence (p < .00001; r = 0.19; CI: 0.14 - 0.25)
• Adherence via interview versus self-report higher association
• Continuous measures versus dichotomies higher
• Not limited to those with clinical depression
Systematic Review

- Active drug use = worse HAART outcomes (former DU, OST or support = better outcomes)

Meta analysis:
- 38 studies; 14,960 patients
- Drug users mean adherence 60%
- Comparable to meta analysis of PLWH in N. America, reporting 55% (overlapping CIs; Mills et al., 2006)
Mental Health / Substance Use Can Interfere with Health Behavior Intervention Models

Information \rightarrow Motivation \rightarrow Behavioral Skills \rightarrow Health behavior / Adherence

Depression / Anxiety, poverty, poor social conditions, substance use dx

Initial ART Adherence Intervention Trials

- Minimal interventions – MGH/Fenway work
  - “Life-Steps” – single session adherence intervention; significant effects but comparison group “caught up” over time (Safren et al., 2001)
  - Pager study – significant but modest effects (Safren et al., 2003)
- Meta analyses of adherence interventions: significant but modest effects
  - Simoni (2006): 19 RCTs
  - Amico (2006): 25 studies

Safren et al., 2001, Behaviour Research and Therapy; Safren et al., 2003; AIDS Care; Amico et al., 2006. JAIDS; Simoni et al., 2006. JAIDS
CBT-AD Overview

Modules: 12 sessions, each 50 minutes long

Each CBT module for depression integrates adherence counseling

1. Psychoeducation and Motivation.......... 1 session
2. Adherence Training / Life-Steps......... 1 session
3. Behavioral Activation ...................... 2 sessions
4. Adaptive thinking (cognitive restructuring).4 sessions
5. Problem Solving............................ 2 sessions
6. Relaxation Training.......................... 1 session
7. Maintenance & Relapse Prevention....... 1 session
Initial Outcome of CBT-AD

- Significant acute improvement in adherence (MEMS) and depression in intent-to-treat analyses
- Similar pattern of results for completer analyses
- Those who “crossed-over” caught up
- Intervention-associated improvements were generally maintained at 6 and 12 months

Note: effect size conventions .5 = medium, .8 = large, calculated with change scores
CBT for adherence and depression in HIV-infected IDU (N=89): Acute outcomes

**MEMs based adherence – above:**
HLM analysis of MEMs Weeks 0-10 = greater improvement in treatment versus control condition (slope = 0.887, t(86)= 2.38, p = .02)

**Depression:** Pre-Post
Treatment: Significantly greater improvements in depression in treatment versus control condition [MADRS (F(1,79)=6.52, p<.01)] (replicated with clinical global impression [(F(1,79)=14.77, p<.001)] )

Safren et al., 2012– JCCP
Outcomes after intervention discontinuation (6 and 12 month)

- **Depression:** gains were maintained

- **MEMs based adherence:** gains not maintained

![Graph showing MEMs Adherence (% Past 2 Weeks)](image)

- **Viral load:** No differences across conditions
- **CD4:** the CBT-AD condition had significant improvements in CD4 cell counts over time compared to ETAU ($\gamma_{slope} = 2.09$, $t(76) = 2.20$, $p = .03$)
  - 61.2 CD4 cell increase intervention condition
  - 22.4 CD4 cell decrease control condition
ART for HIV Treatment versus HIV Prevention

ACTG5175 – TREATMENT 1,571 (201 from U.S.) participants, 9 countries, 4 continents, 3-arm non-inferiority trial: Rio de Janeiro and Porto Alegre, Brazil; Port-au-Prince, Haiti; Chennai and Pune, India; Blantyre and Lilongwe, Malawi; Lima, Peru; Durban and Johannesburg, South Africa; Chiang Mai, Thailand; Harare, Zimbabwe and 31 United States sites

HPTN052 Prevention: 13 Sites, 9 Countries, 1,763 sero-discordant couples:
Gaborone, Botswana; Kisumu, Kenya; Lilongwe and Blantyre, Malawi; Johannesburg and Soweto, South Africa; Harare, Zimbabwe; Rio de Janeiro and Porto Alegre, Brazil; Pune and Chennai, India; Chiang Mai, Thailand; and Boston

Major findings (Campbell et al., 2012; PLOS Medicine):
• QD PI regimen (ATV+DDI+EC+FTC) inferior to BID standard of care (EFV+3TC/ZDV) NRTIs + NNRTI
• QD NNRTI regiment (EFV+FTC/TDF) had similar efficacy to standard of care (EFV+3TC/ZDV)

Major finding (Cohen et al., NEJM 2011):
• Early ART prevents HIV transmission in sero-discordant heterosexual couples (1 infection in the early ART arm, 27 infections in delayed)
## ACTG 5175 (treatment trial): Significant Multivariable Risk Factors of Pill Count Non-Adherence

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>Week</strong></td>
<td>1.015</td>
<td>(1.008, 1.021)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>QOL_health</strong></td>
<td>0.991</td>
<td>(0.986, 0.996)</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-once daily NRTIs + PI</td>
<td>0.651</td>
<td>(0.518, 0.818)</td>
<td>0.0002</td>
</tr>
<tr>
<td>2-once daily NRTIs + NNRTI</td>
<td>0.491</td>
<td>(0.388, 0.621)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3-twice daily standard of care</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latin America/Caribbean</td>
<td>1.023</td>
<td>(0.736, 1.443)</td>
<td>0.891</td>
</tr>
<tr>
<td>Asia</td>
<td>0.877</td>
<td>(0.618, 1.245)</td>
<td>0.464</td>
</tr>
<tr>
<td>Africa</td>
<td>0.520</td>
<td>(0.366, 0.739)</td>
<td>0.0003</td>
</tr>
<tr>
<td>United States</td>
<td>1.000</td>
<td></td>
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1. Model includes random intercept (covariance=unstructured)
HPTN052 (prevention trial): Longitudinal multivariable model: Significant Odds Ratios for 100% Pill Count Adherence
Overview of adherence and efficacy of major PrEP clinical trials

<table>
<thead>
<tr>
<th>Trial name</th>
<th>PrEP formulation</th>
<th>Population</th>
<th>N</th>
<th>Estimated adherence</th>
<th>HIV reduction rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PrEP</td>
<td>TDF tablets</td>
<td>Serodiscordant couples</td>
<td>4,758</td>
<td>97% (clinic pill count) 82% (drug concentration)</td>
<td>67% (TDF) 75% (FTC/TDF)</td>
</tr>
<tr>
<td></td>
<td>FTC/TDF tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF2-CDC</td>
<td>FTC/TDF tablets</td>
<td>Heterosexual men and women</td>
<td>1,200</td>
<td>84% (clinic pill count)</td>
<td>63%</td>
</tr>
<tr>
<td>iPrEx</td>
<td>FTC/TDF tablets</td>
<td>MSM</td>
<td>2,499</td>
<td>95% (self-report) 89–95% (clinic pill count) ~50% (drug concentration)</td>
<td>44%</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study</td>
<td>TDF tablets</td>
<td>Injection drug users</td>
<td>2,413</td>
<td>84% (self-report diaries) 95% (DOT; 87% of study)</td>
<td>49%</td>
</tr>
<tr>
<td>CAPRISA 004</td>
<td>1% TDF gel</td>
<td>High-risk women</td>
<td>889</td>
<td>72.2% (returned applicators)</td>
<td>39%</td>
</tr>
<tr>
<td>FemPrEP</td>
<td>FTC/TDF tablets</td>
<td>High-risk women</td>
<td>1,951</td>
<td>95% (self-report) &lt;50% (drug concentration)</td>
<td>Study stopped for futility</td>
</tr>
<tr>
<td>VOICE</td>
<td>TDF, FTC/TDF tablets; 1% TDF gel</td>
<td>Women in high prevalence areas</td>
<td>5,029</td>
<td>90% (self-report) &lt;30% (drug concentration)</td>
<td>TDF tablets and gel</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>stopped for futility; FTC/TDF tablets NS</td>
</tr>
</tbody>
</table>
The adherence-efficacy relationship

- **CAPRISA:** HIV risk reduction was 99% when PrEP is taken 7 days a week (modeling data).
- **iPrEX:** HIV risk reduction was 99% when PrEP is taken 7 days a week (modeling data).
- **Partners PrEP:** HIV risk reduction was 90% if TDF/FTC was detectable.
- **Bangkok:** HIV risk reduction was 74% if TDF was detectable.

### Adherence HIV risk reduction

<table>
<thead>
<tr>
<th>Adherence</th>
<th>HIV risk reduction</th>
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<tbody>
<tr>
<td>&gt;80%</td>
<td>54%</td>
</tr>
<tr>
<td>50-80%</td>
<td>38%</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>28%</td>
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*Slide courtesy of Jessica Haberer*
Partners in PrEP Ancillary Adherence Substudy

- 3 Study sites in Uganda
- Adherence monitoring: Intervention “triggered” by low (<80%) unannounced pill count adherence
  - Monthly contact with interventionist
  - Number of sessions tailored and variable
  - Optional couples session(s)
  - Utilized principles of cognitive behavioral therapy (e.g., problem solving and motivational interviewing)
  - Standardized provision of information while still tailoring counseling messages to individual needs (12 modules)
  - Designed to allow delivery by a variety of study staff members with various levels of training
Partners in PrEP Ancillary Adherence Substudy Results

- HIV Infections
  - 14 in 404 participants on placebo (333 person-years)
  - 0 infections in 750 participants on active drug (616 person-years)

- PrEP efficacy within this adherence sub-study was 100% (95% CI 83.7-100%, p<0.001)
Partners in PrEP Intervention Characteristics

- Median number of sessions = 10 (IQR range = 5-16)
- Median session length
  - Session 1 = 40 minutes (IQR 30-50)
  - Length decreased to median 20 minutes (IQR 15-30) by session 4
- Most frequently endorsed barriers to adherence at Session 1:
  - Travel 49.0%
  - Forgetting 44.0%
  - Remained most frequently endorsed barriers across all sessions.
Optimizing PrEP Adherence in MSM: Fenway Project “Prepare”

- Intervention content
  - CBT-oriented adherence problem-solving skills
  - brief motivational interviewing
  - sexual risk-reduction strategies.
- Optional modules
  - mental health and substance-use barriers to adherence.
Optimizing PrEP Adherence in MSM: Fenway Project “Prepare”

- Intervention content (based on LifeSteps)
  - CBT-oriented adherence problem-solving skills
  - Brief motivational interviewing
  - Sexual risk-reduction strategies.
- Optional modules
  - Mental health and substance-use barriers to adherence.
Project PrEPare: Real Time Assessment of Sexual risk and PrEP Adherence

Is this a good time for a survey? 1:Yes, 2:No.

Please enter your PIN.

Did you have sex in the past 24 hours? 1:Yes, anal, 2:Yes, vaginal, 3:Yes, both anal and vaginal, 4:No.

Did you use a condom with all sex acts in the past 24 hours? 1:Yes, 2:No.
Early experience with first set of participants:

- High adherence
- Continued self-reported sexual risk
Summary

Experience with ART for treatment = adherence is complicated
- Interventions to promote adherence need to take into consideration psychosocial context of nonadherence
- Next steps: Interventions addressing syndemics in those with high risk and uncontrolled virus

Experience with ART as prevention
- Failed trials = failed adherence
- Our experience in Boston = continued risk and continued high adherence in high risk MSM on PrEP
- Consistent with iPrEX U.S. data
- Next steps: Interventions for those with non-adherence but interest in taking PrEP likely also will need to address the psychosocial context