UK community perspective on PrEP and PROUD

Simon Collins

www.i-Base.info

Overview

- Community perspective on PrEP:
  3 myths and 5 community issues (Glasgow)
- The PROUD study and UK experience
- Update from CROI - February 2015
  - outstanding issues
- A few US ads (Glasgow)

Andrew, Andy B, Andy C, Chris M, Chris P, Richard, Chris W, Space,
Nick, Dolly, Wesley, Colvin, Jimi, Kevin, Mike, Paul, Mark, Steve.

Tsai C-C et al, Science 1995

Daily weight-based daily PMPA (tenofovir) SC for one month in 35 macaques inoculated IV with SIV (10 x 50% infectious dose): 5 arms, follow up 40-56 weeks.

Dose	Day started	n	% infected
20mg/kg	48 hrs pre	n=5	0
30mg/kg	48 hrs pre	n=10	0
30mg/kg	4 hrs post	n=5	0
30mg/kg	24 hrs post	n=5	0
Control	48 hrs pre	n=10	100

1. Tsai C-C et al, Prevention of SIV Infection in Macaques by (R)-9-(2-Phosphonylmethoxypropyl)adenine. Science 1995. (NIH funded).

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PrEP timeline

1995–2005: First macaque data with tenofovir. [1, 2, 3]

- Other ARVs may work but AZT did not.
- Driven by independent research & community needing alternatives to condoms.
- Never an industry priority.

2002: FDA approve tenofovir as ARV.

- Question to Bill Gates at CROI: “When I have sex with my HIV positive boyfriend should I take an HIV drug to protect me” – Dr Mike Youle. [4]
- Largest studies public/private funded. [5]

2012: US approval for tenofovir/FTC as PrEP.

1. Tsai C-C et al, Science 1995; 2. Van Rompay K et al, AIDS Res Hum Retroviruses 1998; 3. Otten R et al. J Vir, 2000. 4. Keynote lecture, CROI 2002, Seattle; 5. NIH, Gates Foundation. US CDC and Thailand MOPH.

People at high risk: women, transwomen, gay men, PWID

Situations when many people are at especially high risk. Not partner-dependent.

"…to benefit those who are less empowered to insist on condom use… HIV serodiscordant couples, sex workers, women wishing to conceive, and individuals unwilling to use condoms"
– Mike Youle, 2003

1. Youle M, JIAPAC, 2(3) 102-105, 2003. PWID: People Who Inject Drugs

Myth 1: pharma marketing

- Not pharma-driven: often donated ARV compounds.
- Limited commercial benefit.
- No PrEP marketing in US by Gilead.
- % use via patient assistance programmes.
- Broad use unlikely until after tenofovir patent expires in 2017.
- Target price close to condoms + lube or oral birth control or Viagra etc

Myth 2: Does PrEP work?

- Efficacy: does PrEP work if you take it?
- Yes in animals (all protected). [1, 2]
- Yes >95% with 4 doses a week (iPrEX). [3]
- No benefit if low adherence: research challenge to enrol people at risk. [4, 5]
- PROUD and IPERGAY report 86% efficacy: no infections on PrEP, no behavior changes. [6, 7]
- Good safety, few side effects or drug resistance.

1. Garcia-Lerma JG et al, PLoS Med, 2008; 2. Radzio J et al, PLoS One 2012. 3. Grant R et al, IAS 2014, Melbourne. 4. Van Damme L et al, FEM-PrEP, NEJM, 2012; 5. Marrazzo J et al, VOICE, CROI 2013.; 6. Abs 23LB, CROI 2015 ; 7. Abs 23LB CROI 2015.

Safety concerns

- Safety is a serious risk.
- HIV testing & safety monitoring essential.
- Potential for acute toxicity, interactions with NSAIDs (diclofenac). [1, 2]
- Risk:benefit will change depending on HIV risk.
- Potential pressure on sex workers to use PrEP instead of condoms. [3]
- Monitoring impact on STIs is important.
- Off-label use already occurring: street versions, PEP access, shared use.

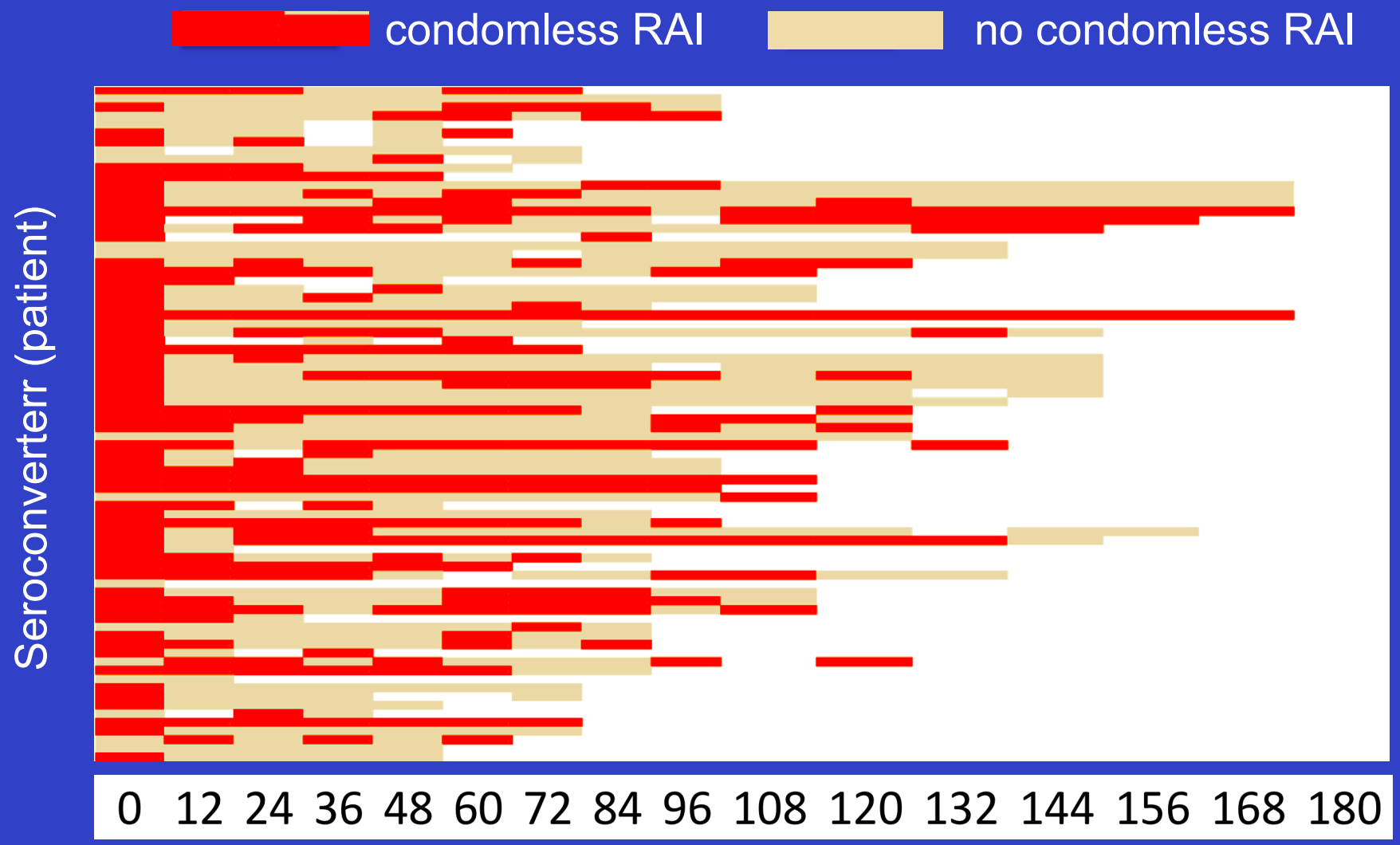
1. Morelle J et al, Clin Nephrol 2009; 2. Bickel M et al, HIV Med 2013; 3. US working group on PrEP and women, 2103.

Myth 3: medicalising sex

- OPTION = CHOICE.
- PrEP not for everyone: ~ 50% interest. [1, 2]
- Not to universally replace condoms.
- Not as lifelong treatment.
- Aim to “come through a higher risk period without HIV complicating the rest of life”.

1.Aghaizu A , BHIVA 2012. 2. Thng C, BHIVA 2012.

iPrEX: HIV risk is not constant



Grant R et al, CROI 2013, Atlanta.

Five community issues

- Dosing and PK: information to know how to use PrEP
- Deciding who should use PrEP?
- Condoms, language and STIs
- Quality of life: reduce fear, anxiety
- Cost and access: now and after 2017

Issues 1: PK of oral PrEP

PK = pharmacokinetics = absorption, metabolism and clearance of drugs in bodies

- Two drugs with different PK profiles.
- Levels in blood vs inside cells (active DP/TP)
- Tissue type: rectal >> vaginal/cervical >> plasma.
- Time to reach protective levels, how long levels last, single vs multiple dosing?
- Variability between different people: age, sex, weight
- Daily PrEP overcomes this complexity.

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Issue 2: Who should use PrEP?

- Defining need and risk is essential for access
- **Situation-based risk** is more useful to define HIV risk – rather than stereotypes [1, 2]

  - recent receptive anal sex without a condom?
  - relationship status/change in status?
  - sexual history: STIs, history of abuse?
  - recent PEP?
  - home life, employment, lifestyle stress?
  - alcohol and drug use, etc.

Issue 3: Condoms & STIs

- Condoms are effective but not popular.
- PrEP challenges 30 years of important public health and community work: but PrEP is an additional resource.
- Recommending PrEP should be used with condoms is not helpful. [1, 2]
- But no risk compensation in PrEP studies (used as a reason not to publicise condoms).
- Other STIs are important but the primary short term aim is to dramatically reduce HIV.

1. US CDC PrEP guidelines, 2014; 2. WHO PrEP guidelines, 2014,

Issue 4: Quality of life

- For three decades the impact of the fear of infection on QoL has been difficult to measure: before, during and after sex.
- PrEP and TasP can change this.
- Potential to normalise HIV: stigma remains high in high risk groups.
- Control over HIV risk is a motivation.
- Intimacy is a motivation.

Quality of Life

"I'm a doctor and I've started PrEP" [1]

"I am a 60-year-old gay man who has spent those same three decades trying to keep myself from becoming infected with HIV. I am tired of being scared, so I am starting on PrEP".
— Dr Howard Grossman, July 2014

1. Grossman H, I'm an HIV Physician. And I'm Starting PrEP. TheBody.com. July 2014.

Quality of Life

"It's not 1994, just go on PrEP, get over it."

– Dom, "New Looking", HBO

Storyline includes HIV positive character Eddie

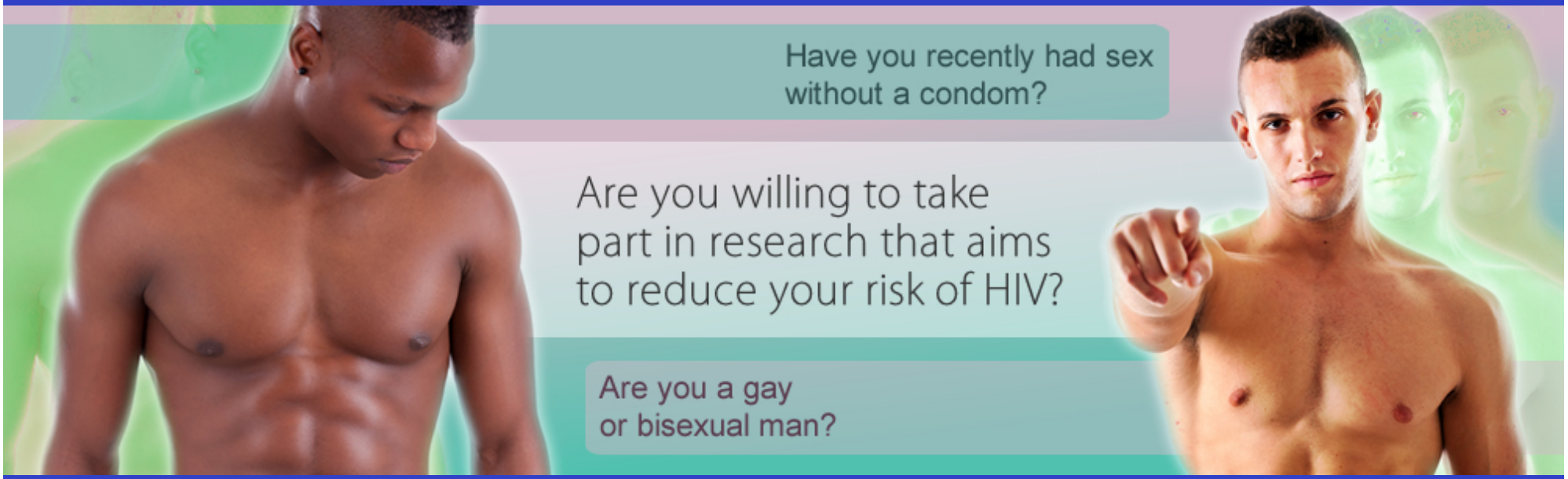
Quote from "New Looking", HBO.

Issue 5: Cost and access?

- In short term (now) community demand will affect how soon PrEP is available – role to generate demand?
- Highly cost effective now in people at high risk Very low NNT [3] (NNT=250 is cost effective)
- 2017 patent: generic $70 vs $4000/year.[1,2]
- Likely $200-300 ($25 a month).

1. CHAI, ARV Ceiling Price List, August 2014; 2. Hill A et al, CROI 2006; 3. . Buchbinder SP et al. Lancet, June 2014.

UK PROUD study



PROUD

Examining the impact on gay men of using Pre-Exposure Prophylaxis (PrEP)

www.proud.mrc.ac.uk

UK PROUD study

- Pilot study – to test enrolment and behaviour (3000 people needed to show efficacy)
- 545 MSM and trans women – all for 2 years
- Randomised to immediate or deferred PrEP after 12 months (plus sexual advice, condoms, support, questionnaires etc for all)
- 79% white, 80% employed, 60% graduate
  10 partners in previous 3 months
  Highly aware of HIV: ~ 3 tests in last year
  30% had used PEP, 30% recent STIs

www.proud.mrc.ac.uk

UK PROUD study

- Nov 2012 – trial starts
- Nov 2013 – over 300 people enrolled
- May 2014 – Safety group formed
- Oct 2014 – Deferred arm stopped due to early efficacy
- Oct 2014 – IPERGAY study stops placebo arm stopped due to early efficacy

www.proud.mrc.ac.uk

UK PROUD IDMC

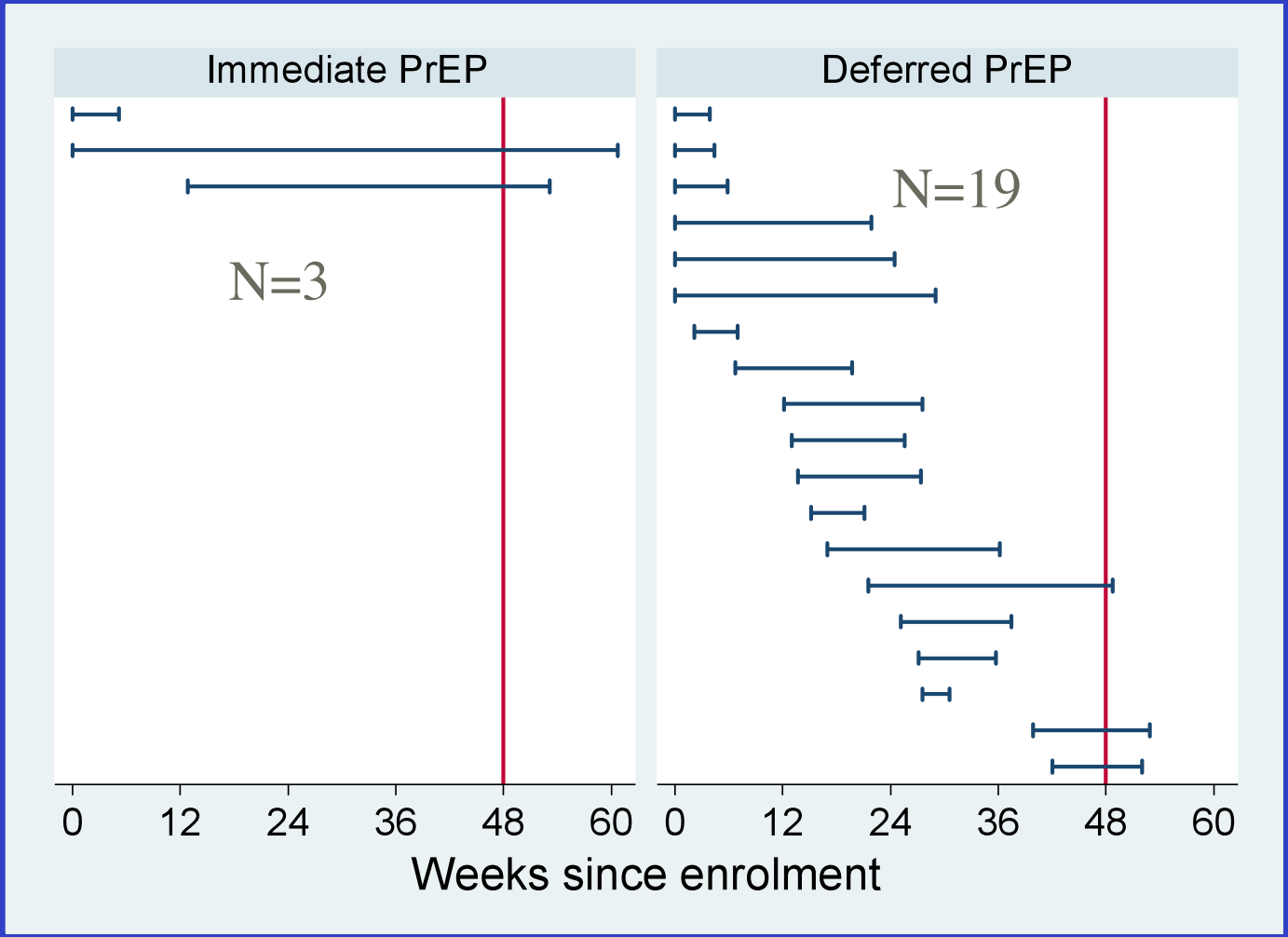
- Independent Data Monitoring Committee
- Small group (3) experts to oversee safety issues – can see unblinded results
- Set up in May 2014 as HIV rate was higher than expected
- Decided criteria / rules for stopping – this is major decision for any study
- Recommended stopping in October 2014 because efficacy was already proven with no likelihood that longer follow-up would change

UK PROUD study

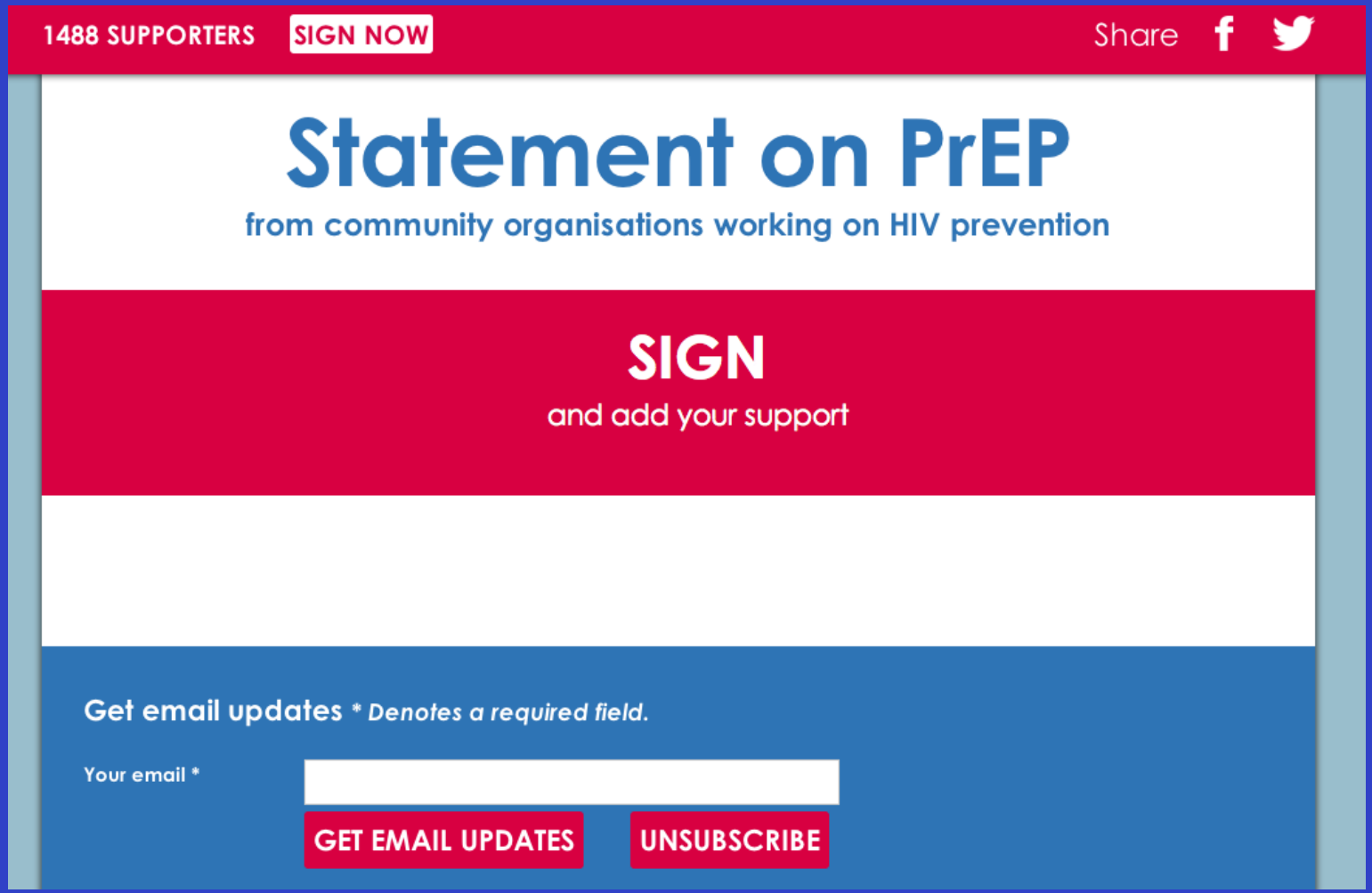
Results from CROI 2015: (at month 12 or Oct 2014 stop date)

- 453 patient years of follow up
- 22 HIV infections: 3 in PrEP vs 19 in deferred
- HIV rate: 1.3 vs 8.9 per 100 PY
- 86% risk reduction (90%CI 58%-98%), p=0.0002
- NNT = 13 (to prevent 1 infection over 1 year)

New HIV infections



PrEP community statement – more than 1200 signatures in a few weeks



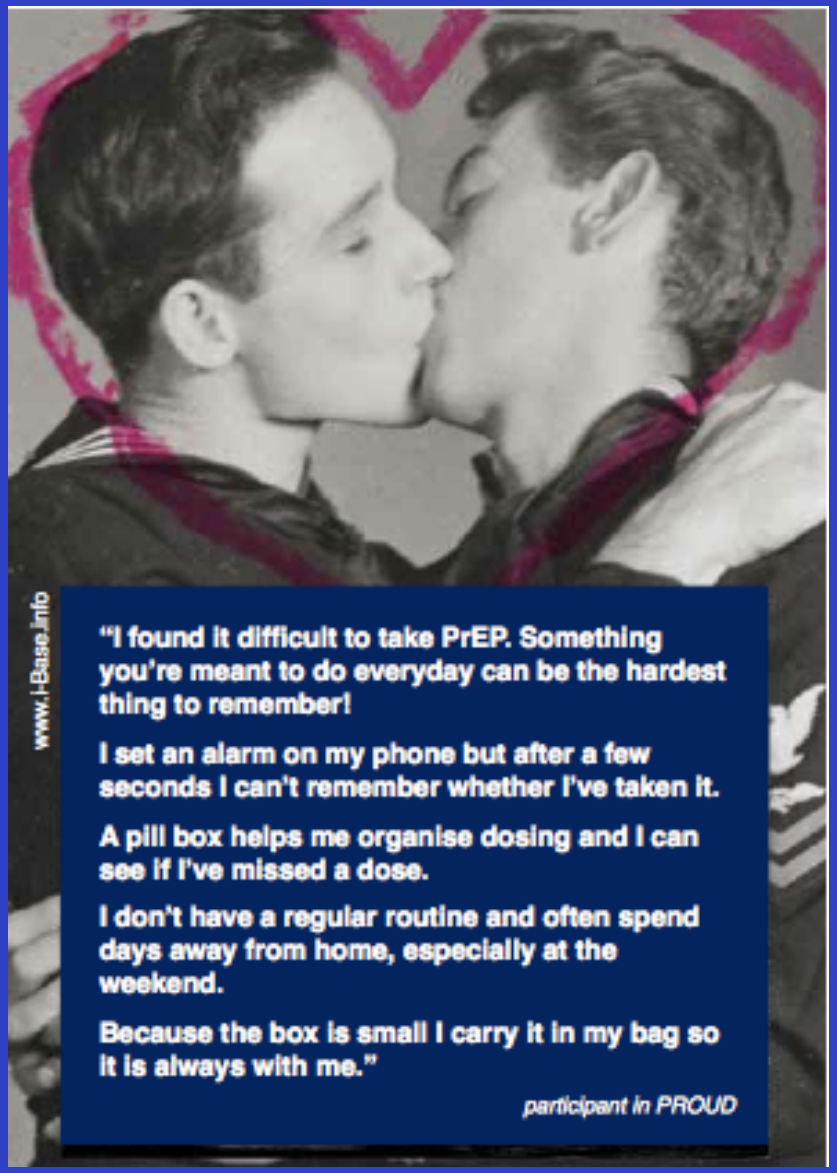
www.prepaccess.org.uk

ACT-UP London, for NHS PrEP meeting, December 2014

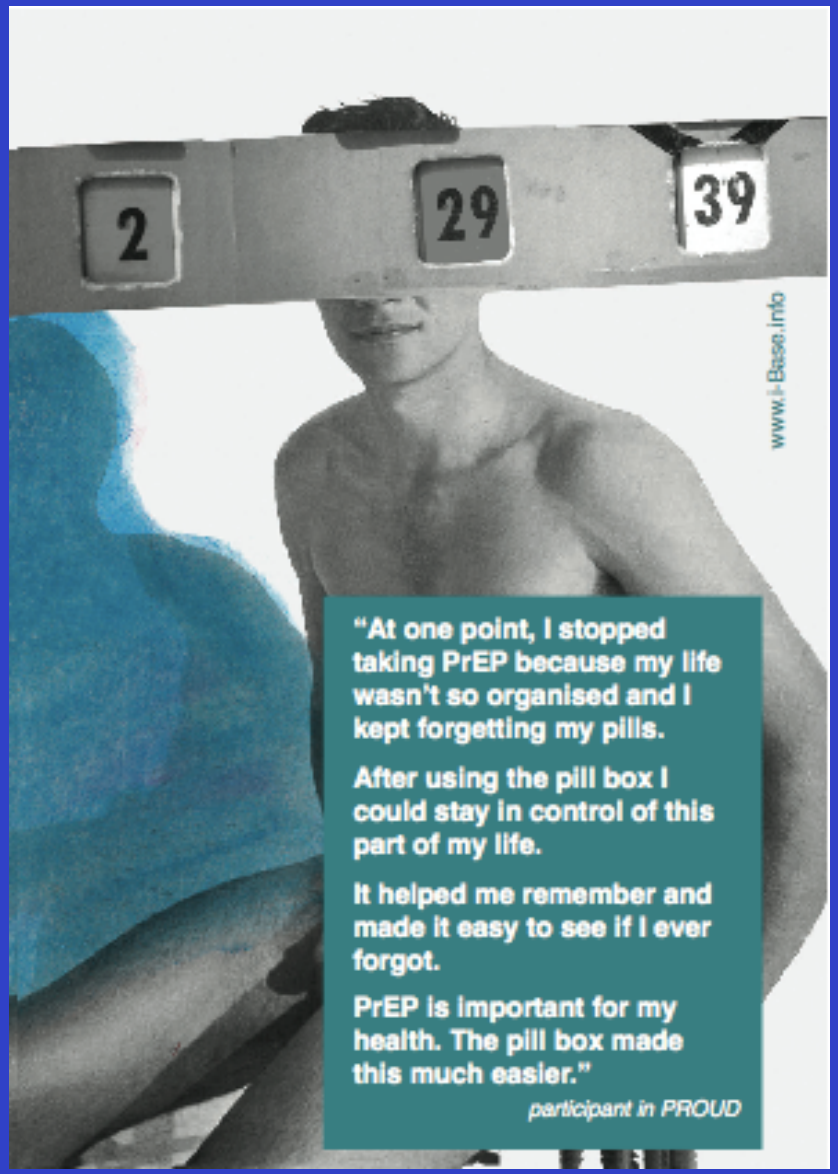
Adherence

Develop adherence support – worked for ART.

4+ doses a week for men
6-7 doses a week for women


"I found it difficult to take PrEP. Something you're meant to do everyday can be the hardest thing to remember!
I set an alarm on my phone but after a few seconds I can't remember whether I've taken it.
A pill box helps me organise dosing and I can see if I've missed a dose.
I don't have a regular routine and often spend days away from home, especially at the weekend.
Because the box is small I carry it in my bag so it is always with me."
participant in PROUD
www.i-Base.info


"I am HIV positive but I wish PrEP was available years ago.
I'm doing really well as I've been on meds for years. I rarely miss a dose because I use a pill box that shows if I've taken them.
I find this makes a big difference.
It seems crazy to miss out from the protection from PrEP when something that is this easy to use can help."
HIV+ advocate at i-Base
www.i-Base.info



www.i-Base.info

i-base

i-Base supports the PROUD study.
We know that a pill box makes life easier for people taking meds.

The results from using PrEP are really impressive. We hope this pill box helps.

Life can be exciting, tough and challenging. In 2015, it doesn't need to include HIV...

Information about HIV treatment and PrEP

0808 800 6013

questions@i-Base.org.uk

www.i-Base.info

any feedback: feedback@i-Base.org.uk
any questions: questions@i-Base.org.uk

CROI 2015

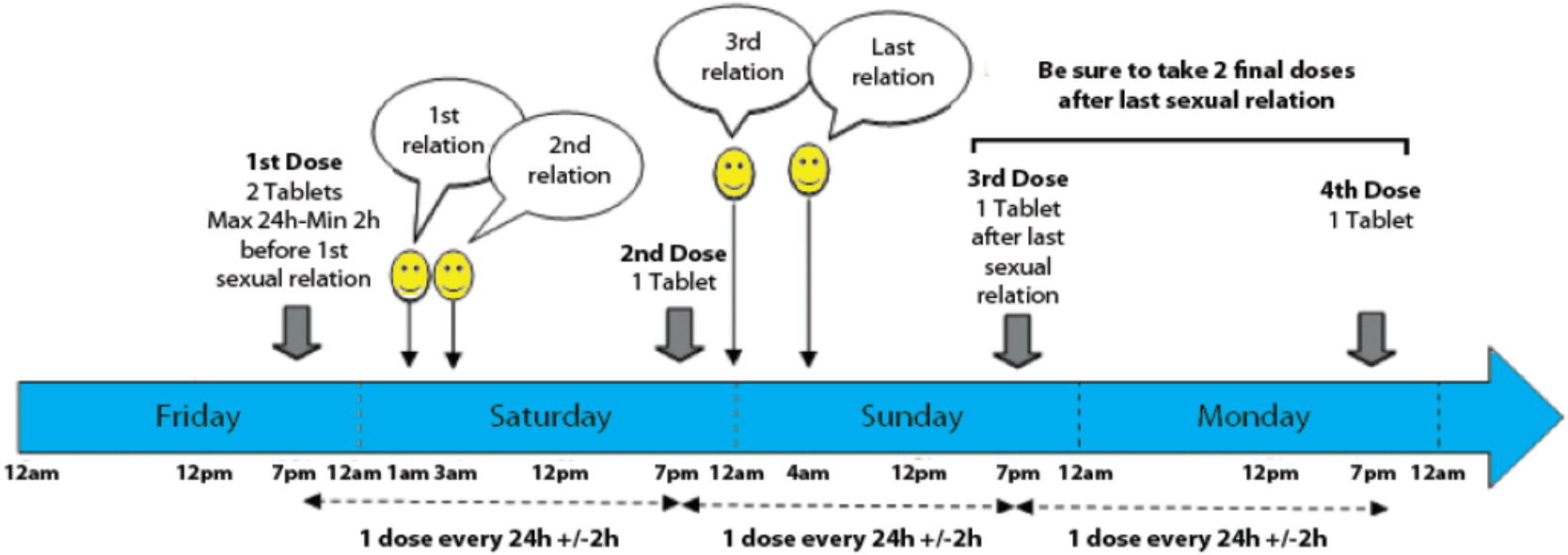
www.croiconference.org

- PROUD & IPERGAY studies [1, 2]
  - 86% efficacy
  - no infections in people taking PrEP
  - no behaviour changes
- Reducing HIV in San Francisco [3]
- Bridging PrEP for serodifferent couples. [4, 5]
- Daily vs intermittent in practice [6]
- Tenofovir gel –FACT 001 study. [7]
- Men vs women. [8]

CROI 2015: 1. Abs 23LB; 2. Abs 23LB; 3. Abs 25; 4. Abs 24; 5. Abs 989; 6. Abs 978LB; 7. Abs 26LB. 8. Abs 20.

ipergay
ANRS

- **Regimen = Two Truvada 2 to 24 hours before sex, one tablet within 24 hours after sex, and another tablet within 48 hours after sex.**

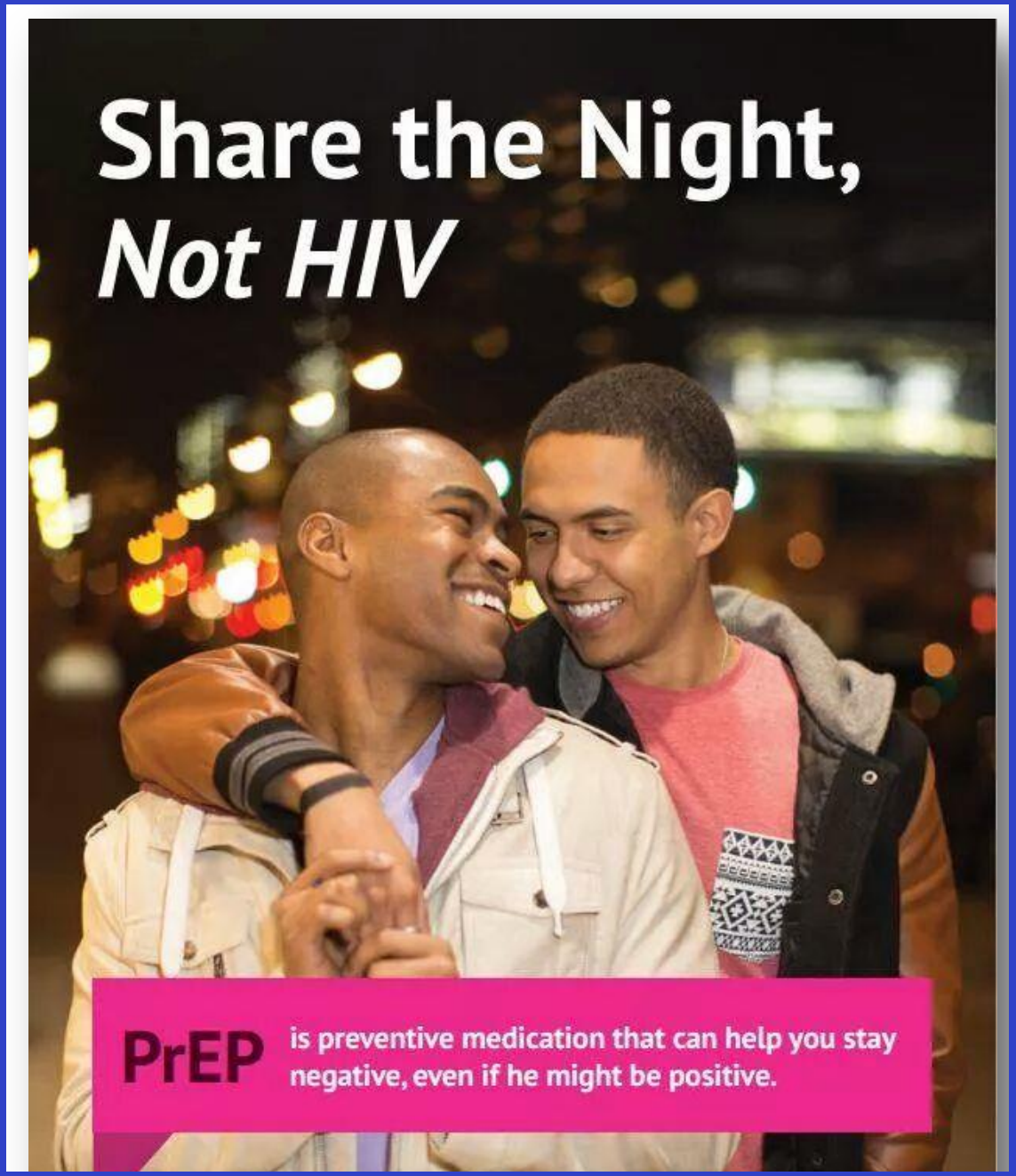


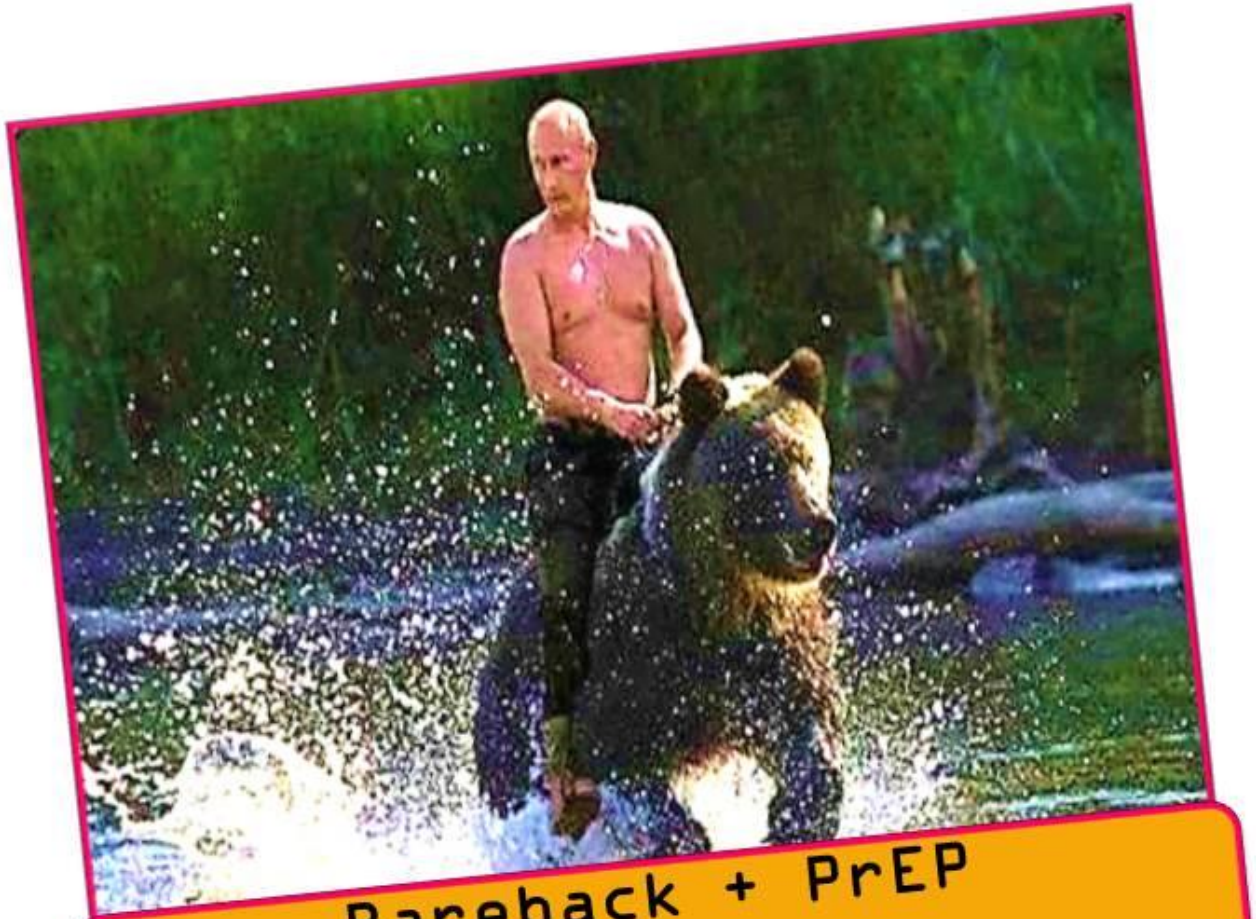
IPERGAY questions

- One-time sex involves minimum of 4 pills: double-dose before, 1 same day, 1 day after
- Most follow-up used 4 doses a week
- Doesn't provide answer to very intermittent use
- Safety issues with double-dose?
- Interpretation: more evidence to support 4-7 dose/week for men with 1-2 week lead and 7 doses/week for women with 3 wk lead in

Conclusions

- PrEP clearly works but you need to take it.
- Cost effective if risk is high: low NNT.
- Generics make PrEP even more affordable.
- Support for adherence.
- EU regulatory block: why this bottleneck?
- Future: PrEP may include different drugs, long-acting injections, formulations.
- Community roles for awareness, education and access.


Share the Night,
Not HIV
PrEP
is preventive medication that can help you stay negative, even if he might be positive.



Bareback + PrEP
= Safer Sex

Learn about PrEP
click myprepexperience.blogspot.com

My PrEP experience


THURSDAY, OCTOBER 17, 2013
6:00 PM TO 9:00 PM • FREE EVENT
CLICK HERE TO
RSVP
AND FOR MORE INFO!
HOSTED BY
PRINCE
MAGNETO EBONY
AND
FATHER
MEMPHIS KHAN
Raw Sex
DID IT JUST GET SAFER?
RSP
Care 2 PREVENT
YPS
THE PrEP EXPERIENCE TALK SHOW & MINI BALL
TALK SHOW GUESTS INCLUDE EXPERTS STUDYING PREP AND PEOPLE
USING PREP TO PREVENT HIV INFECTION.
UNIVERSITY OF CHICAGO | SCHOOL OF SOCIAL SERVICE ADMINISTRATION
969 E. 60TH ST


Name a common side effect from taking PrEP.
Peace of mind.
Learn about PrEP – www.myprepexperience.blogspot.com

My PrEP experience

myprepexperience.blogspot.com

Find out how PrEP can protect you -

In this sample of men who are in a relationship with a perceived HIV-negative man, we found that ***intimacy motivation was the strongest predictor*** *of adopting PrEP.*

"Intimacy Motivations and Pre-exposure Prophylaxis (PrEP) Adoption Intentions Among HIV-Negative Men Who Have Sex with Men (MSM) in Romantic Relationships"
– Annals of Behavioral Medicine
August 2014

Thank you

www.i-base.info

www.ukcab.net

PrEP efficacy

- iPrEX: n=2499; med fu 1.2 yrs. [1]

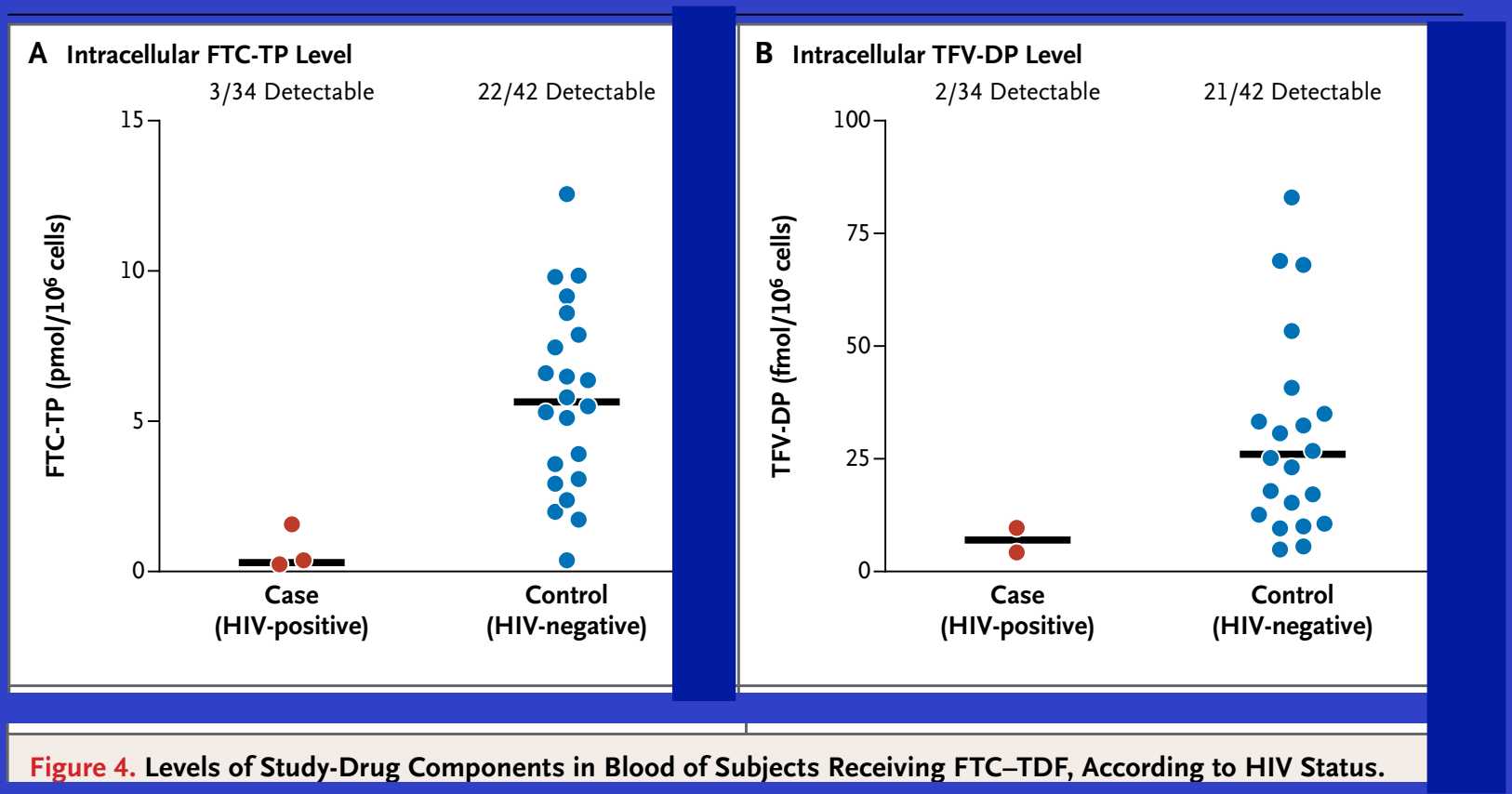


Figure 4. Levels of Study-Drug Components in Blood of Subjects Receiving FTC–TDF, According to HIV Status.

1. Grant R et al, NEJM, 2010.

Efficacy in iPrEX-OLE [1]

Table 1: Incident HIV infections in pts on PrEP by dry blood spot drug exposure

Drug levels (fmol/punch)	BLQ	LLOQ -350	350-699	700-1249	>1250
Estimated weekly dose	none	<2	2-3	4-6	7
% of follow-up time	25%	26%	12%	21%	12%
Patient years	384	399	179	316	181
Number of new infections	18	9	1	0	0
HIV incidence (95% CI)	4·70(2·99-7·76)	2·25(1·19-4·79)	0·56(0·00-2·50)	0·00(0·00-0·61)	0·00(0·00-1·06)
Risk reductions (95%CI)		**44% (-31 to 77%)**	**84% (21 to 99%)**	**100% (86-100%)**	

Key: BLQ: below limit of quantification; LLOQ: lower limit of quantification;

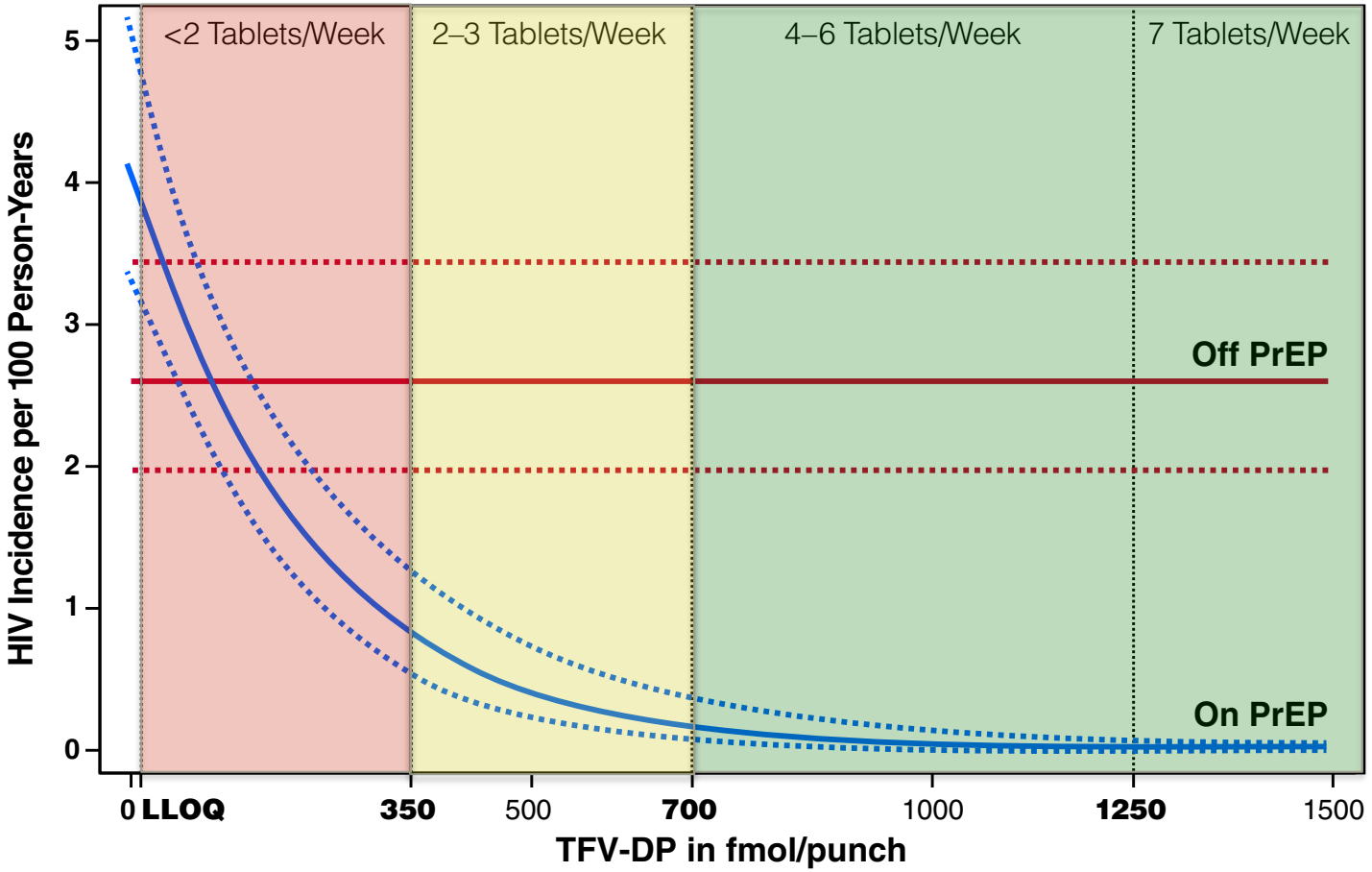
1. Grant R et al, iPrEX-OLE, IAS 2014, Melbourne.

Funding: US NIH

HIV incidence and drug concentrations

Grant et al. IAS, 2014, Lancet ID July 2014.

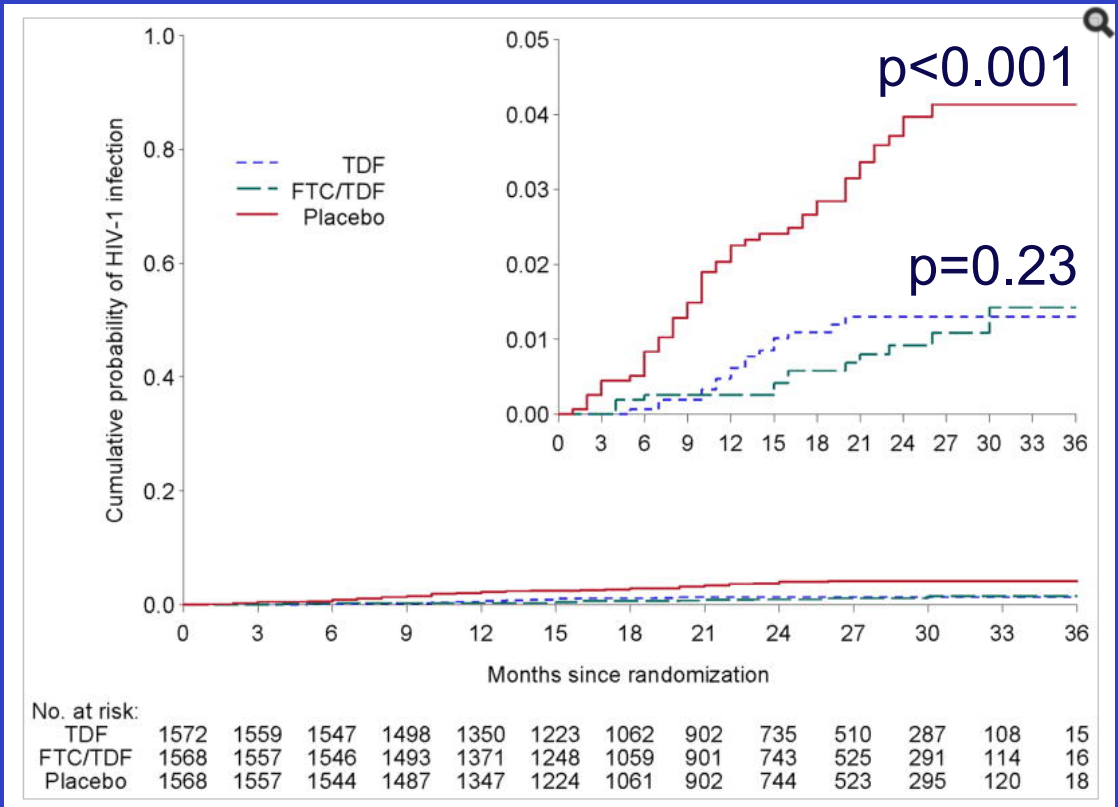
Funding:
US NIH



Follow-up %	26%	12%	21%	12%
Risk Reduction	44%	84%	100%	100%
95% CI	-31 to 77%	21 to 99%	86 to 100% (combined)	

Efficacy in Partners PrEP[1]

Table 2: Kaplan-Meier curve for the primary modified ITT analysis



Heterosexual study in Kenya and Uganda.
N=4758.
38% HIV neg partners were women.

		+ve
	PCB	52
75%	TDF/FTC	13
67%	TDF	17

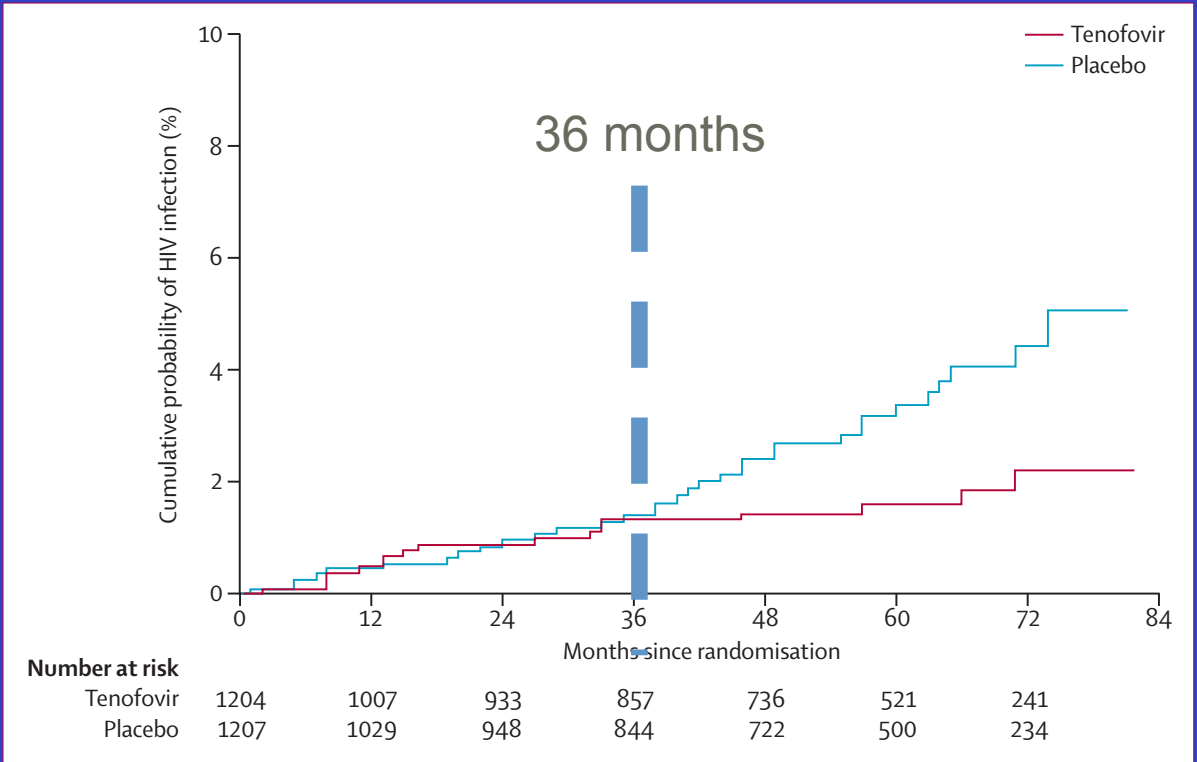
31% vs 81% detectable TNF at seroconversion visit

1. Baeten JR et al, NEJM, 2012.

Funding: Bill & Melinda Gates

Bangkok tenofovir study

Figure 2: Kaplan-Meier estimates of time to HIV infection (modified ITT)



3 years follow-up:
27 infections (13 vs 14)

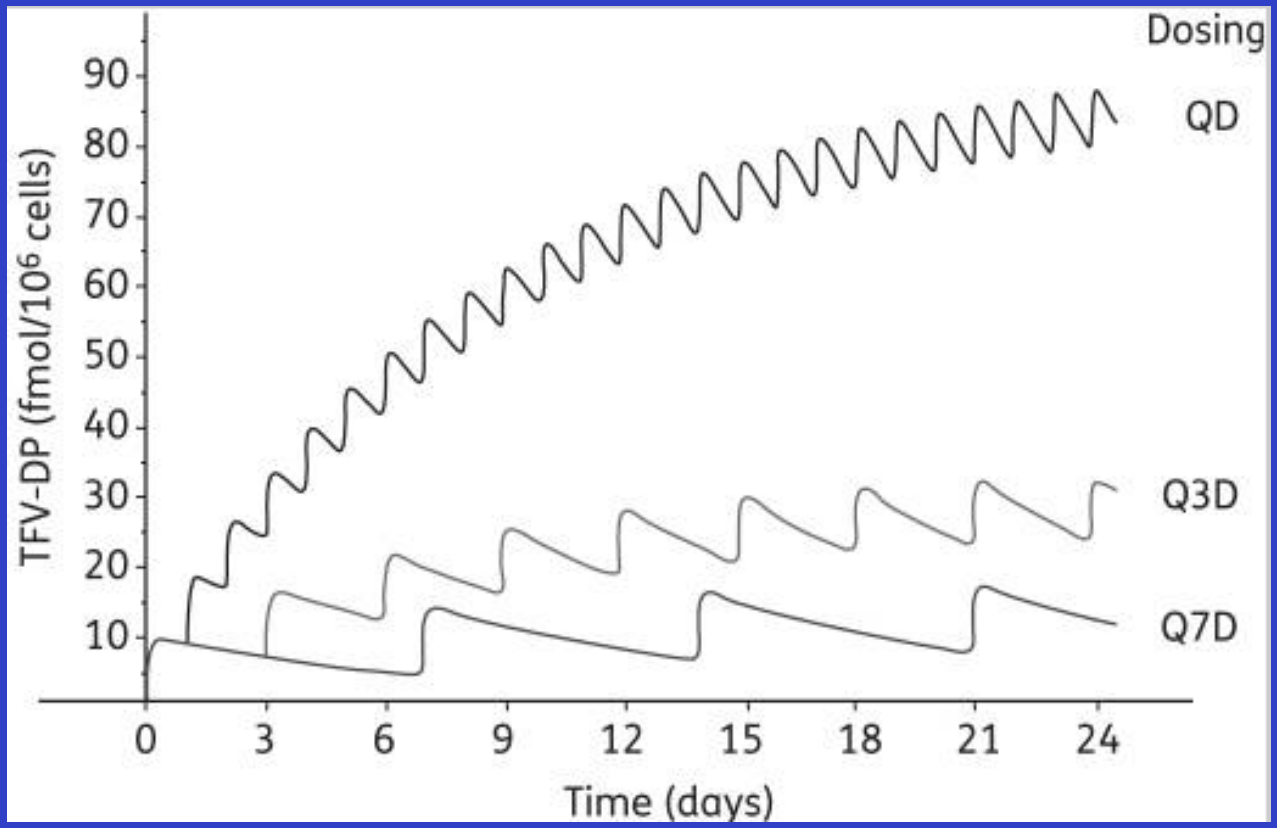
5 years follow-up:
50 infections (17 vs 33)

16 infections averted overall

15 infection averted in final two years (4 vs 19)

1. Choopanya K et al Bangkok tenofovir study (Lancet 2013).

How drug levels in cells vary by 1, 3, and 7 days/week dosing



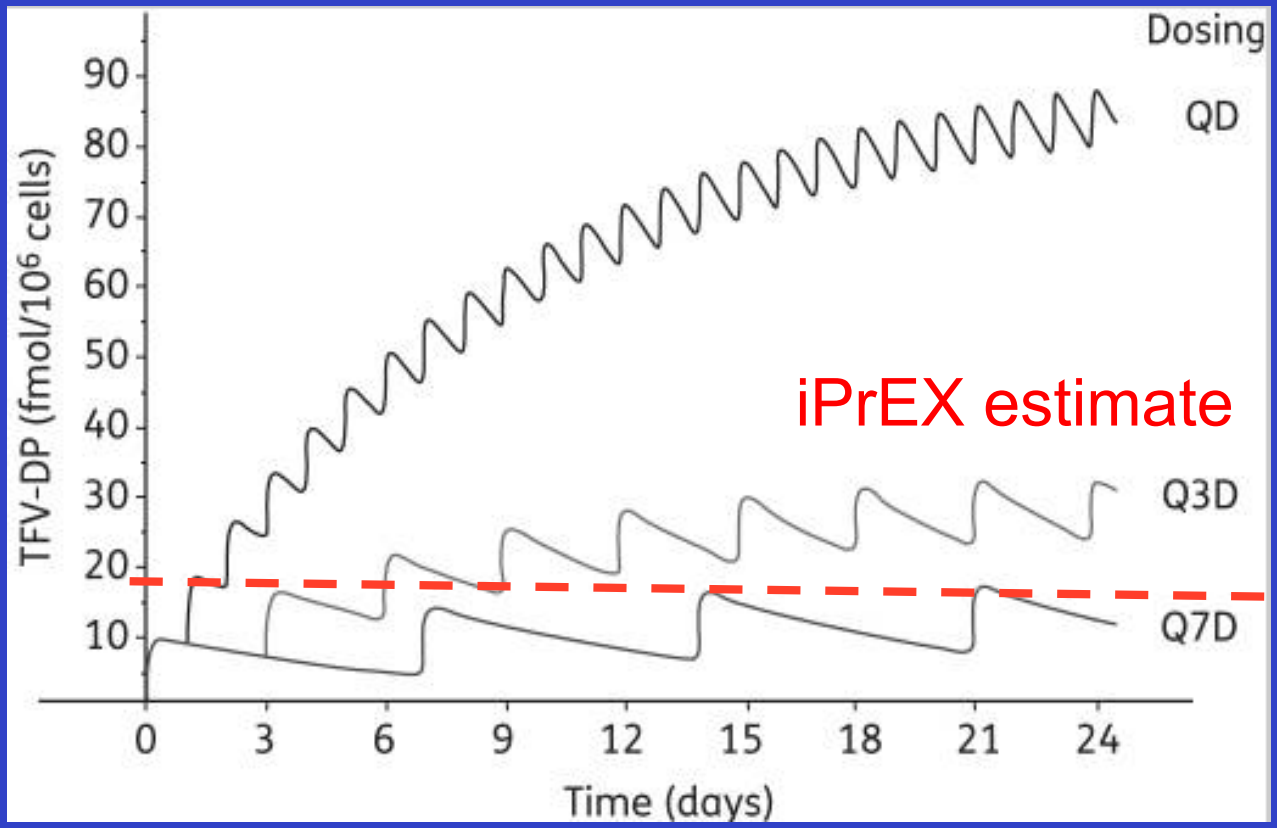
TFV
Daily (QD)

Every 3 days (Q3D);

Once weekly (Q7D).

1. Anderson PL, J Antimicrob Chemother 2011; 66: 240–250; 2. 2. Anderson P et al, CROI 2012.

How drug levels in cells vary by 1, 3, and 7 days/week dosing



TFV
Daily (QD)

Every 3 days (Q3D);

Once weekly (Q7D).

In iPrEX – 4 doses a week ~16 fmol/M (95%CI 3-28) [2]

1. Anderson PL, J Antimicrob Chemother 2011; 66: 240–250; 2. 2. Anderson P et al, CROI 2012.