

ORAL

Behavioral Threats to PrEP Success

Behaviors that Promote PrEP Success

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No conflict of interest



CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Treatment as Prevention and Pre-Exposure Prophylaxis

Bio-Medical interventions that
are self-administered are
Bio-Behavioral interventions



CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Treatment as Prevention and Pre-Exposure Prophylaxis

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?

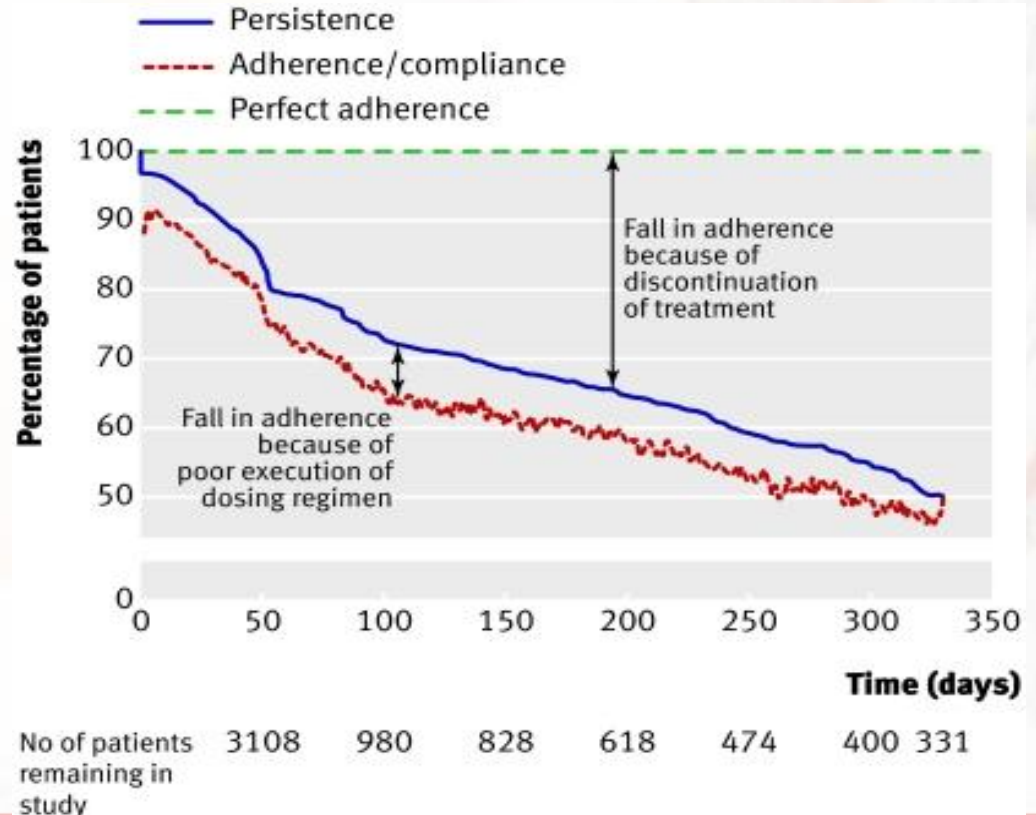
- Assuming a once daily one tablet regimen
 - HIV negative confirmation at start
- How well do people follow the regimen?



PrEP Adherence

What?

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

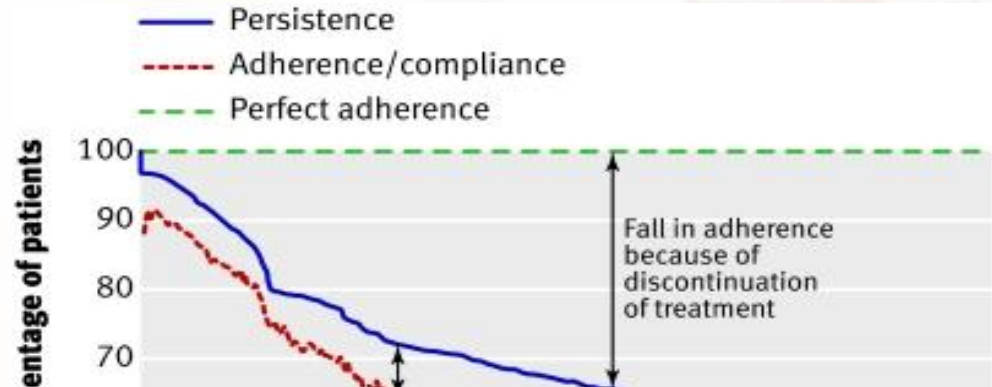


Vrijens B, Vincze G, Kristanto P, et al. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories.: [BMJ. 2008 May 17; 336\(7653\): 1114–1117.](#) Published online 2008 May 14. doi: 10.1136/bmj.39553.670231.25

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

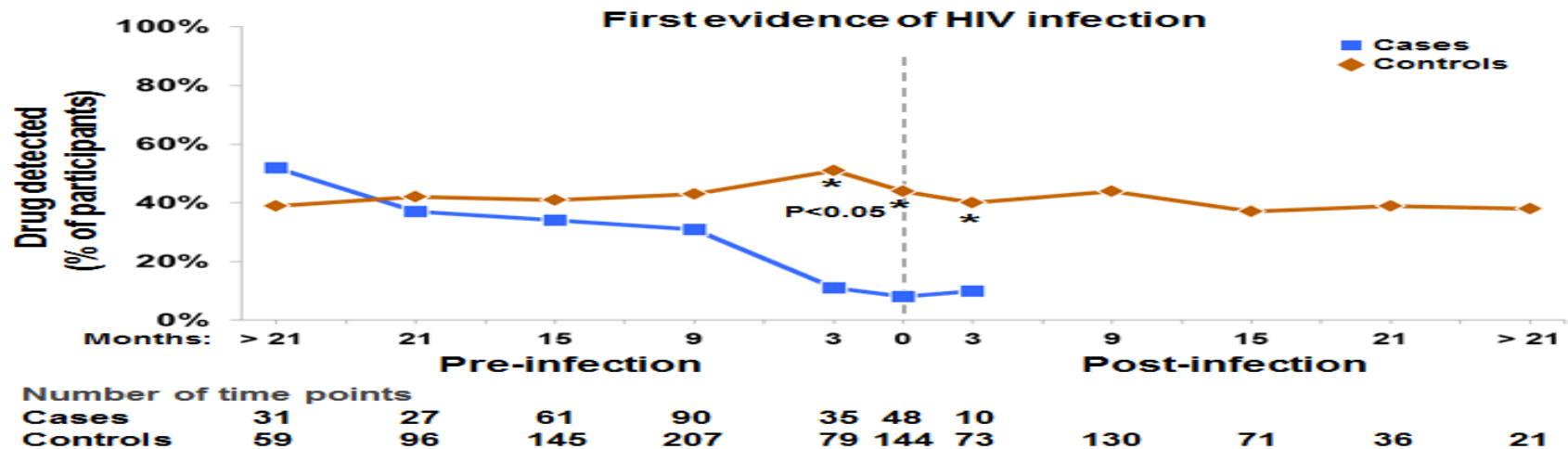
Why worry?

- 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 $\sim 44\%$ of participants with any drug detected
 - 18% estimated to have been taking it daily



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PrEP Adherence

Evidence base?

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

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

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?

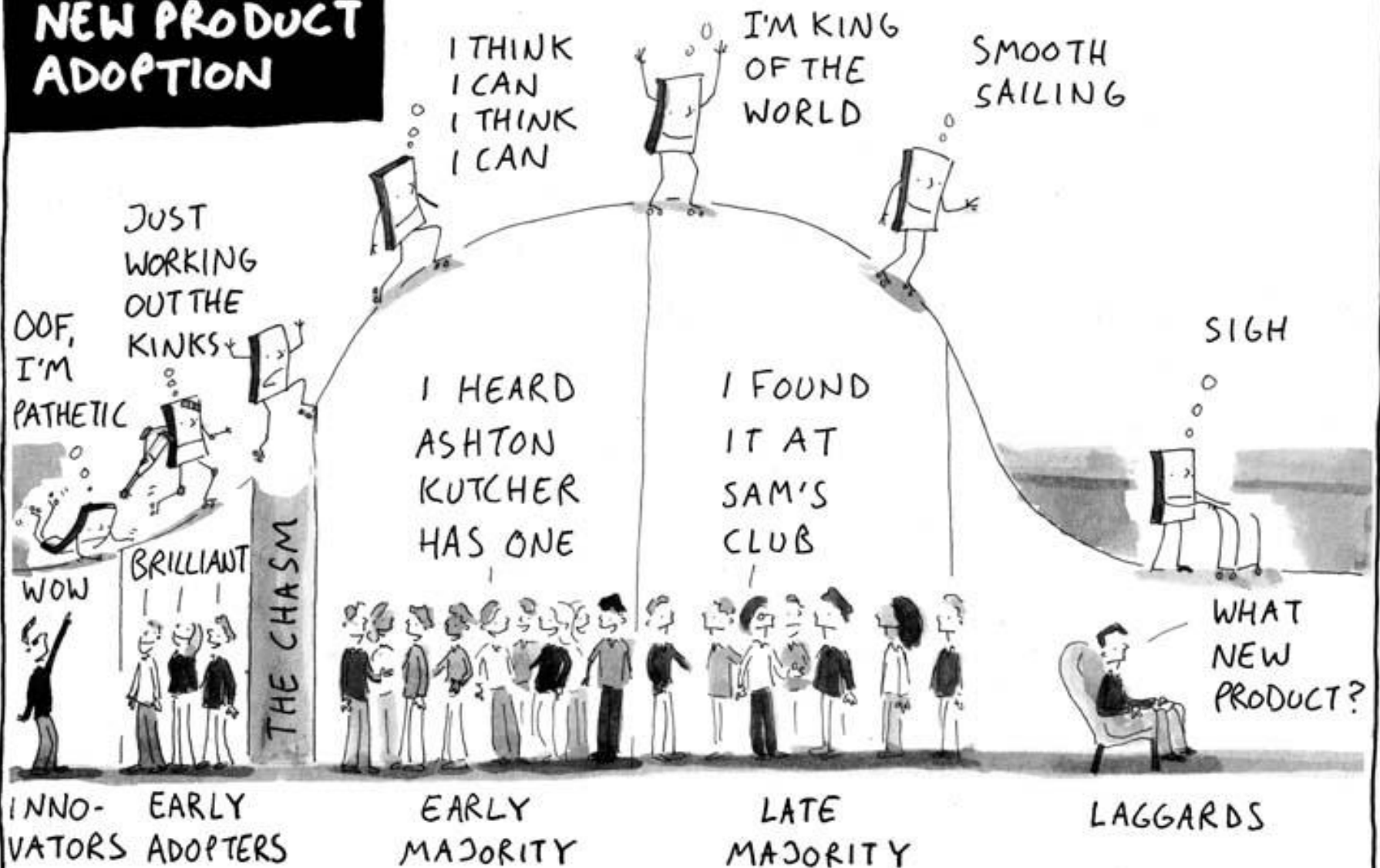
- We may not know what adherence will look like for the typical PrEP user for several years



BRAND CAMP

by Tom Fishburne


NEW PRODUCT ADOPTION



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.


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Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

Weekly
January 28, 2011 / 60(03);65-68

PrEP Adherence

Monitor?

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



PrEP Adherence

| What | Why | How | Knowledge gaps |
|--|----------------|---|--|
| Execution (following dosing while on-PrEP) | Low protection | <ul style="list-style-type: none"> • Drug det • Pharm data • Self-report • [EDM?] | <ul style="list-style-type: none"> • What will rates of adherence be? • What proportion of PrEP users may need adherence support? • Measures? |
| Safe/Unmonitored cycling | Resistance | <ul style="list-style-type: none"> • [EDM?] • Self-report • Pharm data | <ul style="list-style-type: none"> • What proportion of PrEP users stop and safely re-start? • How to best measure this in practice? • Proportion of PrEP users developing resistance with unsafe restarts? |

- 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
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Change in Risk Behavior

What?

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Change in Risk Behavior

What?

BMJ

BMJ VOLUME 332 11 MARCH 2006 bmj.com

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

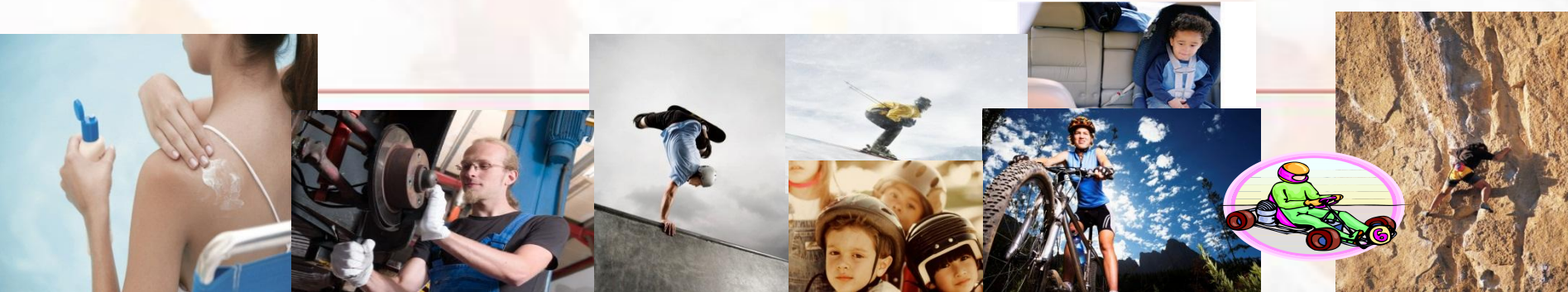
The benefits of new methods of prevention of HIV could be jeopardised if they are not accompanied by efforts to change risky behaviour



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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



Risk Compensation

Sexually Transmitted Diseases, December 2008, Vol. 35, No. 12, p.1009–1010

DOI: 10.1097/OLQ.0b013e31818eb752

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Editorial

Disinhibition and Risk Compensation

Scope, Definitions, and Perspective

MATTHEW HOGBEN, PhD, AND NICOLE LIDDON, PhD



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Risk Compensation

Sexually Transmitted Infections
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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.^{6,7} Other examples are drug use, where people feel they cannot avoid a harm and then do so.⁸ In both examples, the outcome is behavioral change through lack of caring, although the causes

Risky ‘people’?
Volitional?
Homeostasis?

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-



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.

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

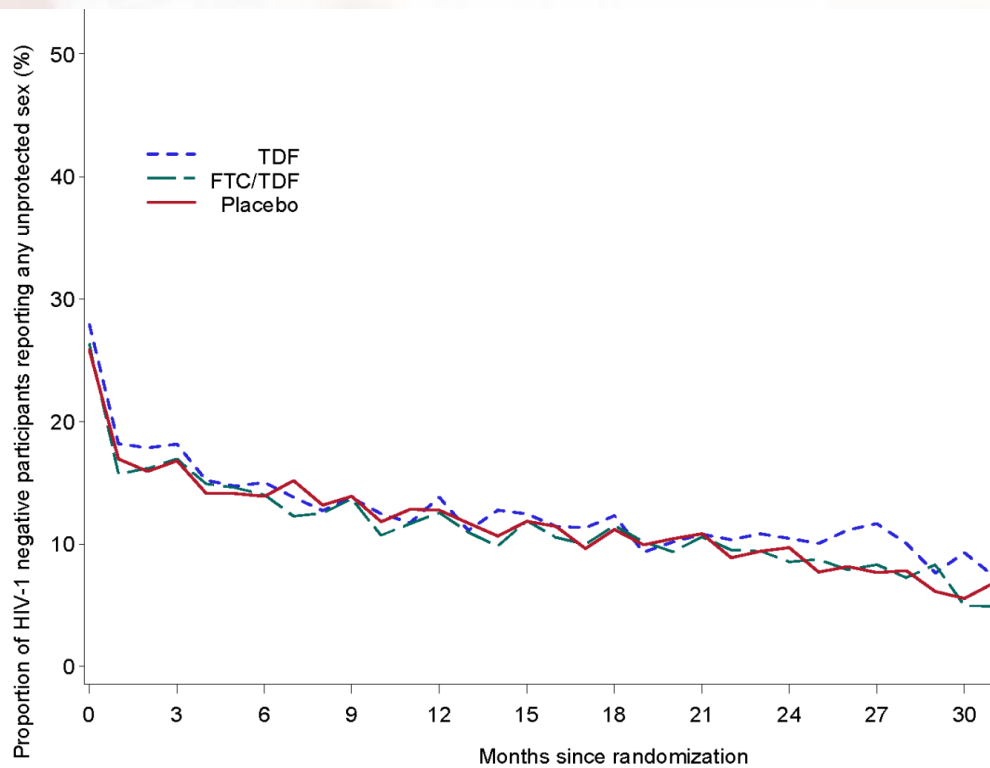
INCREASE
HIV infections



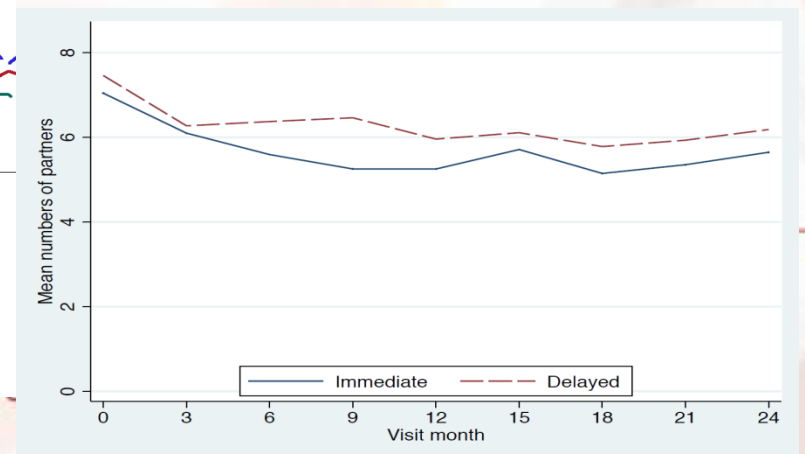
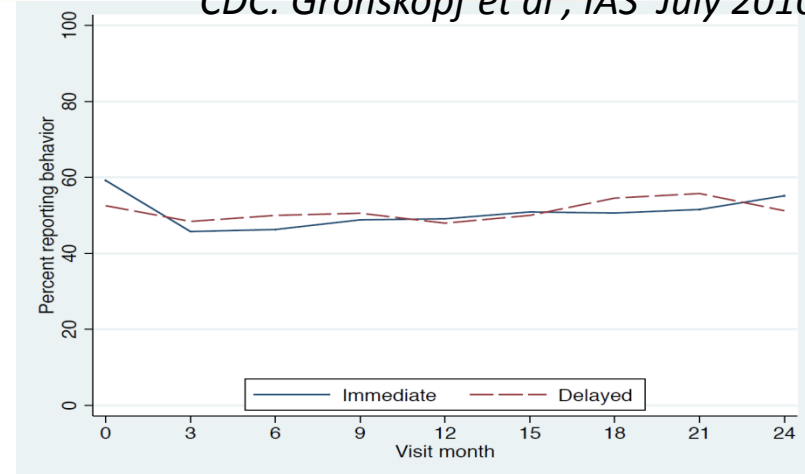
Offset and Changes in Risk

Evidence Base

- Specific to PrEP...we do not yet know.



CDC: Grohskopf et al, IAS July 2010

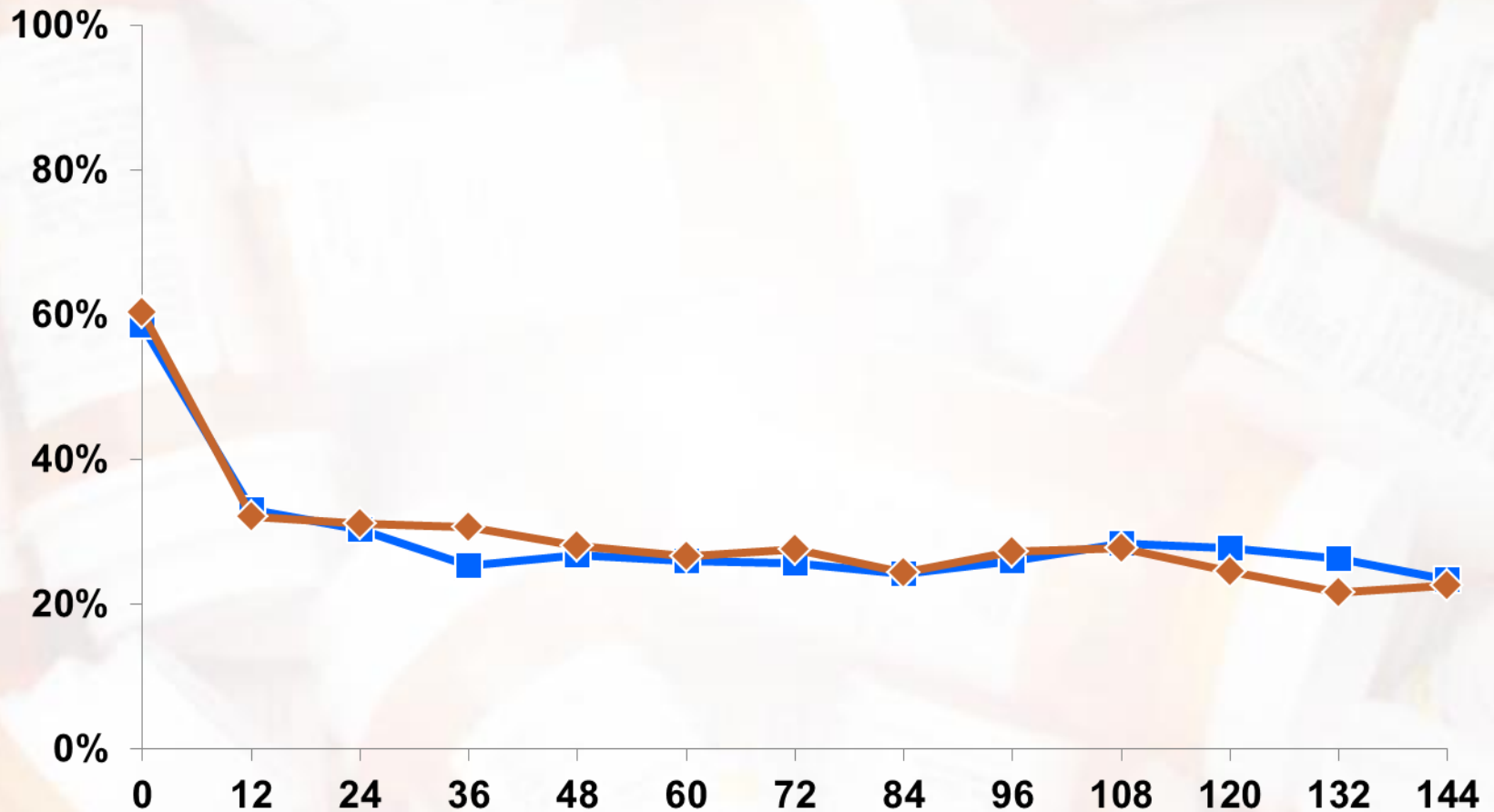


Responses:

| | | | | | | | | | | | |
|---------|------|------|------|------|------|------|------|-----|-----|-----|-----|
| TDF | 1584 | 1517 | 1487 | 1439 | 1296 | 1174 | 1017 | 862 | 700 | 490 | 280 |
| FTC/TDF | 1579 | 1523 | 1492 | 1434 | 1324 | 1196 | 1020 | 862 | 715 | 506 | 283 |
| Placebo | 1584 | 1521 | 1500 | 1434 | 1304 | 1174 | 1021 | 869 | 724 | 509 | 289 |

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



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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

| What | Why | How | Knowledge gaps |
|---|--|--|---|
| PrEP User: Decreased prevention practices with inadequate adherence | Risk assessment is inaccurate (misconception) | <ul style="list-style-type: none"> • Self-report • Monitor beliefs | <ul style="list-style-type: none"> • Will people overestimate their level of personal protection from PrEP? • Will changes in beliefs result in greater risk for HIV? |
| Community: Decrease in prevention practices as a result of presumed effects of PrEP in a community | Risk assessment is inaccurate (misconception) | <ul style="list-style-type: none"> • Survey | <ul style="list-style-type: none"> • Do community level beliefs change? • Does risk behavior change? |



Oral Preexposure Anti-HIV Prophylaxis for High-Risk U.S. Populations: Current Considerations in Light of New Findings

Gavin M. Myers, M.A.¹ and Kenneth H. Mayer, M.D.¹⁻³

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. This



Safety/Prevention Synergies?

| What | Support |
|---|---|
| Adherence | Education: benefits, risks and strategies Support: Skills building and motivation Monitoring |
| Safe Cycling | Education: benefits, risks and strategies Promote ease for safe restarts (responsive) Monitoring |
| Sexual Health Protection as multiple strategies | Compendium approach- what are you considering doing for protection from other STIs? |
| Help support decision making and respect choices | Must provide accurate information Frame adherence and risk reduction realistically Offer help Support choice |

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
- Albert Liu, SFDPH, EPIC study PI
- HPTN 067 Study team
- Sarit Golub, Hunter College



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