

**Pre-Exposure Prophylaxis For HIV:
Emerging Interpretations of
Findings**

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PrEP Awareness Low Even Among Sexually Active HIV- MSM Post-iPrEx Results

Study	HIV risk group	Location	n	PrEP knowledge (%)	PrEP use (%)
Kellerman (2004) ²⁷	80% gay/bisexual	Baltimore MD	104	20	6.8
	18% heterosexual	Detroit MI	170	19	2.0
		Oakland CA	139	18	1.6
		San Francisco CA	628	29	7.0
		Overall	1041	25	5.0
Nodin (2006) ²³	MSM	New York City NY	72	0.3	NR
Liu (2006) ¹⁹	MSM	San Francisco CA	403	20.0	NR
		San Diego CA	363	16.0	NR
		Overall	766	18.0	1.7
Mimiaga (2007) ²²	MSM	Boston, MA	227	18.9	<1.0
Golub (2007–2009) ¹⁷	MSM	New York City NY	180	23.2	1.7
Al-Tayyib (2008) ²⁵	MSM	Denver CO	425	21.4	NR
Barash (2009) ¹⁴	MSM	Seattle WA	215	22.3	2.0
Whiteside (2009–2010) ²⁹	90% heterosexual (56% male) 8% gay/bisexual	Columbia SC	27 ^c	22.2	NR
Brooks (2009) ^{15,16}	MSM	Los Angeles CA	50	0.0	0.0
Bautista (2011) ²⁸	MSM	Atlanta GA	418	30.0	2.0
Krakower (2010–2011) ²⁶	MSM	U.S. sample ^d			
		Pre-iPrEx results	289	12.5	0.7
		Post-iPrEx results	3387	19.0	0.9
		Overall	3676	18.5	0.9

Campbell, et al, *AJPM*, 2013

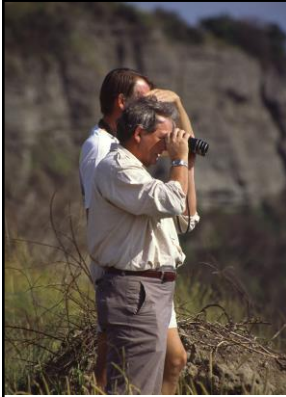
Concerns About PREP

- Not Protective Enough
- Too Few Use it Effectively
- Side Effects and Toxicity
- Drug Resistance
- Risk Compensation
- Access and Cost
- Stigma

Efficacy of Oral FTC/TDF PrEP “Intention to Treat” includes those who opt out

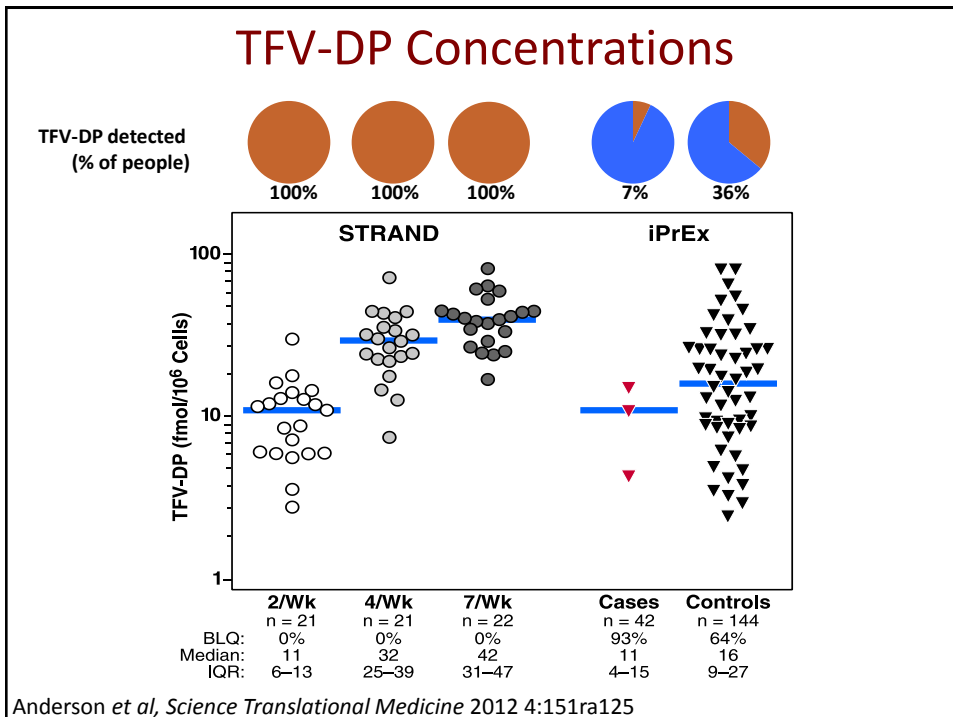
Trial	Population	Efficacy (%)	95% CI
iPrEx	MSM	42	18% to 60%
Partners PrEP	Men	84	49% to 94%
	Women	66	19% to 82%
TDF2	Men	80	25% to 97%
	Women	49	22% to 81%
FEM-PrEP	Women	6	-52% to 42%
VOICE	Women	-4	-50% to 30%

Grant RM, et al. *N Engl J Med.* 2010;363(27):2587-2599; Baeten JM, et al. *N Engl J Med.* 2012 July 11. [Epub ahead of print]; Thigpen MC, et al. *N Engl J Med.* 2012 July 11. [Epub ahead of print]; Van Damme L, et al. *N Engl J Med.* 2012 July 11. [Epub ahead of print], Marrazzo CROI 2013.



Intention to Treat: Analysis from the Investigators Perspective

- All who were offered PREP
- All who did not take any PREP
- All who took some PREP
- All those who left the study and came back later, sometimes months later after infection.
- No information about how PREP was taken is considered

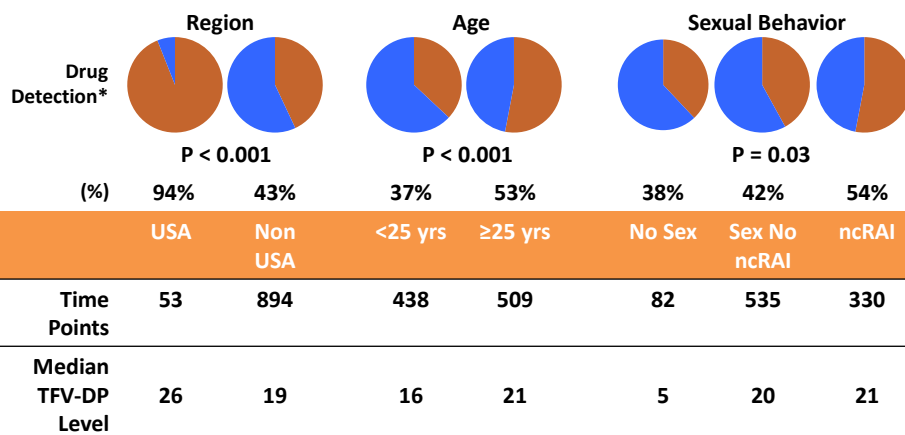


HIV Risk Reduction By Drug Concentration

Drug Concentration Commensurate with Doses	HIV Risk Reduction	95% Confidence Interval
2 per week	76%	56% to 96%
4 per week	96%	90% to >99%
7 per week	99%	96% to >99%

Anderson *et al*, *Science Translational Medicine* 2012 4:151ra125

TFV-DP Detection



*Detection of TFV/FTC/TFV-DP or FTC-TP in plasma or PBMC

How Clinical Trial Culture May Undermine PrEP Use

- Strong Culture of Compliance
 - Strict compliance with protocols
 - No negotiation around adherence
- Placebo and Blinding
 - Deception can be useful
- Visit Incentives
 - Money
 - Respect from authority
 - Swag
 - Community Activities

Ways to Increase Adherence in Clinical Practice

- Give the active drug
- Give information about safety and efficacy
- Client centered negotiation
- PrEP access as the main visit incentive

HIV and risk behaviour

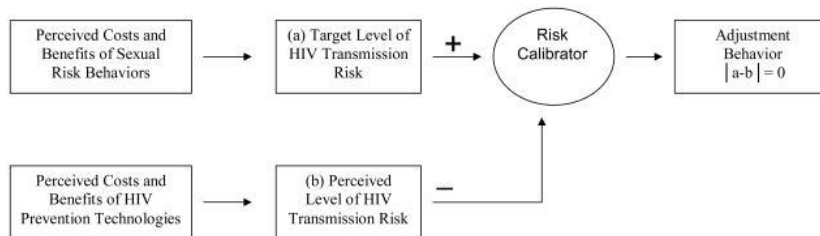
Risk compensation: the Achilles' heel of innovations in HIV prevention?

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

BMJ VOLUME 332 11 MARCH 2006 bmj.com

- Assumes a Rational Process In Sexual Decisions
- Predicts \uparrow Risk Behavior if \downarrow Risk Perception

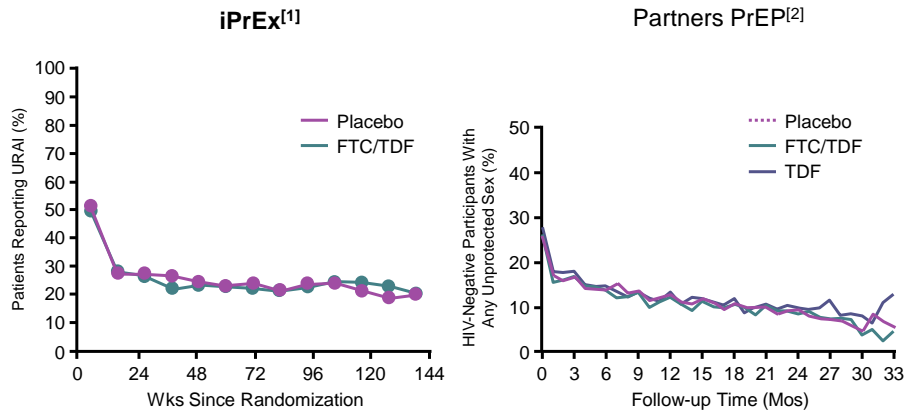


Adapted from Eaton et al, 2004

Denial
Cure for Fear



No Evidence of Risk Compensation in PrEP Clinical Trials



1. Grant R, et al. CROI 2011. Abstract 92. 2. Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print].

Why Behavior Becomes Safer During PREP Use?

- Less denial of HIV
 - Paralyzing fear replaced by action
 - Pills can serve as a daily reminder of imminent
 - Risk mitigation strategies thought through in calm moments over many days.
 - Acceptable solutions to the threat
- Social support
 - Regular consistent contact with testing, counseling, and peers focused on HIV
 - Acceptance of social and sexual goals



Reasons Given For Not Wanting PrEP: CASI at OLE enrollment, Check all that apply.

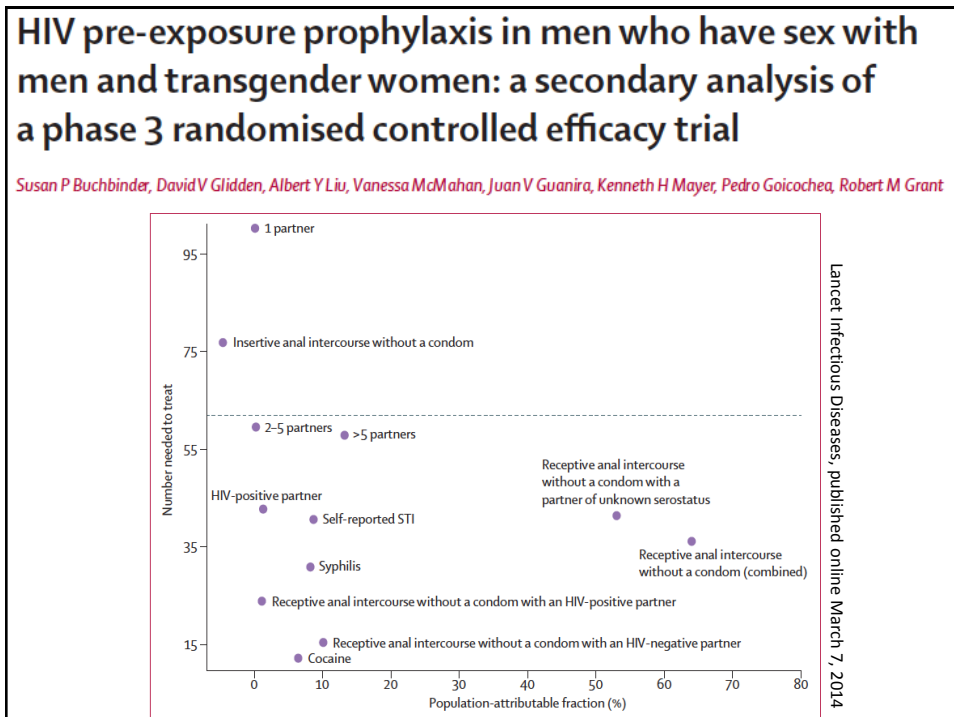
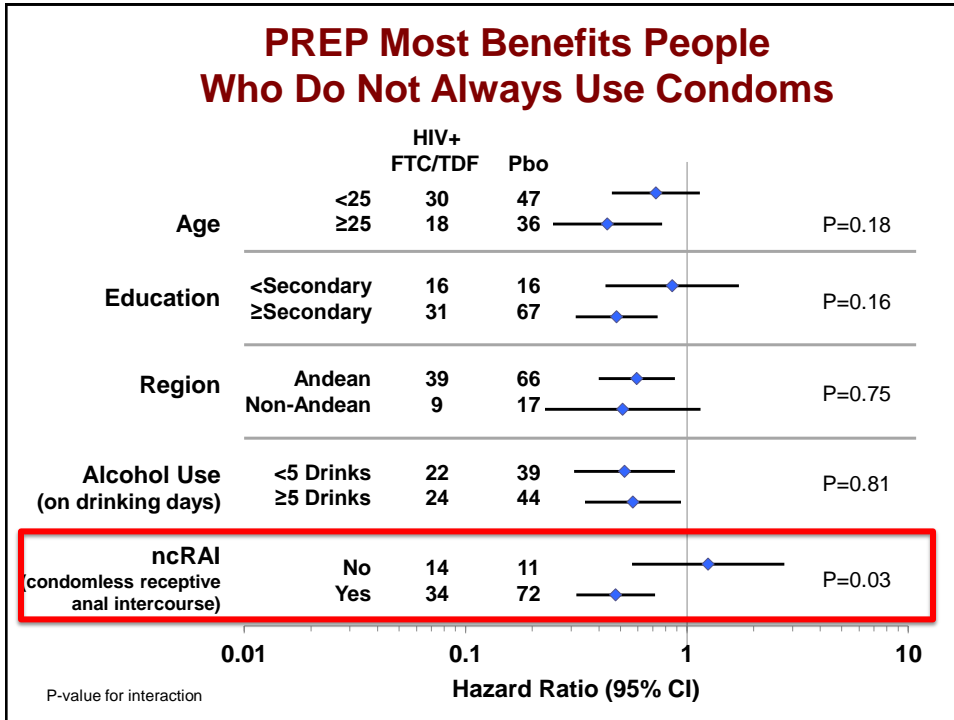
	%
I am concerned about side effects from the pills	49%
I can avoid HIV in other ways	14%
I don't like taking pills	12%
I am concerned that people will think that I am HIV positive because I am taking Truvada	7%
I am concerned that people will know that I have sex with men and/or trans people because I am taking Truvada	3%
I fear developing resistance to HIV medications if I became positive	9%
I don't want to take a pill every day	15%
None of the above	14%
Decline to state	16%

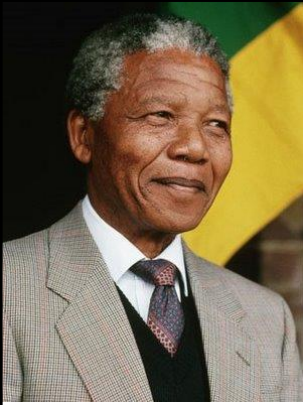
Grant et al, IAS Kuala Lumpur 2013



Oral FTC/TDF PREP Safety

- Trends toward safer behavior.
- Drug resistance only if infected before starting.
 - Such resistance limited to FTC, wanes in 6 months.
- No effect on liver, glucose, amylase, blood counts.
- Creatinine elevations in 1:200 users are reversible.
 - Do not recur when PREP is resumed.
 - No evidence of proximal tubulopathy.
- Nausea or Abdominal Cramping in <10%,
 - Resolved after the first weeks of use,
 - Not dose limiting.
- No alteration in lipids or body fat distribution.
 - 1% decrease in BMD in 6 months, does not progress, partially reverses when stopping.





It is never my custom to use words lightly. If twenty-seven years in prison have done anything to us, it was to use the silence of solitude to make us understand how precious words are and how real speech is in its impact upon the way people live or die.

Nelson Mandela,
International AIDS Conference
Durban, July 2000

A New HIV Prevention Lexicon?

- **Stigmatizing Words**
 - Them
 - Their needs
 - High risk people
 - Risk behavior
 - Targeting them
 - Discordant couple
 - Adherence
- **Alternative Words**
 - Us
 - Our desires
 - Popular, affectionate people
 - Intimate sex
 - Prioritizing and marketing
 - Courageous in love
 - Use

Conclusions

- The Efficacy Findings of Clinical Trials Require Interpretation
 - Intention to Treat is one Interpretation
 - Well suited for regulatory decision
 - As Taken
 - Better suited for informing prospective users
- Oral FTC/TDF PREP protects MSM from HIV if taken, and it can be taken.
 - The efficacy of PREP is in the hands and mouths of users.

