Behavioral Threats to PrEP Success

Behaviors that Promote PrEP Success

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No conflict of interest
Bio-Medical interventions that are self-administered are Bio-Behavioral interventions
What would limit the success of effective PrEP?

Two main threats:
1. Adherence and patterns of use
2. Increased exposures to HIV in the context of inadequate adherence
• PrEP Adherence and Patterns of Use
  – What is it
  – Why worry about it
  – Current evidence base
  – What to look for in practice or research

• Increases in Risk (risk compensation or safety offset)
  – What is it
  – Why worry about it
  – Current evidence base
  – What to look for in practice or research

• Strategies to amplify PrEP success
PrEP Adherence

What?

• Assuming a once daily one tablet regimen
  – HIV negative confirmation at start

• How well do people follow the regimen?
PrEP Adherence

**What?**

- “Execution” – how closely did someone follow the regimen?
- “Persistence” – how long did someone stay on-treatment?

PrEP Adherence

What?

- “Execution” – how closely did someone follow the regimen?

- Expect periods of use/non-use

Safe Cycling

Following “prescribed” HIV testing prior to re-initiation

PrEP Adherence

Why worry?

• Following daily regimen or close to daily is highly associated with protection

94% reduction in HIV risk
(95% CI: 79 to 99%)

Any Drug Detection by Group and Time
PrEP Adherence

Why worry?

• Low adherence would not lead to high levels of protection

• Unmonitored stopping and re-starting PrEP could lead to resistance if infected prior to re-start

• Also worried about potential mis-belief that using some PrEP is still highly effective
PrEP Adherence

Evidence base?
WHAT DO WE KNOW SO FAR....

- No studies yet of actual rates of PrEP use
- Adherence to blinded study product in PrEP trials suggests anywhere from >86% to as low as <26%
- iPrEx estimated ~44% of participants with any drug detected
  - 18% estimated to have been taking it daily
## PrEP Adherence

**Evidence base?**

- Adherence from other fields?
  - 55 – 77% adequate execution
  - 40 – 65% will persist [35% may cycle in 3m]

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>COHORT</th>
<th>RATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART adherence</td>
<td>US</td>
<td>~55% [Mills 2006]</td>
</tr>
<tr>
<td>Drug Using PLWH</td>
<td></td>
<td>~60%  [Malta 2008]</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td></td>
<td>~77% [Mills 2006]</td>
</tr>
<tr>
<td>PEP</td>
<td>HCW</td>
<td>~67%  [Lacombe 2006]</td>
</tr>
<tr>
<td></td>
<td>Non-occupational</td>
<td>~78%  [Lacombe 2006]</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td>Continued script for 6 months</td>
<td>~45%  [Dempsey 2010]</td>
</tr>
<tr>
<td></td>
<td>Continued script for 3 months</td>
<td>~65%  [Murphy 2008]</td>
</tr>
<tr>
<td>Injectable Contraceptive</td>
<td>Got second injection</td>
<td>~40%  [Murphy 2008]</td>
</tr>
</tbody>
</table>

- 55 – 77% adequate execution
- 40 – 65% will persist [35% may cycle in 3m]
PrEP Adherence

Evidence base?

- Emerging
  - iPrEx OLE
  - Demonstration projects
  - HPTN067 ADAPT study (daily arm with EDM)
  - Other studies in preparation (daily with EDM)
PrEP Adherence

Evidence base?

- We may not know what adherence will look like for the typical PrEP user for several years.
We may not know what adherence will look like for the typical PrEP user for several years.
PrEP Adherence Monitor?

• Guidelines presently available in US identify monitoring of adherence and re-start as critical.

PrEP has the potential to contribute to effective and safe HIV prevention for MSM if 1) it is targeted to MSM at high risk for HIV acquisition; 2) it is delivered as part of a comprehensive set of prevention services, including risk-reduction and PrEP medication adherence counseling, ready access to condoms, and diagnosis and treatment of sexually transmitted infections; and 3) it is accompanied by monitoring of HIV status, side effects, adherence, and risk behaviors at regular intervals.
PrEP Adherence *Monitor*

- How to monitor is less clear
  - Drug detection
  - Self-report
  - Pharmacy based measures (MPR)
  - EDM
  - Unmonitored re-starts?
# PrEP Adherence

<table>
<thead>
<tr>
<th>What</th>
<th>Why</th>
<th>How</th>
<th>Knowledge gaps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Execution (following dosing while on-PrEP)</td>
<td>Low protection</td>
<td>• Drug det&lt;br&gt;• Pharm data&lt;br&gt;• Self-report&lt;br&gt;• [EDM?]</td>
<td>• What will rates of adherence be?&lt;br&gt;• What proportion of PrEP users may need adherence support?&lt;br&gt;• Measures?</td>
</tr>
<tr>
<td>Safe/Unmonitored cycling</td>
<td>Resistance</td>
<td>• [EDM?] &lt;br&gt;• Self-report&lt;br&gt;• Pharm data</td>
<td>• What proportion of PrEP users stop and safely re-start?&lt;br&gt;• How to best measure this in practice?&lt;br&gt;• Proportion of PrEP users developing resistance with unsafe restarts?</td>
</tr>
</tbody>
</table>
• PrEP Adherence and Persistence/Cyclical use
  – What is it
  – Why worry about it
  – Current evidence base
  – What to look for in practice or research

• Increases in Risk (risk compensation or safety offset)
  – What is it
  – Why worry about it
  – Current evidence base
  – What to look for in practice or research

• Strategies to amplify PrEP success
PreP has the potential to contribute to effective and safe HIV prevention for MSM if 1) it is targeted to MSM at high risk for HIV acquisition; 2) it is delivered as part of a comprehensive set of prevention services, including risk-reduction and PreP medication adherence counseling, ready access to condoms, and diagnosis and treatment of sexually transmitted infections; and 3) it is accompanied by monitoring of HIV status, side effects, adherence, and risk behaviors at regular intervals.
Change in Risk Behavior

What?

BMJ

HIV and risk behaviour

Risk compensation: the Achilles’ heel of innovations in HIV prevention?

Michael M Cassell, Daniel T Halperin, James D Shelton, David Stanton

The benefits of new methods of prevention of HIV could be jeopardised if they are not accompanied by efforts to change risky behaviour
Risk Compensation

• What is it?
  – Term emerged from traffic safety research.
• Introducing safety features (airbags, anti-lock breaks) and laws (seatbelts) resulted in increased risk behavior
Editorial

Disinhibition and Risk Compensation

Scope, Definitions, and Perspective

MATTHEW HOBGEN, PHD, AND NICOLE LIDDON, PHD
Risk Compensation

Disinhibition and risk compensation with different implications for intervention strategies. Disinhibition derives from psychological terminology; it occurs when people stop trying to avoid risk to themselves or others. Probably the most widely known examples in sexual behavior are centered around the disinhibiting effects of alcohol; an inebriated person may be sexually incautious or aggressive because he or she no longer "cares" about the risk of sexual exposure. Other examples are derived from how people feel they cannot avoid a harm and then not do so. In both examples, the outcome is born through lack of caring, although the causes of unavoidable risk) are very different. Risk compensation, on the other hand, is best understood from a more cognitive perspective. The term applies to those whose diminished susceptibility via a given preventive intervention permits them to increase other risk behaviors. Although both terms are often used inter-

Risky 'people'? Volitional? Homeostasis?
Safety Offset Hypothesis

If cues you use to signal risk diminish, then the caution you exercised before will reduce

Increase in behavior previously avoided or controlled

Net result is null gains in protection/safety (effects are offset by increases in risk)

If you are “feeling” more safe, you simply don’t need to be as careful.

Fred Mannering; Emil Venere
Offset

Why Worry?

Perceived vulnerability to HIV
Cue used to gauge risk

PrEP = Decreased perceived vulnerability to HIV

Decreased practice of behaviors previously used to mitigate risk

INCREASE number of partners
type of partners
total potential exposure events
discussion of HIV status
positioning
condomless sex

INCREASE HIV infections
Offset and Changes in Risk

Evidence Base

• Specific to PrEP…we do not yet know.

CDC: Grohskopf et al, IAS July 2010

Baeten et al, May 2012 FDA Presentation, Washington DC
iPrEx RCT: Unprotected Receptive Anal Intercourse by Treatment Arm and Weeks on study

Grant et al, May 2012 FDA Presentation, Washington DC
Offset and Changes in Risk

Evidence Base

• No increases in risk behavior reported to date in recent PrEP trials

• STI data confirms overall decreases in risk behavior (iPrEx, PiP)

• Restricted to those reporting believing being in active arm, no increase in risk behavior found (iPrEx)
Offset and Changes in Risk

Evidence Base

• Other areas?
  – Safety regulations for automotive/traffic safety, child safety restraints, antilock breaks and airbags: mixed
  – Helmet use skiing/cycling: mixed leaning towards no change in risk behavior
  – Sunscreen: some evidence for offset with net result increased negative outcomes
Offset and Changes in Risk

Evidence Base

Prevention Misconception

Beliefs that the intervention is more effective than it actually is.

- Sunscreen: some evidence for offset with net result increased negative outcomes
# Safety/Prevention Offset

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<tr>
<th>What</th>
<th>Why</th>
<th>How</th>
<th>Knowledge gaps</th>
</tr>
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<tbody>
<tr>
<td><strong>PrEP User: Decreased prevention practices with inadequate adherence</strong></td>
<td>Risk assessment is inaccurate (misconception)</td>
<td>• Self-report</td>
<td>• Will people overestimate their level of personal protection from PrEP?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Monitor beliefs</td>
<td>• Will changes in beliefs result in greater risk for HIV?</td>
</tr>
<tr>
<td><strong>Community: Decrease in prevention practices as a result of presumed effects of PrEP in a community</strong></td>
<td>Risk assessment is inaccurate (misconception)</td>
<td>• Survey</td>
<td>• Do community level beliefs change?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Does risk behavior change?</td>
</tr>
</tbody>
</table>
Oral Preexposure Anti-HIV Prophylaxis for High-Risk U.S. Populations: Current Considerations in Light of New Findings

Gavin M. Myers, M.A., and Kenneth H. Mayer, M.D.

Abstract

This article reviews the status of current research evaluating oral preexposure prophylaxis (PrEP) for prevention of HIV infection in high-risk populations. In animal model studies, the use of antiretrovirals has been shown to be effective in preventing HIV acquisition. Early-phase PrEP studies have established safety in humans. Currently, more than 20,000 men and women will soon be enrolled in studies of oral or topical chemoprophylaxis, testing a variety of drug delivery methods including tenofovir disoproxil fumarate (TDF) gel applied vaginally or rectally, as well as oral PrEP using TDF by itself or coformulated with emtricitabine (FTC). The largest global PrEP trial in men who have sex with men (MSM), known as iPrEx, has demonstrated that oral chemoprophylaxis received active medication, suggesting that PrEP users will need ongoing PrEP clinical monitoring. The prophylactic benefits of TDF/FTC were substantially attenuated by nonadherence, indicating that effective PrEP implementation programs will need to focus on this behavioral variable, in addition to safer sex counseling.
## Safety/Prevention Synergies?

<table>
<thead>
<tr>
<th>What</th>
<th>Support</th>
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<tbody>
<tr>
<td>Adherence</td>
<td><strong>Education</strong>: benefits, risks and strategies</td>
</tr>
<tr>
<td></td>
<td><strong>Support</strong>: Skills building and motivation</td>
</tr>
<tr>
<td></td>
<td><strong>Monitoring</strong></td>
</tr>
<tr>
<td>Safe Cycling</td>
<td><strong>Education</strong>: benefits, risks and strategies</td>
</tr>
<tr>
<td></td>
<td><strong>Promote ease for safe restarts (responsive)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Monitoring</strong></td>
</tr>
<tr>
<td>Sexual Health Protection as multiple</td>
<td><strong>Compendium approach</strong>: what are you considering doing for protection</td>
</tr>
<tr>
<td>strategies</td>
<td>from other STIs?</td>
</tr>
<tr>
<td>Help support decision making and respect</td>
<td><strong>Must provide accurate information</strong></td>
</tr>
<tr>
<td>choices</td>
<td><strong>Frame adherence and risk reduction realistically</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Offer help</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Support choice</strong></td>
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Behavioral Threats to PrEP Success
Watch for…
• Adherence and Safe Cycling
• Development of beliefs of invulnerability or over estimation of protection

Behaviors that Promote PrEP Success
Prepare to…
• Support adherence and provide needed/responsive services
• Discuss PrEP efficacy and effects of inadequate adherence openly
• Explain how to re-start PrEP and why this is recommended
• Frame PrEP use as one of several things to consider for prevention
• Explain limitations of PrEP in protection from other STIs
• Invite opportunity to contribute to one’s decisions; respecting one’s autonomy to decide
Thank you

Special thanks to

- Robert Grant and the iPrEx RCT and OLE team
- Jared Baeten and the PiP team
- Lynn Paxton and the CDC TDF2 study team
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- HPTN 067 Study team
- Sarit Golub, Hunter College