HIV Prevention Strategies

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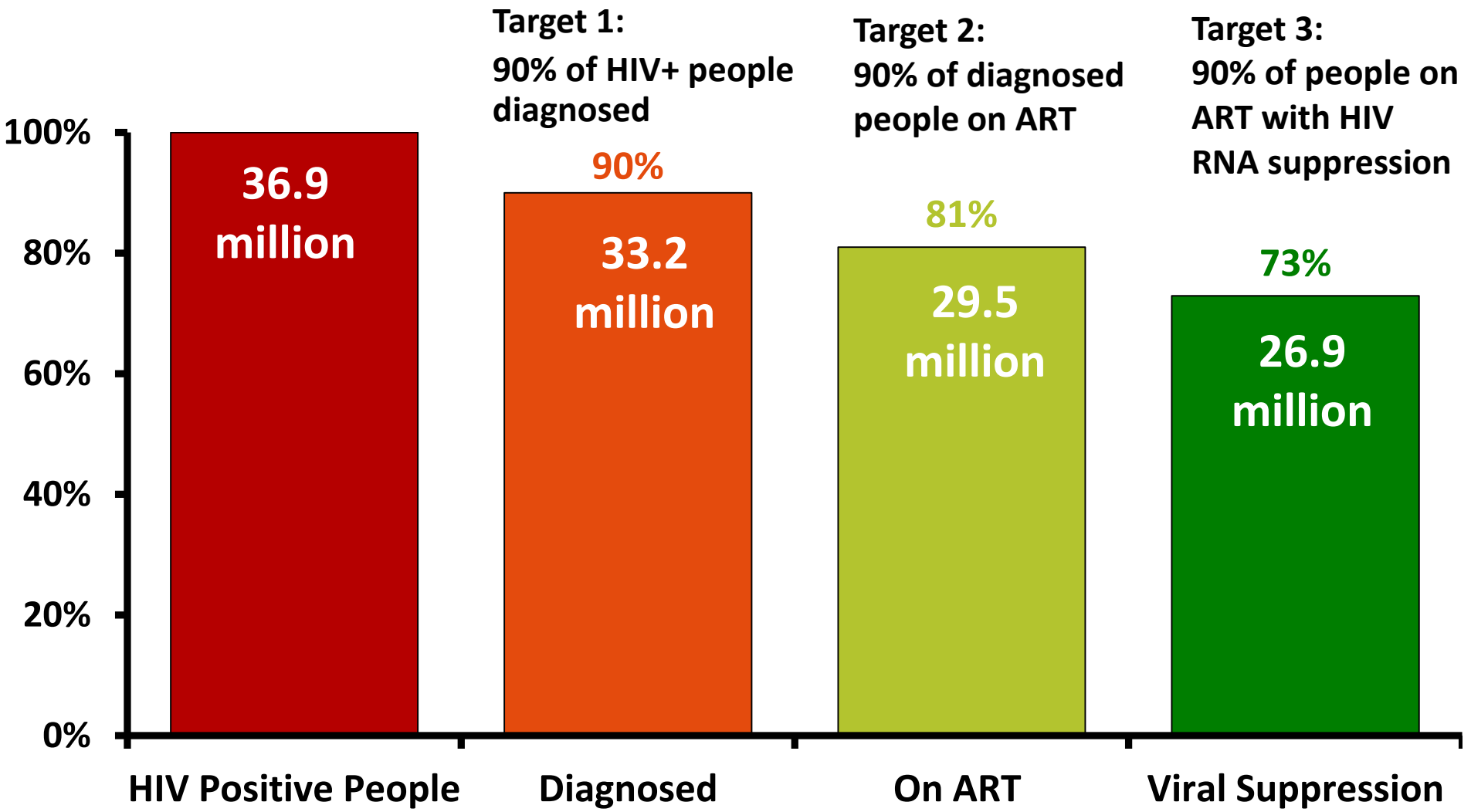
Summary of the global HIV epidemic (2017)

	People living with HIV in 2017	People newly infected with HIV in 2017	HIV-related deaths 2017
Total	36.9 million [31.1 million – 43.9 million]	1.8 million [1.4 million – 2.4 million]	940 000 [670 000 – 1.3 million]
Adults	35.1 million [29.6 million – 41.7 million]	1.6 million [1.3 million – 2.1 million]	830 000 [590 000 – 1.2 million]
Women	18.2 million [15.6 million – 21.4 million]	–	–
Men	16.8 million [13.9 million – 20.4 million]	–	–
Children (<15 years)	1.8 million [1.3 million – 2.4 million]	180 000 [110 000 – 260 000]	110 000 [63 000 – 160 000]

Source: UNAIDS/WHO estimates

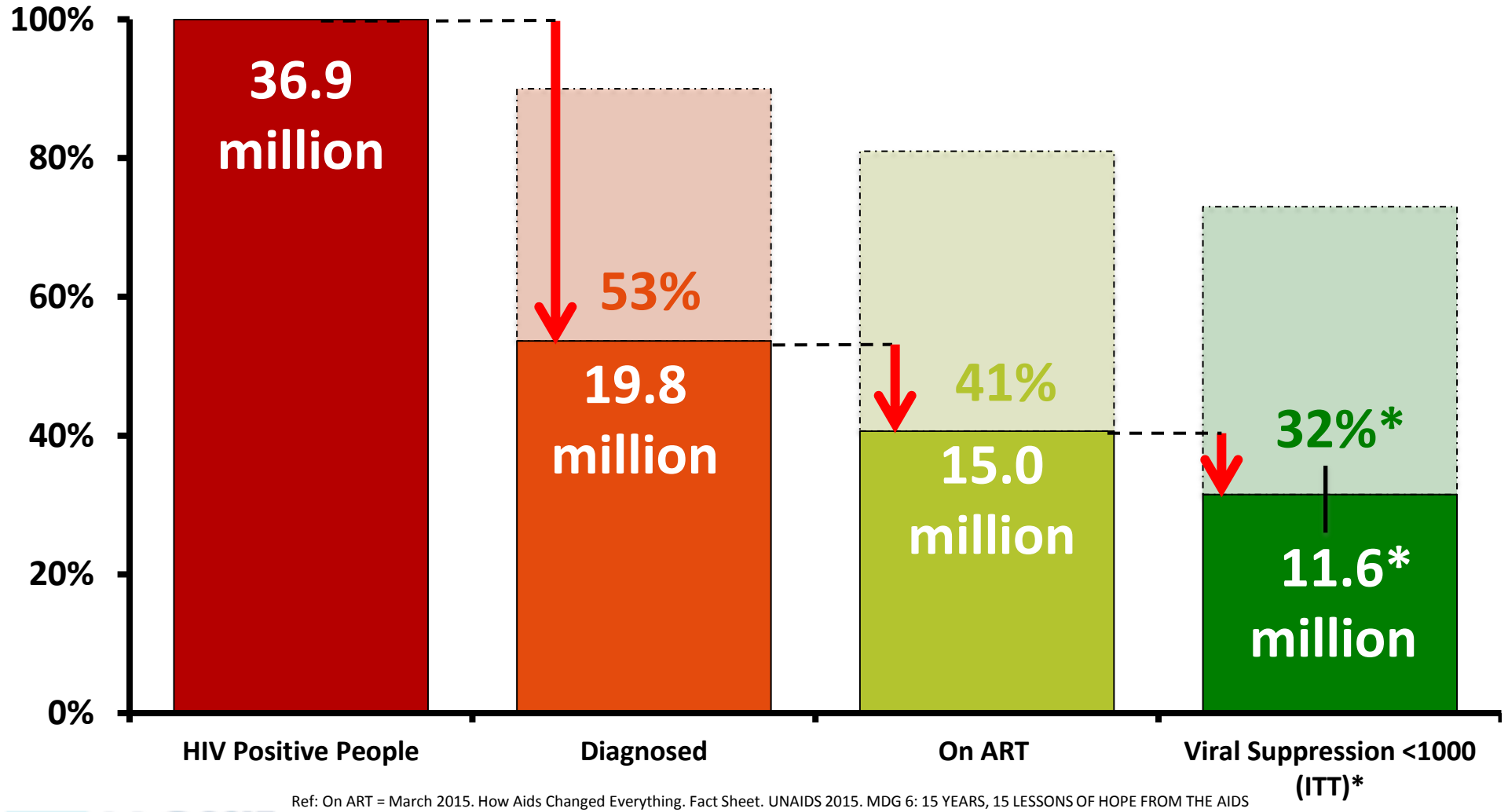
World Health Organization

UNAIDS 90-90-90:
HIV Treatment Targets for 2020 with Global Estimates (2014)



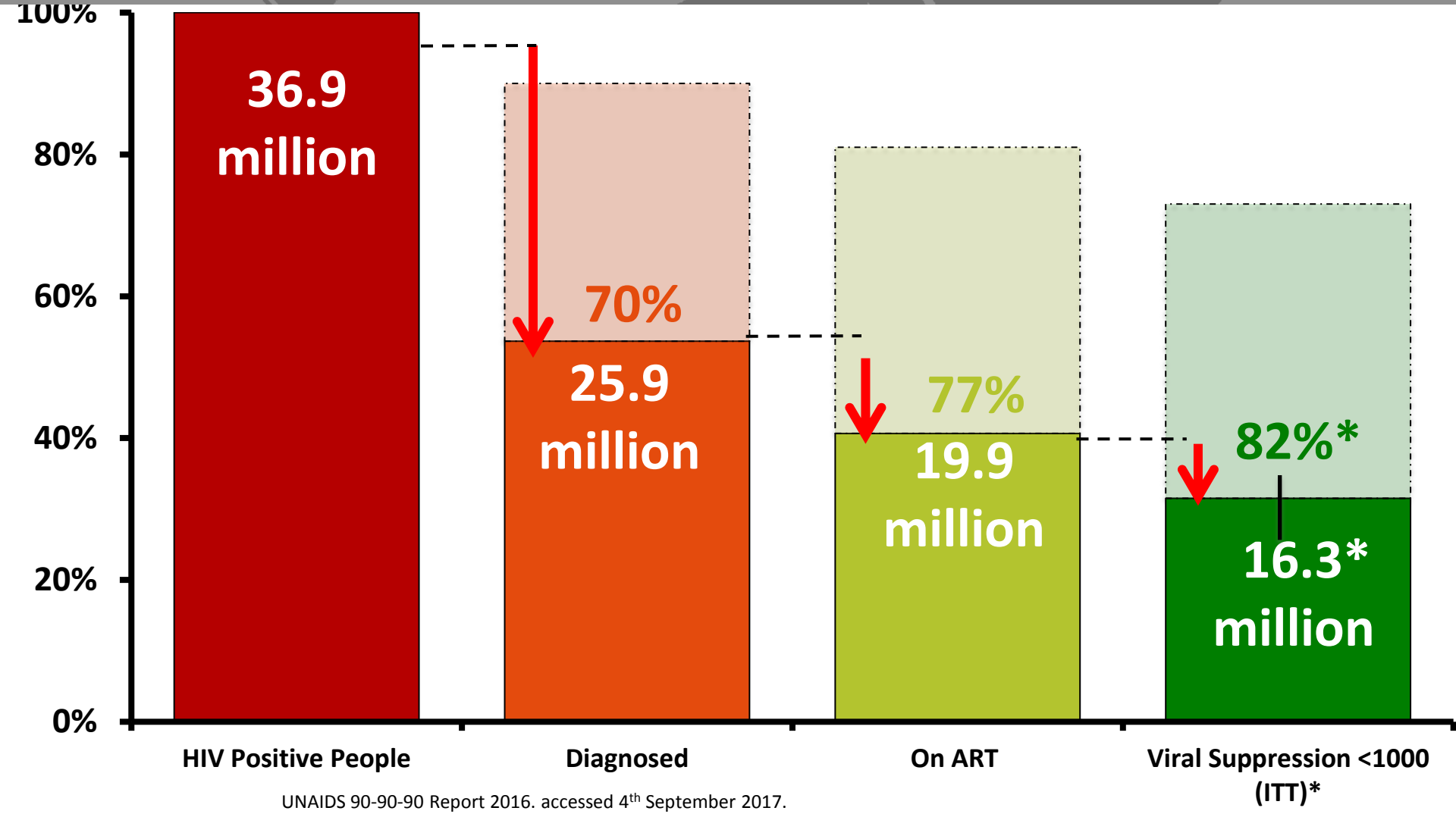
Ref: The Joint United Nations Programme on HIV/AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014; JC2684 (Numbers as of March 2015) How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015.

Global Estimates (2014-15) vs the Gap to reach 90-90-90 Targets



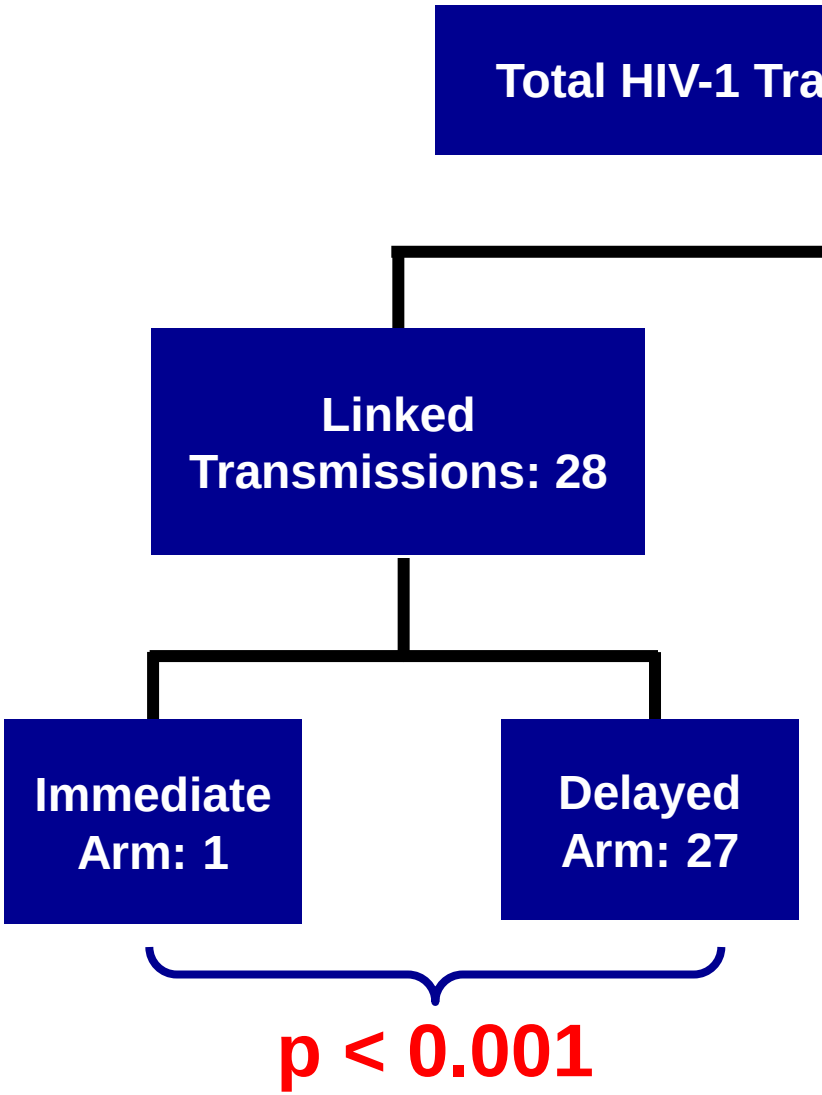
Ref: On ART = March 2015. How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015. * Average viral suppression% Intention to Treat LMIC rate from a Systematic Review by McMahon J. et al. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review." *Bulletin of the World Health Organization* 91.5 (2013): 377-385.

Global Estimates (2017) vs the Gap to reach 90-90-90 Targets



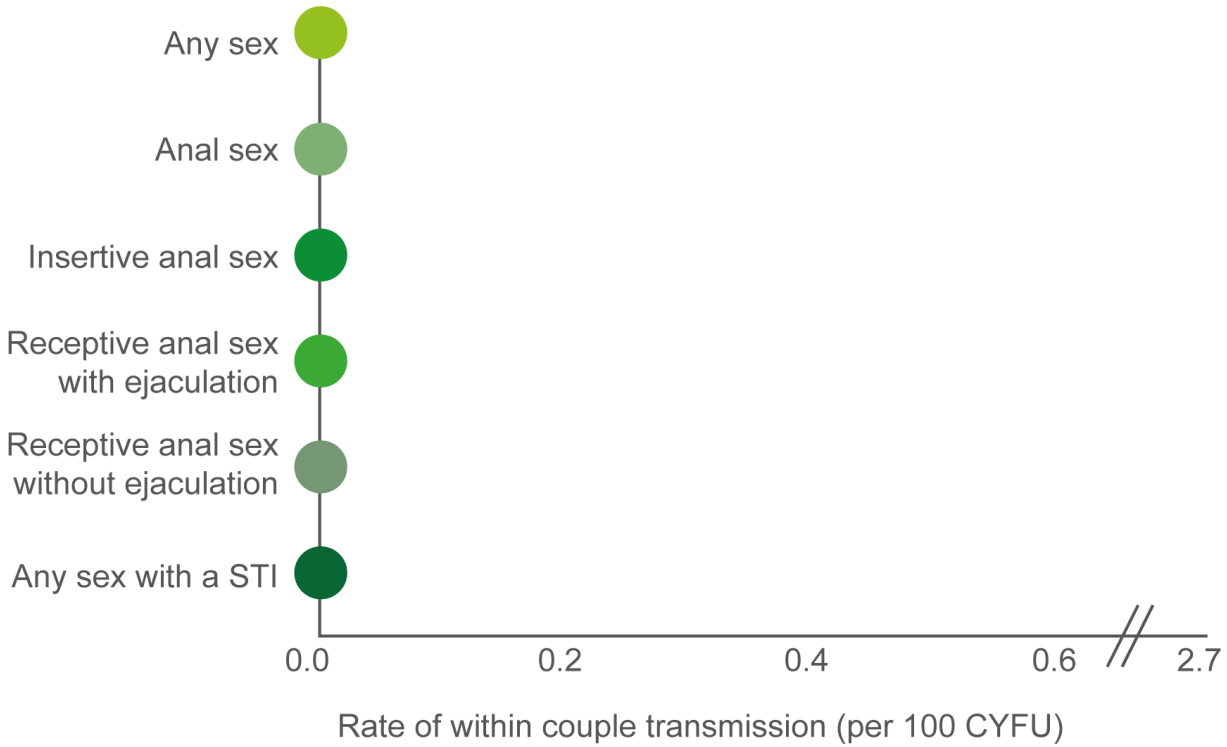
UNAIDS 90-90-90 Report 2016. accessed 4th September 2017.

HPTN 052: HIV-1 Transmission



- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

Rate of HIV transmission according to sexual behaviour reported by the negative partner



	Linked transmissions	Upper 95% CL	CYFU	CLS acts
Any sex	0	0.23	1596	76991
Anal sex	0	0.24	1546	70743
Insertive anal sex	0	0.27	1345	52572
Receptive anal sex with ejaculation	0	0.57	652	20770
Receptive anal sex without ejaculation	0	0.43	867	23153
Any sex with a STI	0	2.74	135	6301

PARTNER

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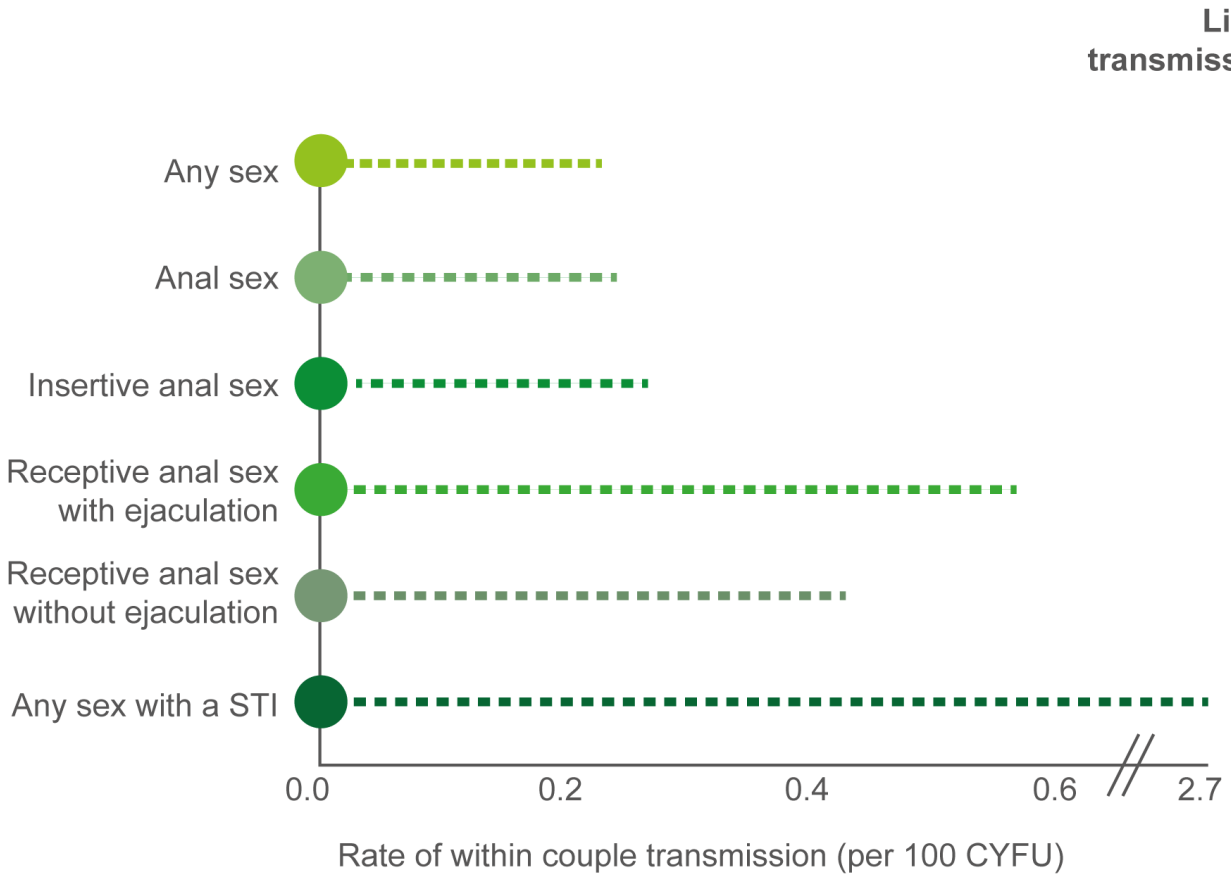

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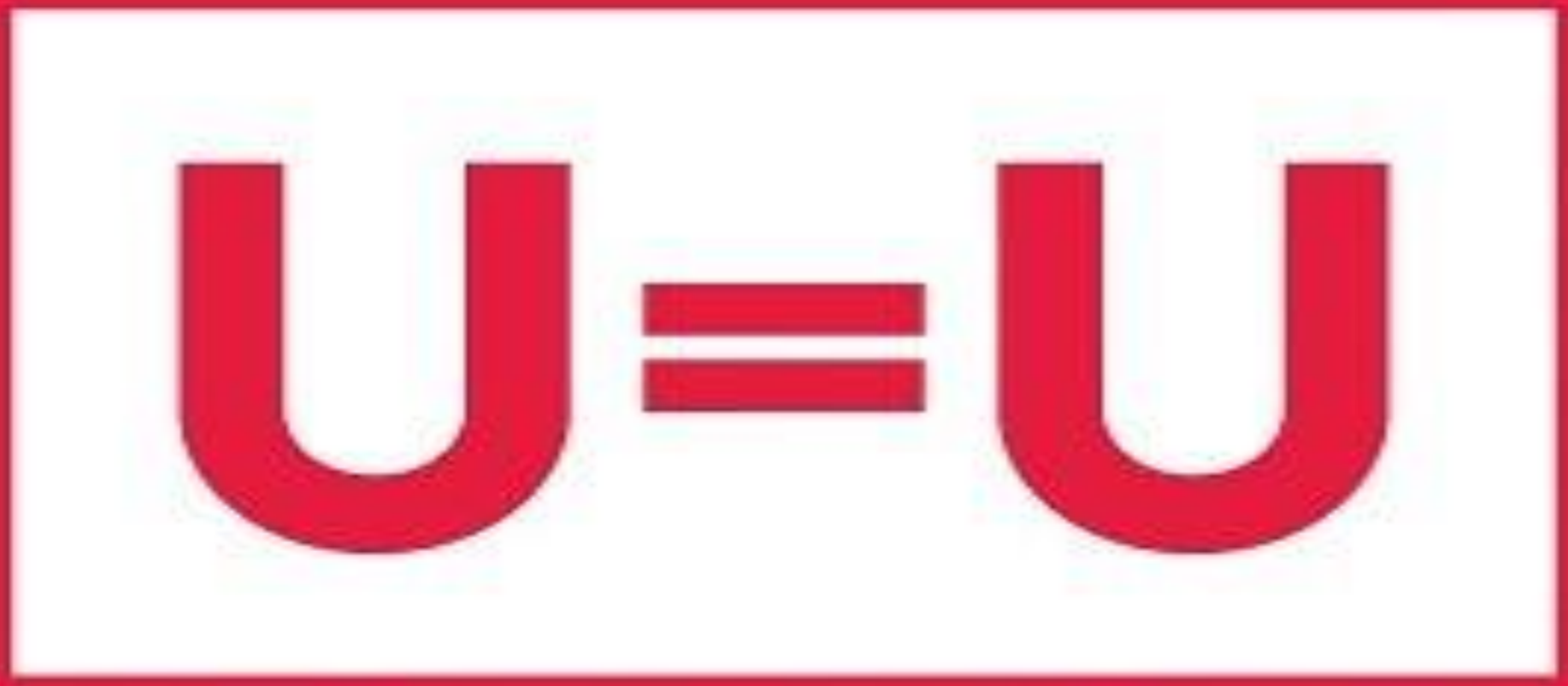
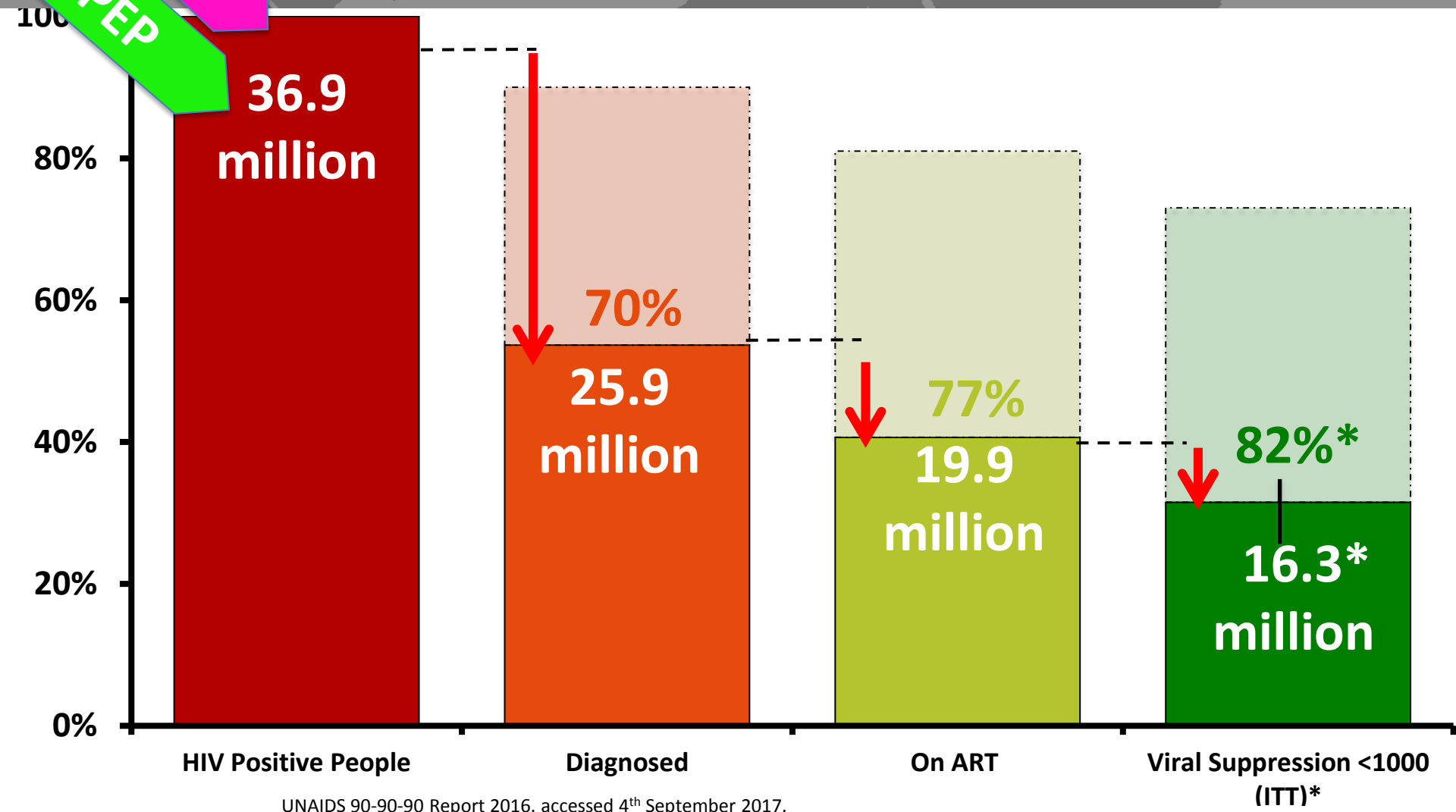
IAS 2018



Global Estimates (2017) vs the Gap to reach 90-90-90 Targets

PrEP

PEP



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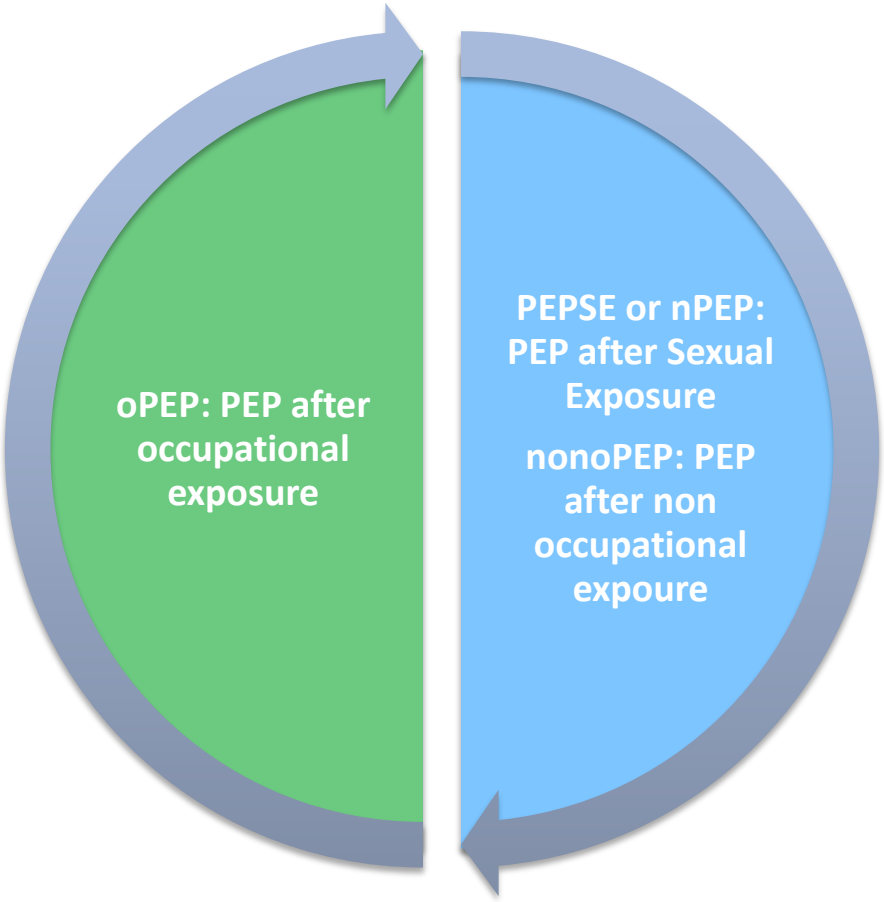
Post Exposure Prophylaxis
PEP

PEP


oPEP: PEP after occupational exposure
PEPSE or nPEP: PEP after Sexual Exposure
nonoPEP: PEP after non occupational expoure

What is considered substantial risk?

Substantial risk

• Exposure of

- Vagina, rectum, eye, mouth or other mucous membrane, non intact skin, or percutaneous

contact

• With

- Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid

that is visibly contaminated with

blood

• When

- The source is known to be HIV infected

Negligible risk

• Exposure of

- Vagina, rectum, eye, mouth or other mucous membrane, intact or non intact skin, or percutaneous contact

• With

- Urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood

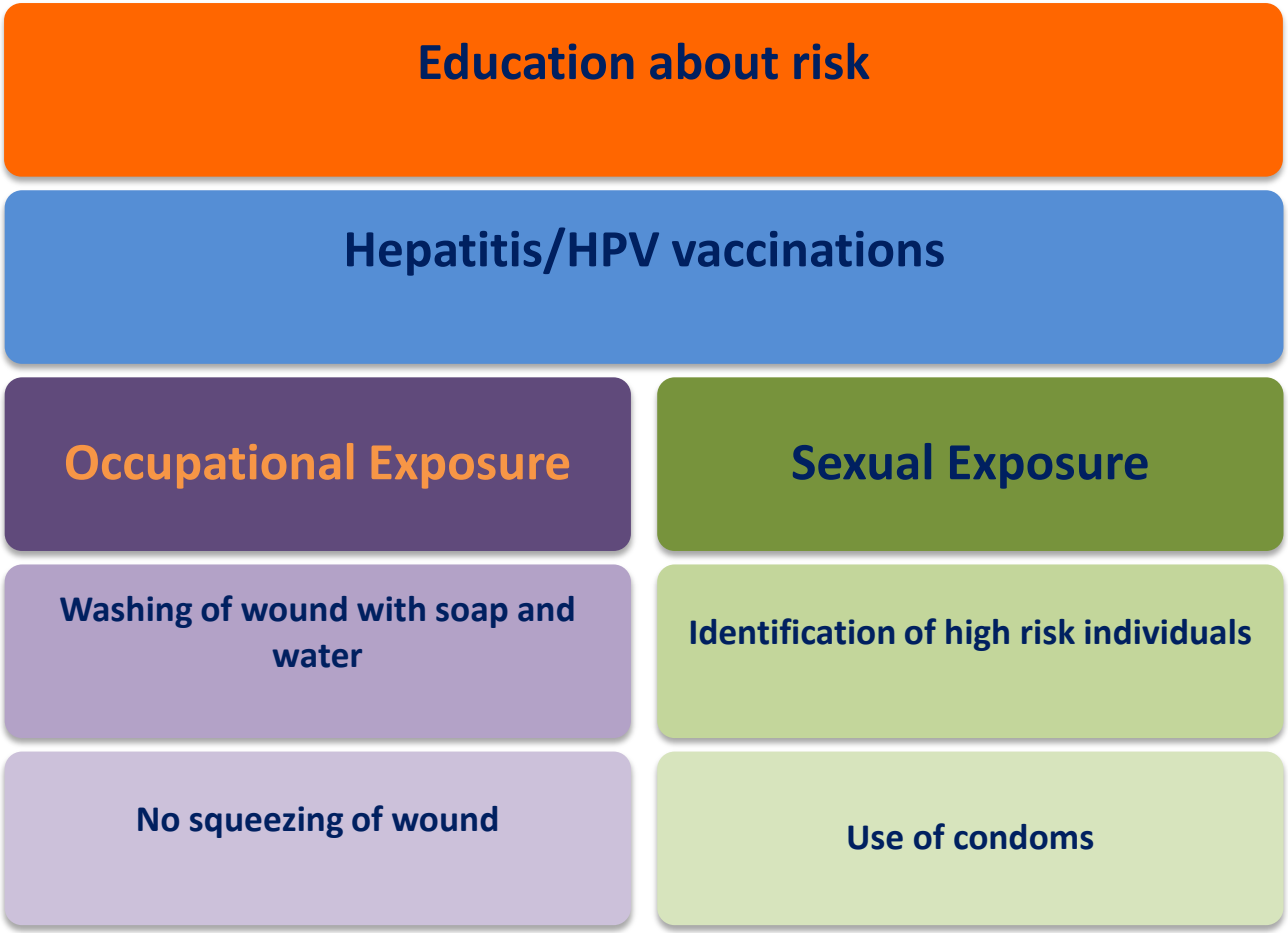
• Regardless

- Of the known or suspected HIV status of the source

Risk of exposure

Type of exposure	Estimated risk of HIV transmission
Receptive anal intercourse	1.1 (0.042– 3%)
Receptive vaginal intercourse	0.1 (0.004– 0.32%)
Insertive vaginal intercourse	0.082 (0.011– 0.38%)
Insertive anal intercourse	0.06 (0.06-0.065%)
Receptive oral sex	0.02 (0– 0.04%)
Insertive oral sex	0
Needle-stick injury	0.3 (0.2-0.5%)
Sharing injecting equipment	0.67%
Mucous membrane exposure	0.63 (0.018-3.47%)

In addition to PEP

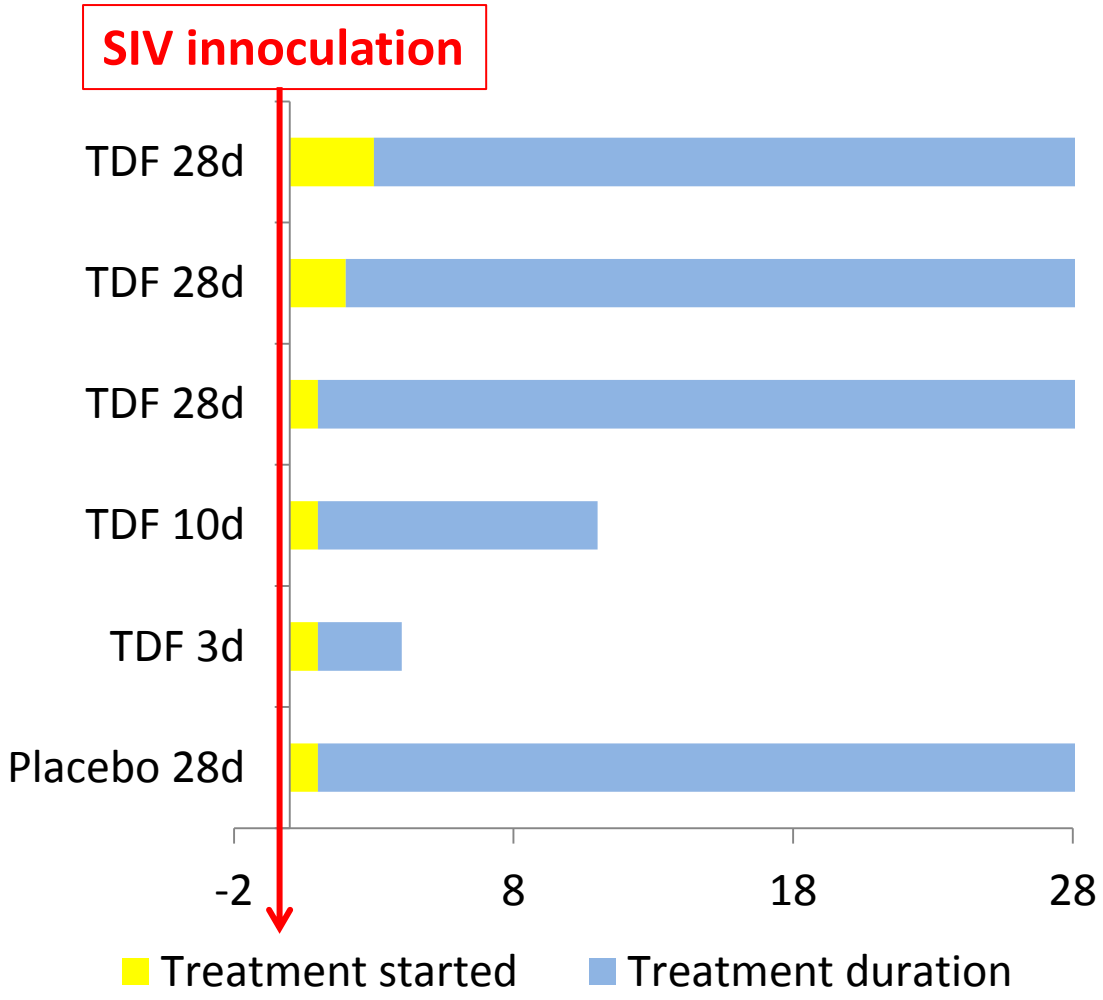


PEP

- No randomized, placebo-controlled clinical trial of PEPSE has been conducted
- Data relevant to PEPSE guidelines are available from
  - animal transmission models
  - perinatal clinical trials
  - observational studies of health care workers receiving prophylaxis after occupational exposures
  - observational and case studies of PEPSE use

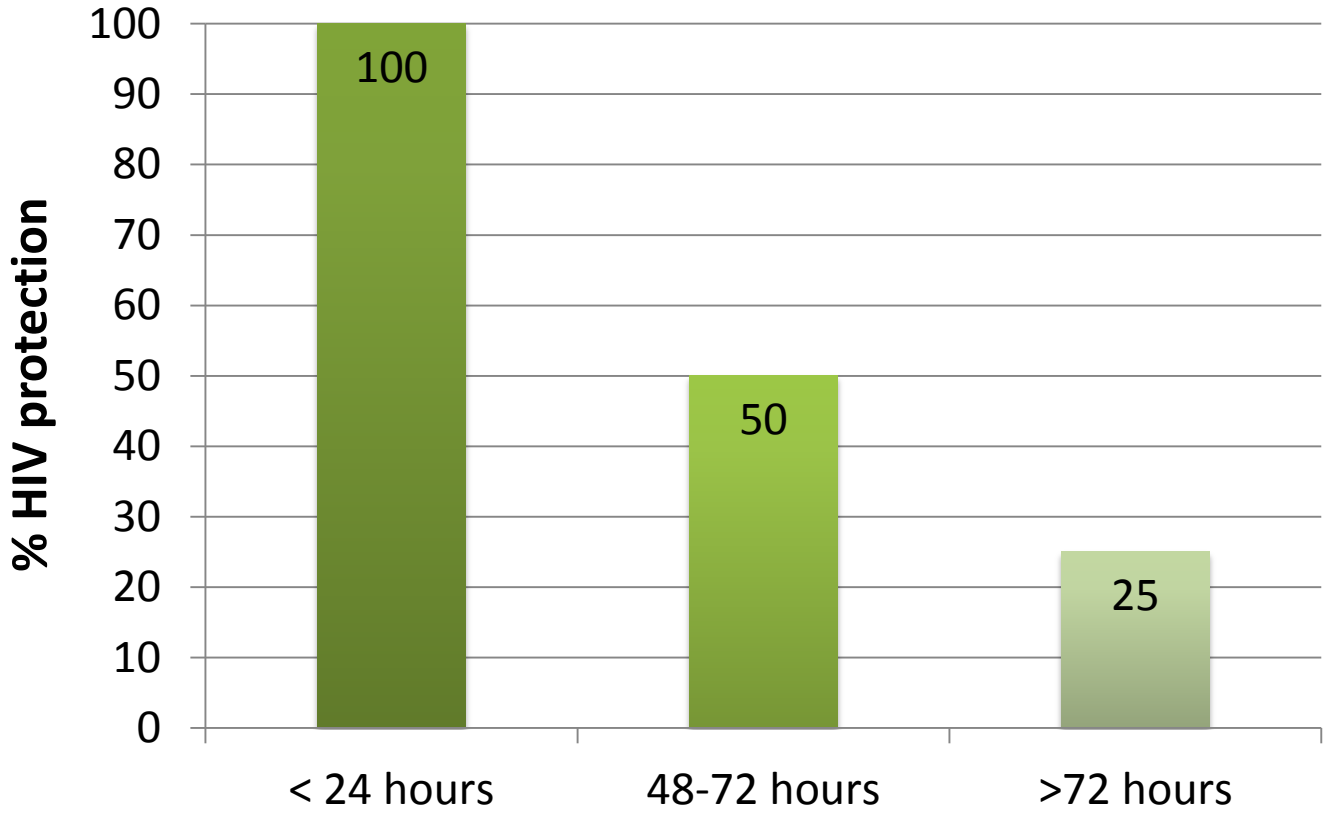
Effectiveness of Tenofovir-DF PEP in Macaques

- Study Features
- N = 24 macaques
- Randomized to 6 treatment arms
- SIV inoculated intravenously
- SIV dose 10x 50% infective dose
- PEP started at 24, 48, or 72 hours
- PEP duration: 3, 10, or 28 days
- PEP regimen: tenofovir-DF SQ
- Analyzed for antibody and viremia



Tsai CC, Fransen K, Diallo MO et al. J Virol 1998;72:4265–73

Macaque animal models – timing of PEP



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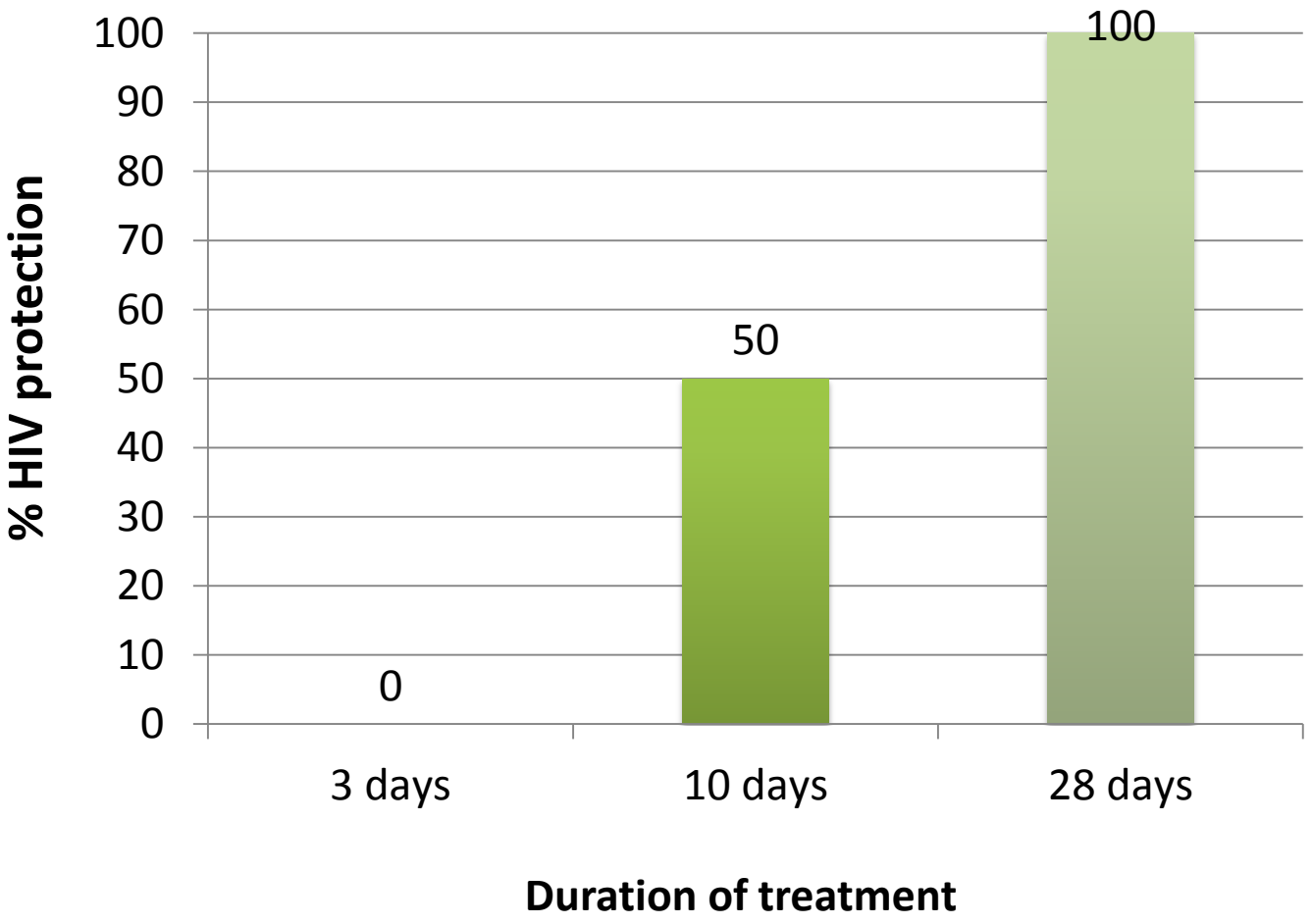
Macaque animal models – duration of PEP



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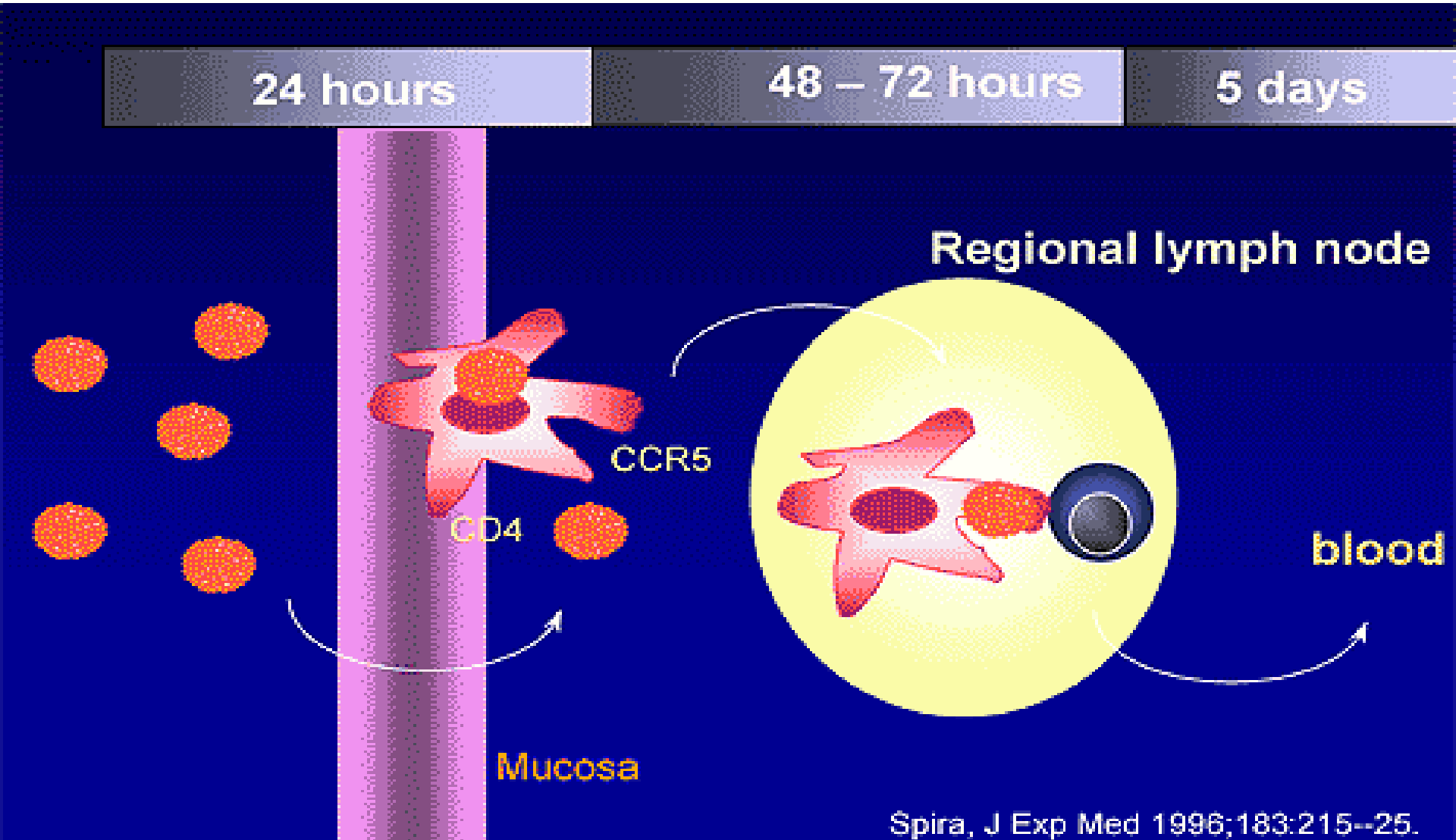
Dynamics following exposure to HIV



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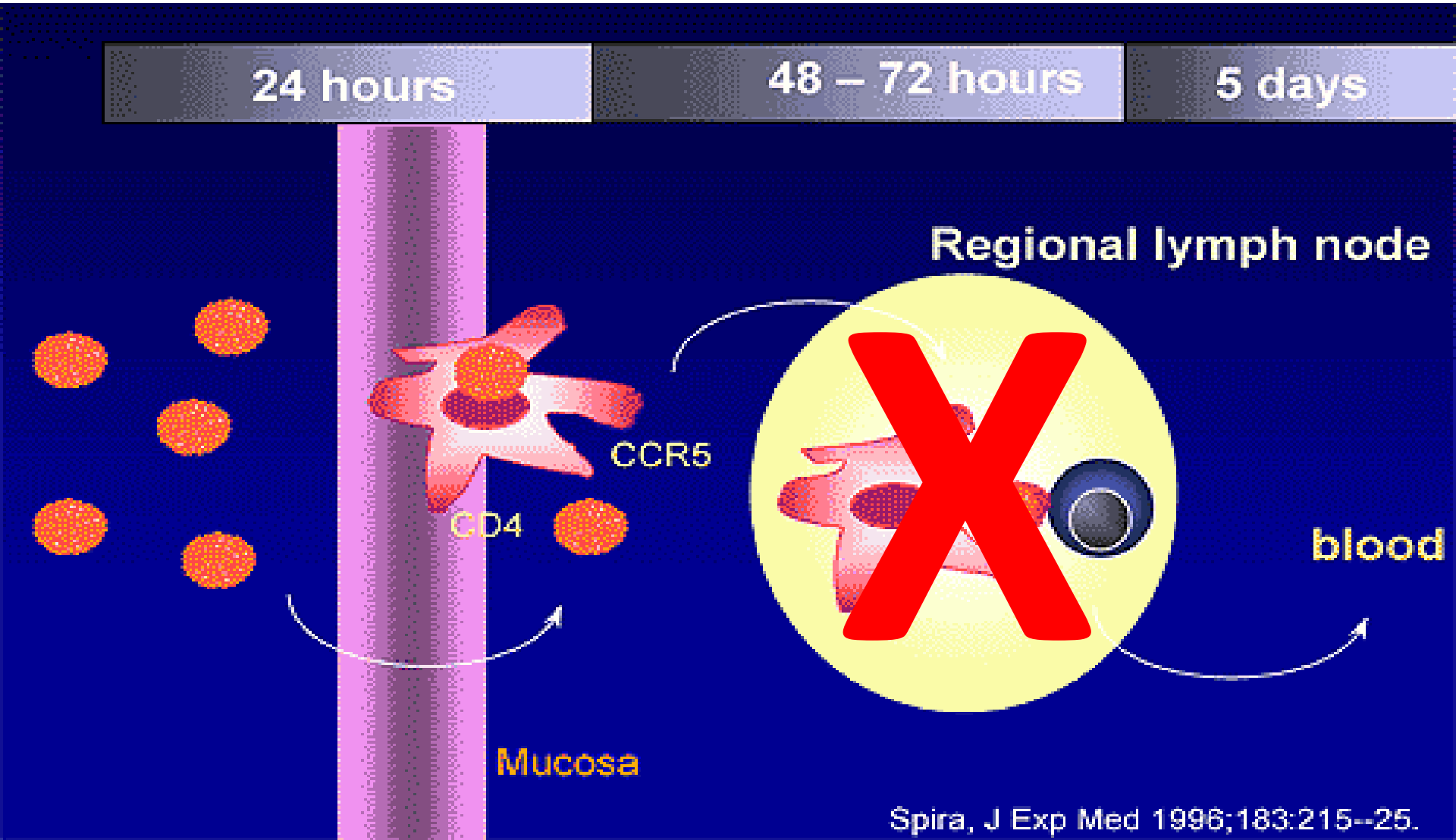
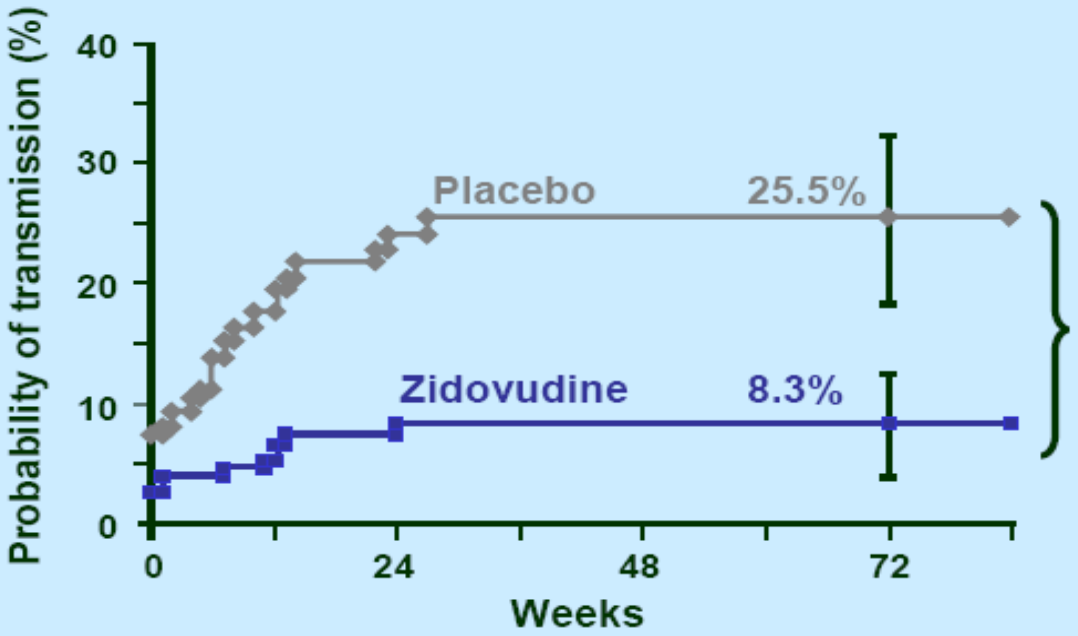


Zidovudine significantly reduces MTCT

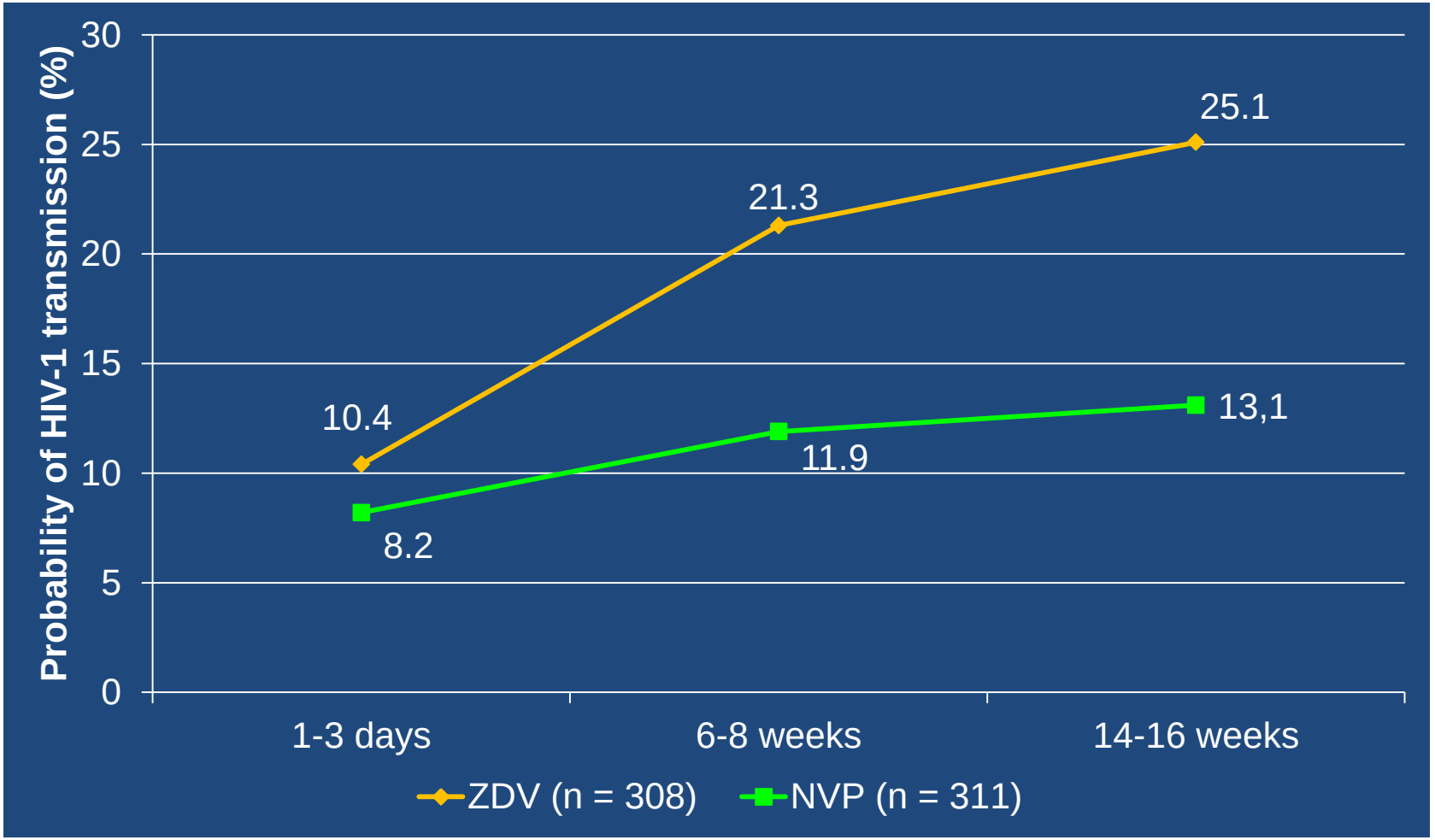
PACTG 076 Study



Placebo (n)	183	84	42	37
Zidovudine (n)	180	105	51	43

Connor EM *et al. NEJM* 1994;331:1173–1180

HIVNET 012: HIV transmission
Intrapartum/postpartum nevirapine vs zidovudine



Stat dose NVP for mother and infant vs ZDV for mother in labour and neonate 1/52

Adapted from Guay et al. Lancet 1999;354:795–802.

Occupational PEP (oPEP)

- A retrospective case-control study
- Zidovudine (ZDV) prophylaxis vs nothing for health care workers with percutaneous exposure to HIV
- Demonstrated an 81% (95% CI = 48%–94%) reduction in the odds of HIV transmission among who received oPEP
- The first study to describe the efficacy of oPEP

Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *New Engl J Med.* 1997;337(21):1485-1490.

MSM PEPSE study Brazil

- 2-year prospective study in Brazil
- 200 seronegative MSM at high risk of HIV were provided with
  - education regarding PEPSE
  - a 4-day starter pack with instructions to initiate its use for a suspected eligible exposure
  - a follow-up 24-day pack (to complete a 28-day course) but only for those men with eligible exposures
  - 68/200 MSM initiated PEPSE
  - Adherence to PEPSE medications was estimated on the basis of questions at the 28-day visit and remaining pill counts
  - The entire 28-day PEPSE regimen was completed by 89% of men with eligible exposures including 1 participant who seroconverted
  - Ten of 11 seroconversions occurred among men who did not initiate PEPSE despite risk exposure

Schechter M, do Lago RF, Mendelsohn AB, et al. Behavioral impact, acceptability, and HIV incidence among homosexual men with access to postexposure chemoprophylaxis for HIV.
J Acquir Immune Defic Syndr. 2004;35(5

PEPSE failure in Men who have Sex with Men (MSM)

- 49 seroconversions were reported after PEPSE use based on case reports and 6 studies of 1535 MSM

- Common findings
  - Ongoing sexual risk
  - Seroconversion occurred long after PEPSE was completed: 91-168 days and >180 days
  - Already HIV positive at presentation

Terzi R, Niero F, Iemoli E, Capetti A, Coen M, Rizzardini G. Late HIV seroconversion after non-occupational postexposure prophylaxis against HIV with concomitant hepatitis C virus seroconversion. *AIDS.* 2007;21(2):262-263.
Donnell D, Mimiaga MJ, Mayer K, Chesney M, Koblin B, Coates T. Use of non-occupational post-exposure prophylaxis does not lead to an increase in high risk sex behaviors in men who have sex with men participating in the EXPLORE trial. *AIDS Behav.* 2010;14(5):1182-1189..
Sonder GJB, Prins JM, Regez RM, et al. Comparison of two HIV postexposure prophylaxis regimens among men who have sex with men in Amsterdam: adverse effects do not influence compliance. *Sex Transm Dis.* 2010;37(11):681-686.
16.):519-525.

Tenofovir-Emtricitabine (TDF-FTC) plus Raltegravir for PEPSE

- 100 participants enrolled at Fenway Health
- 98% male, 83% MSM, mean age 33 yrs
- Prescribed TDF-FTC plus raltegravir for PEPSE
- 85/100 had 3-months follow-up
- None were HIV infected
- 57% finished the regimen as prescribed
- Comparable to historic controls (AZT-3TC or TDF-FTC + PI/r)
- Biggest limitation = missed second dose of raltegravir by 27%
- Well tolerated and fewer side effects than historic controls

Mayer K, et al. J Acquir Immune Defic Syndr. 2012;59(4):354-359.

Considerations of PEP

- Adherence
- Side effects
- Missed doses
- Prescribed medication
- Toxicity
- Cost
- Impact on sexual behaviour

PEPSE and sexual behaviour

- UK nonoPEP Study:
  - 77% reported reduced high-risk activity with casual partners
- Brazil:
  - Baseline: 57% reported high-risk behaviour; 24 months: 40%
- San Francisco:
  - 74% reported reduction in high-risk behaviour; 10% reported an increase

Benn et al, BHIVA 2006; Schecter et al, JAIDS 2004; Roland et al, CID 2005

EACS PEP Guidelines

- Rapid testing of the source person for HCV and HIV (if HIV-status unknown) recommended
- If source person HIV-positive on ART, order resistance testing if HIV-VL detectable
- Individualise PEP according to the source's treatment history and previous resistance tests
- For sexual exposure, if HIV-positive source has documented undetectable HIV-VL, PEP is no longer recommended
- PEP to be started ideally < 4 hours after the exposure and no later than 48/72 hours
- Duration of PEP: 4 weeks
- PEP regimens: TDF/FTC (alternative: ZDV/3TC) + RAL bid, or + DRV/r qd or + LPV/r bid. TDF/FTC + DTG qd may be also considered as an alternative.

- Full sexual health screen in case of sexual exposure
- Follow-up: HIV serology + HBV and HCV, pregnancy test (women) within 48 hours of exposure
- Re-evaluation of PEP indication by HIV expert within 48-72 hours
- Assess tolerability of PEP regimen
- Transaminases, HCV-PCR and HCV serology at month 1 if source person HCV-positive (observed or suspected)
- Repeat HIV serology after 2 and 4 months, syphilis serology after 1 month if sexual exposure

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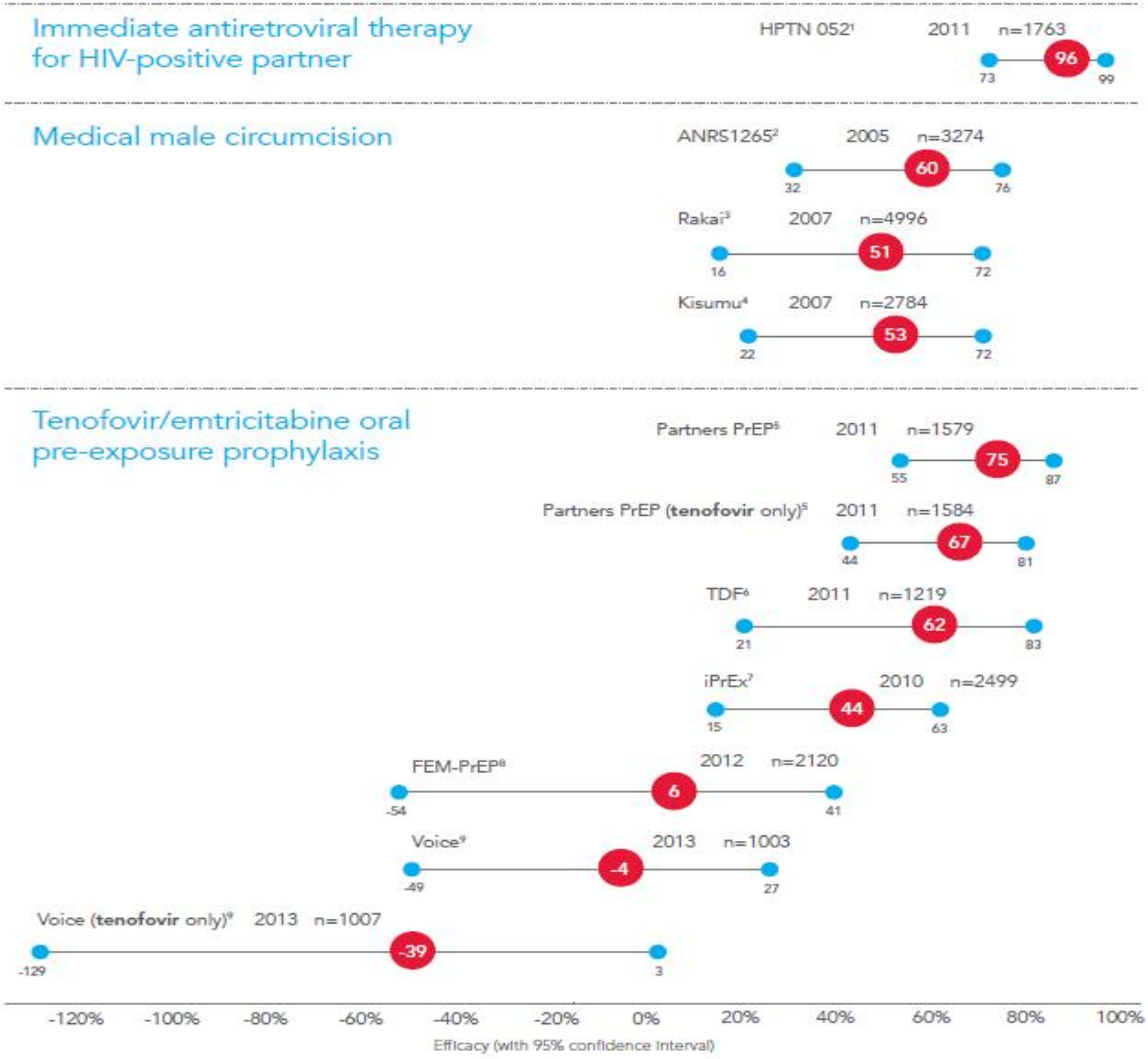
Assess need for PrEP

Pre Exposure Prophylaxis
PrEP

EFFICACY OF AVAILABLE BIO-MEDICAL PREVENTION INTERVENTIONS DERIVED FROM RANDOMIZED CLINICAL TRIALS. MODIFIED WITH PERMISSION FROM MARRAZZO ET AL, JAMA, IN PRESS, 2014.*



Sources: 1. Cohen M, Chen Y, McCauley M, Gamble T, Hosseinipour MC, et al. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med, 2011;365:493–505. DOI:10.1056/NEJMoa1105243 2. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. (2005)

Summary of earlier Oral PrEP studies

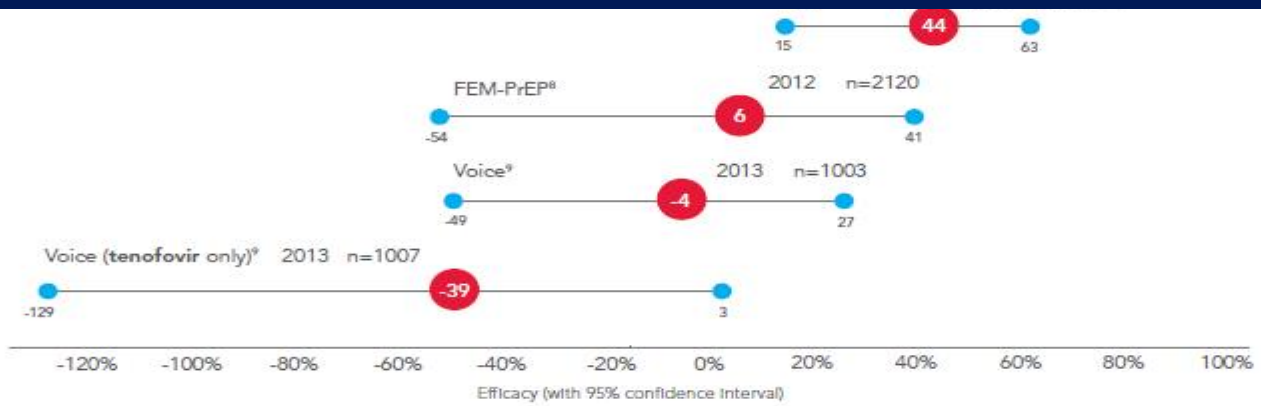
	Risk Group	Setting	n	Reduction in HIV Transmission
iPREX	MSM and transsexual women	US, Brazil, Peru, Ecuador, S Africa, Thailand, China	2499	42% (MITT)
FemPREP	Heterosexual women	Kenya, South Africa,Tanzania.	1951	0% (5% transmission in Truvada and placebo arms)
Partners PrEP Study	Heterosexual men and women	Kenya, Uganda	4736	62-73%
TDF-2	Heterosexual men and women	Botswana	1219	78%

EFFICACY OF AVAILABLE BIO-MEDICAL PREVENTION INTERVENTIONS DERIVED FROM RANDOMIZED CLINICAL TRIALS. MODIFIED WITH PERMISSION FROM MARRAZZO ET AL, JAMA, IN PRESS, 2014.*

Relative risk reduction associated with detectable tenofovir-DF

Partners PrEP study: 90% (95% CI: 56-98%)

iPrEx study: 92% (95% CI: 40-99%)



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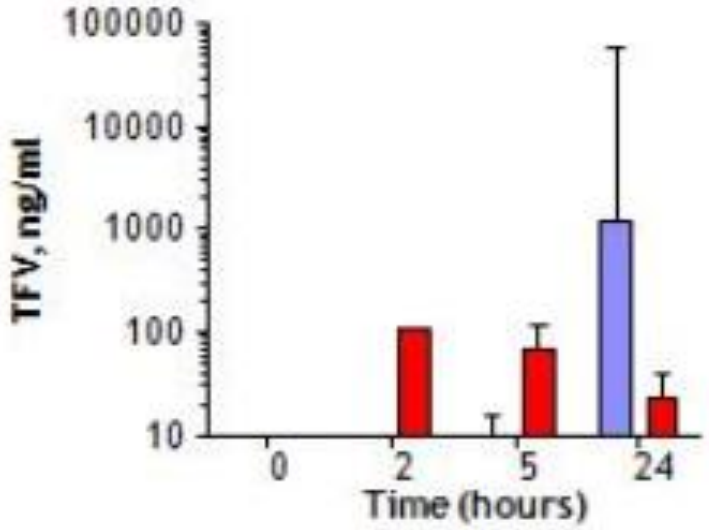
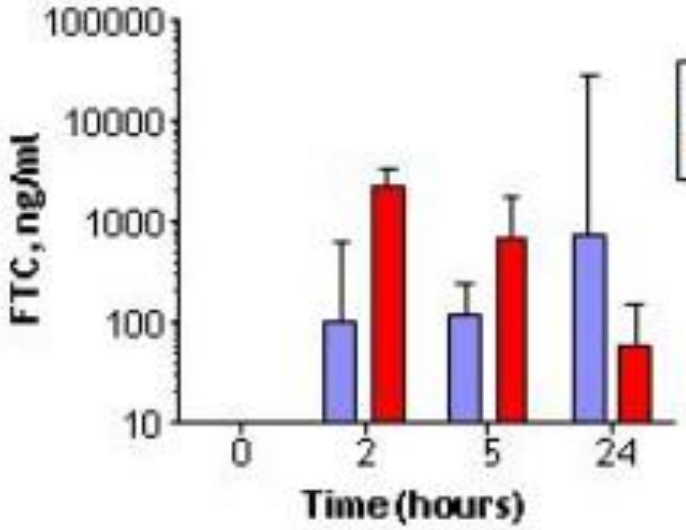
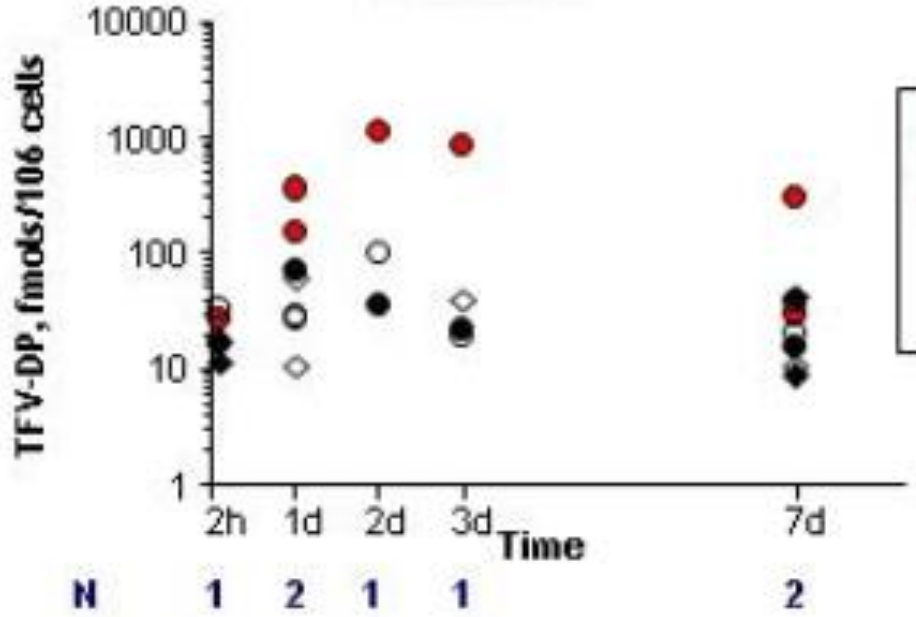
How do we know oral PrEP is effective?

- Animal studies
- Major PrEP trials
  - PROUD
  - Ipergay
  - iPREX OLE

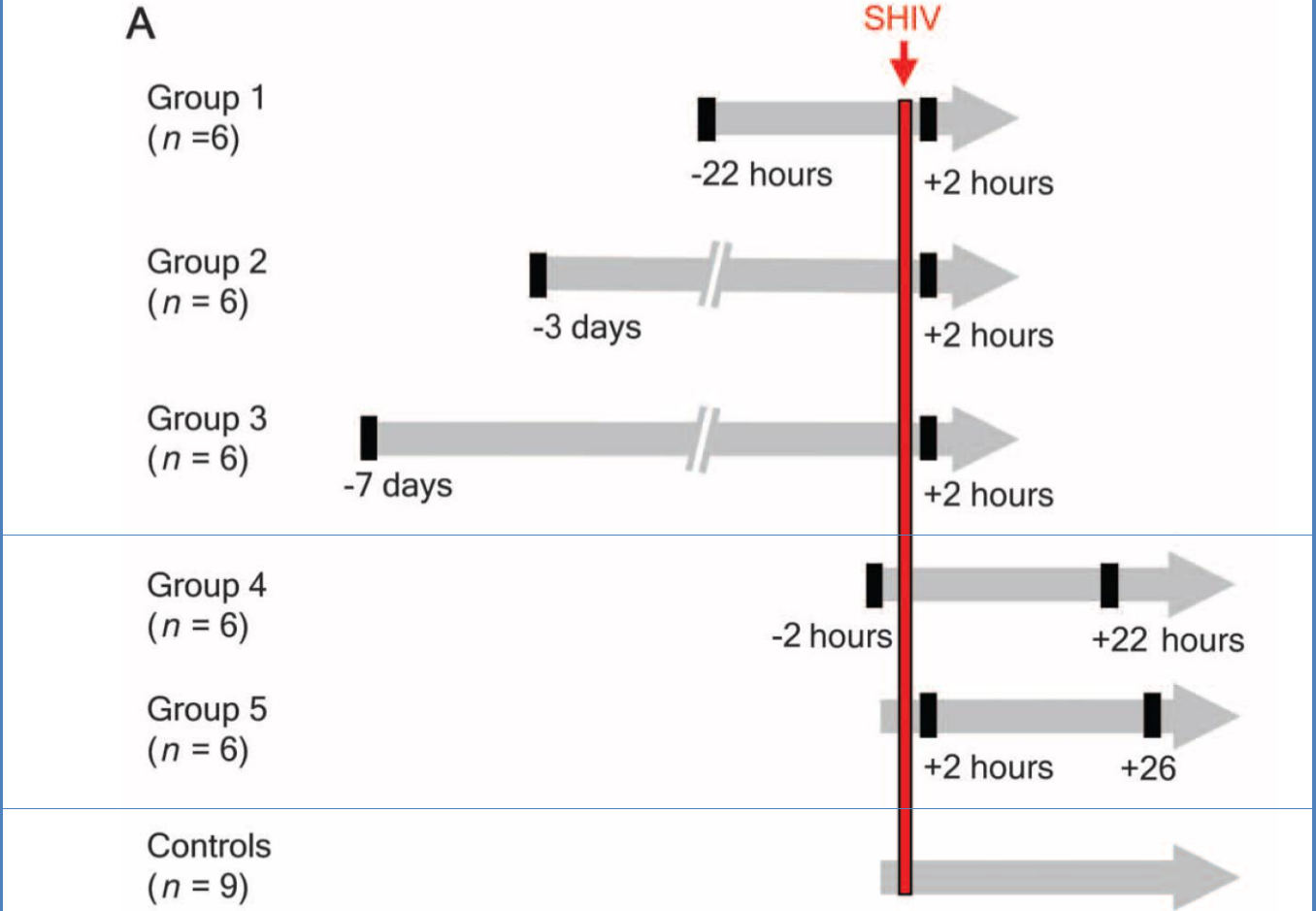
Local and systemic drug concentrations after oral administration of Truvada







Efficacy of intermittent PrEP with Truvada in the repeat low-dose macaque model: design



Slides courtesy of Gerardo Garcia-Lerma*1 CROI 2010 Paper # 83

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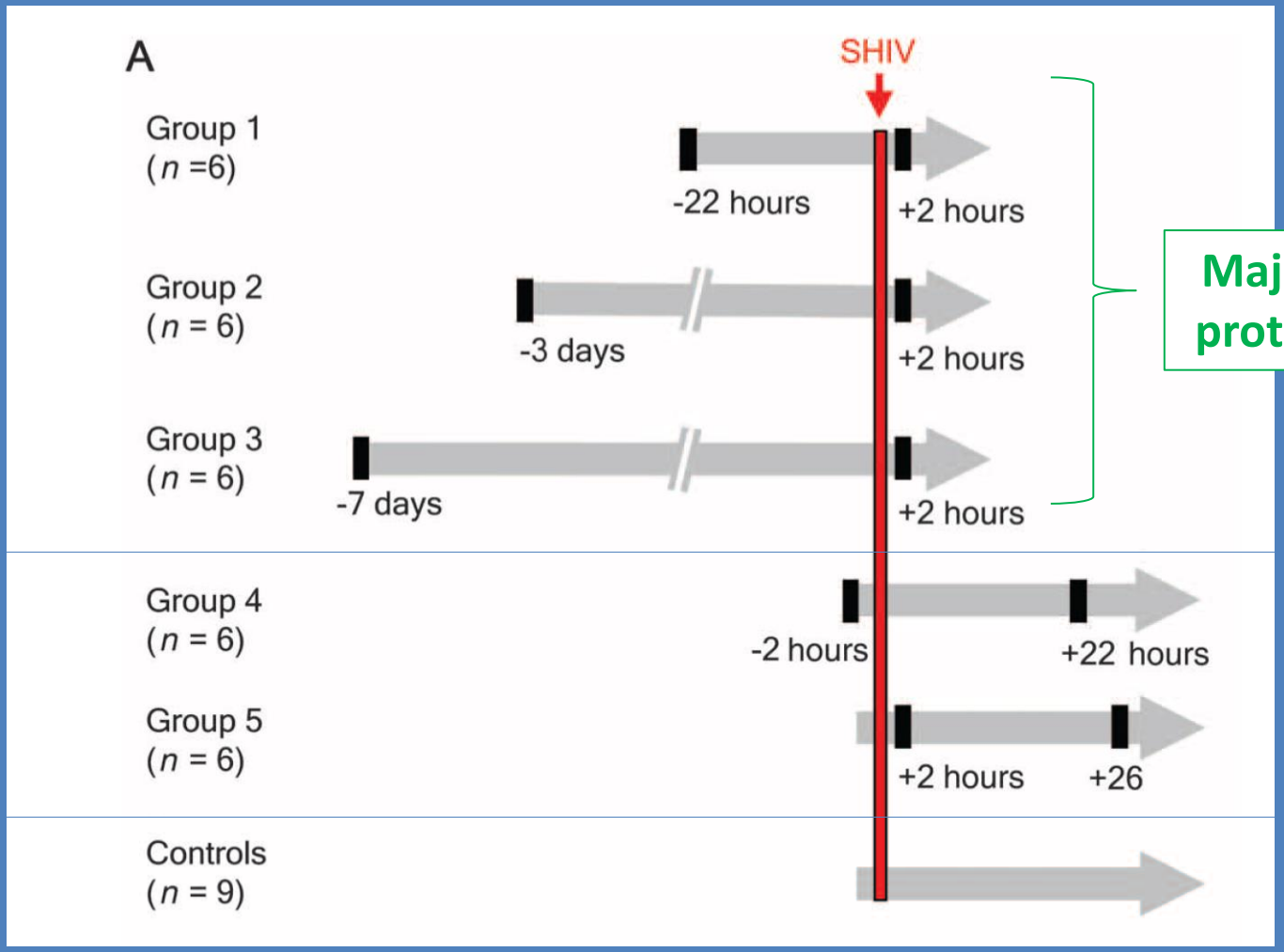

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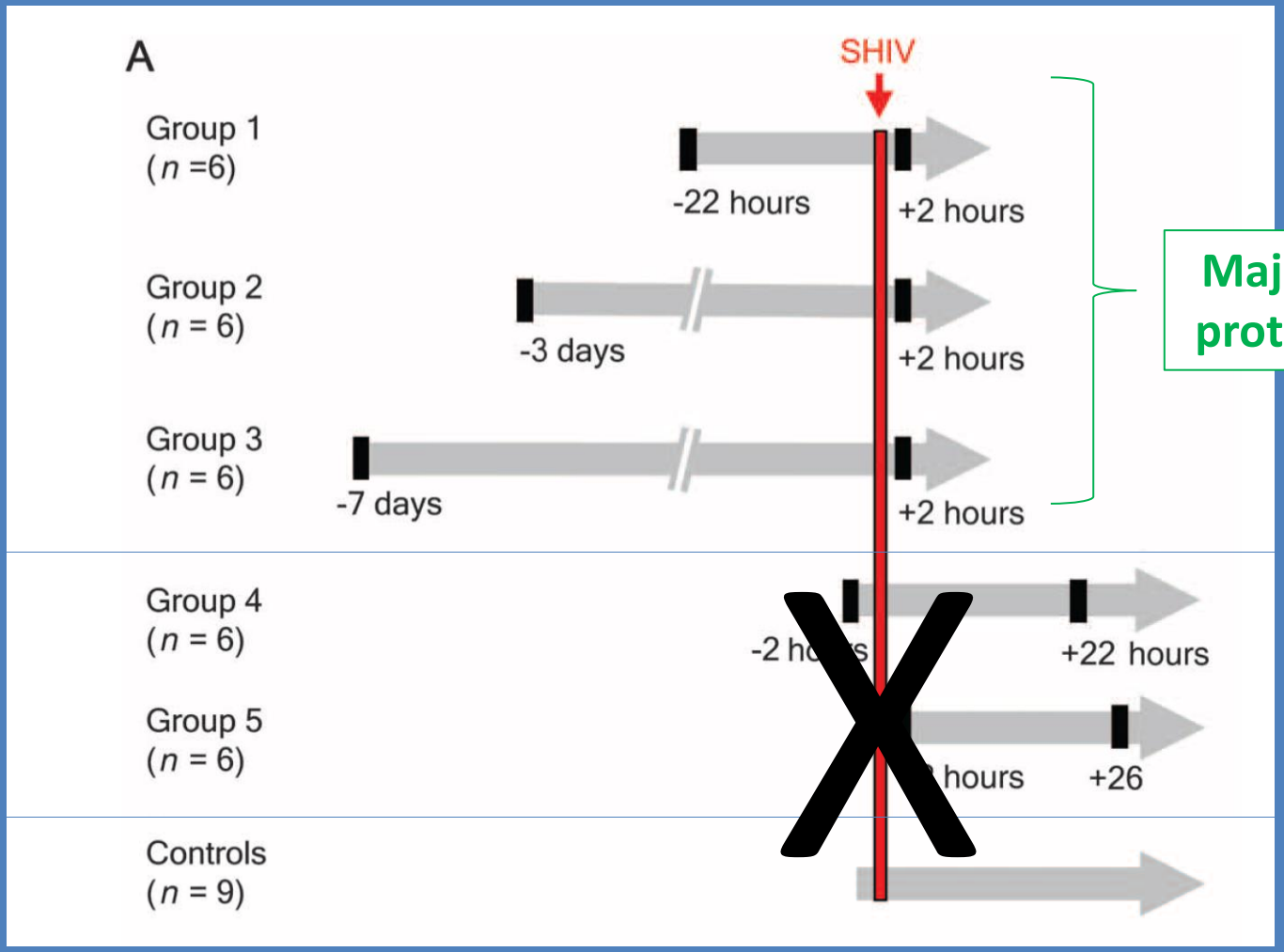

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Public Health England

PROUD

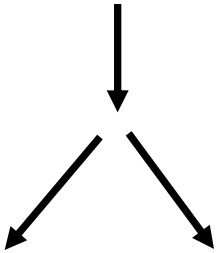
MRC Clinical Trials Unit

Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

- To determine whether PrEP worked as well as iPrEx in this setting (44% reduction in HIV)
- Possibility that effectiveness might be less in real world

PROUD Pilot

MSM reporting UAI last/next 90 days



Truvada **NOW**

N= 267

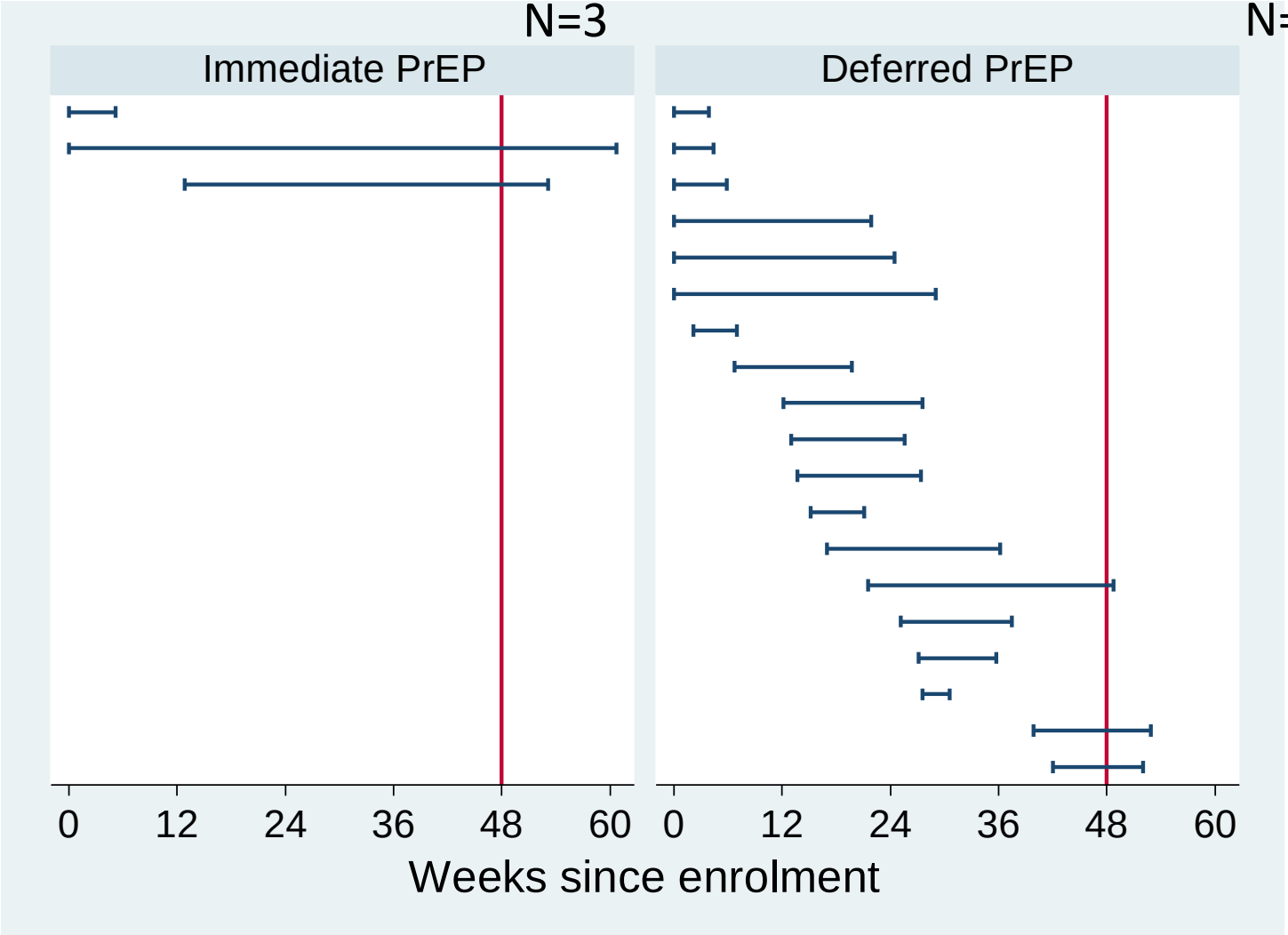
Truvada **AFTER 12M**

N=256

Follow **3 monthly** for up to 24 months

Main endpoints in Pilot: HIV infection in first 12 months

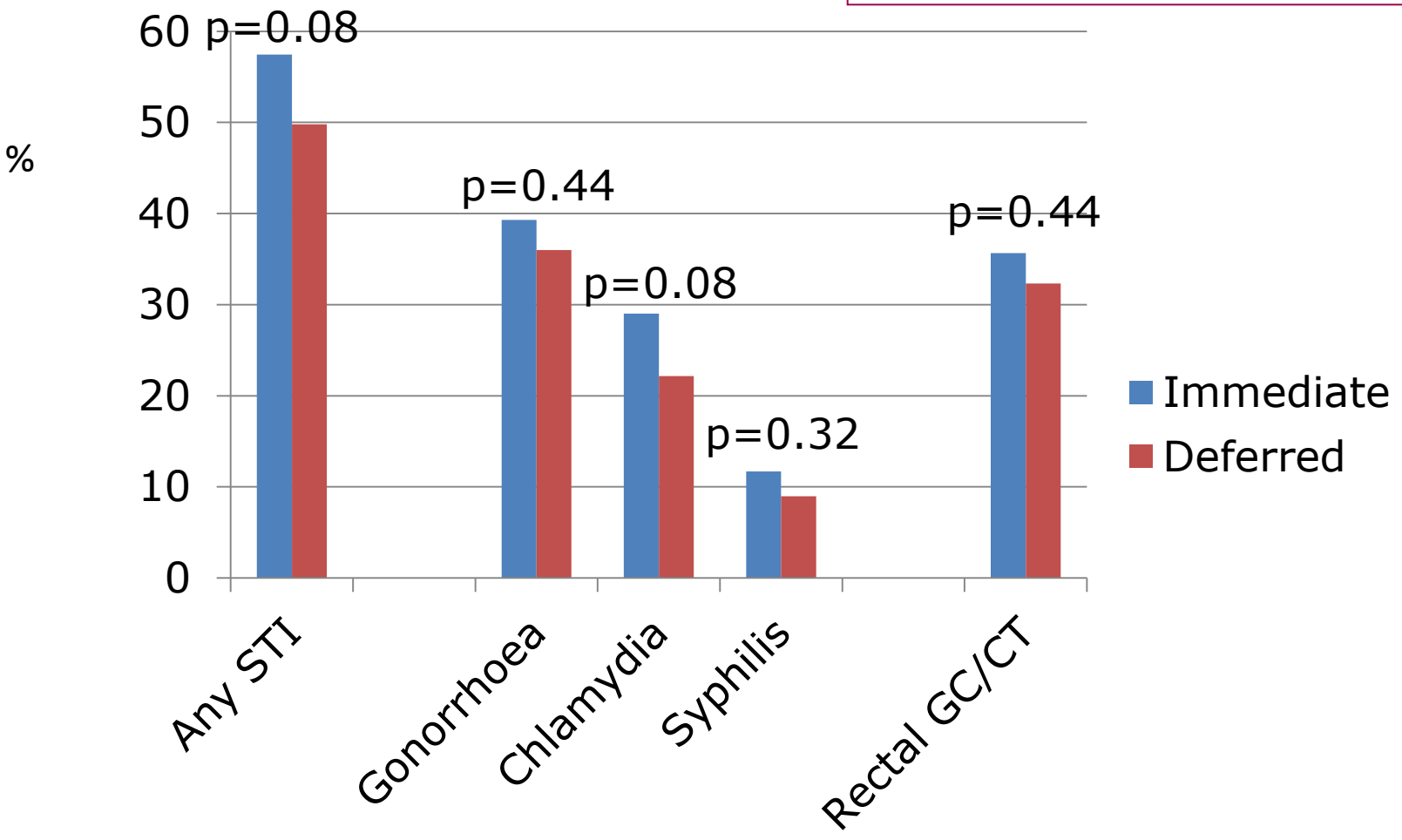
PROUD: new HIV infections



86% reduction in HIV Transmission

PROUD: STIs

Caveat
Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia 974 in the IMM group and 749 in the DEF



ipergay
ANRS
Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

www.ipergay.fr

Study Design

Double-Blinded Randomized Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m

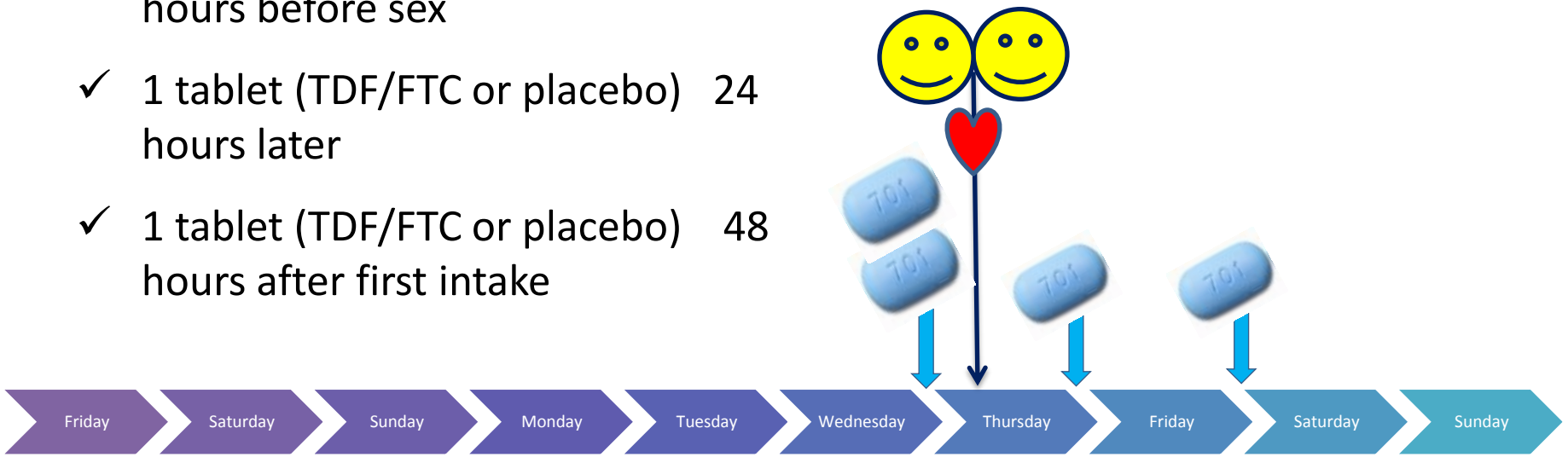
→ **TDF/FTC before and after sex**
N=199

→ **Placebo before and after sex**
N=201

- Follow-up visits: month 1, 2 and every two months thereafter

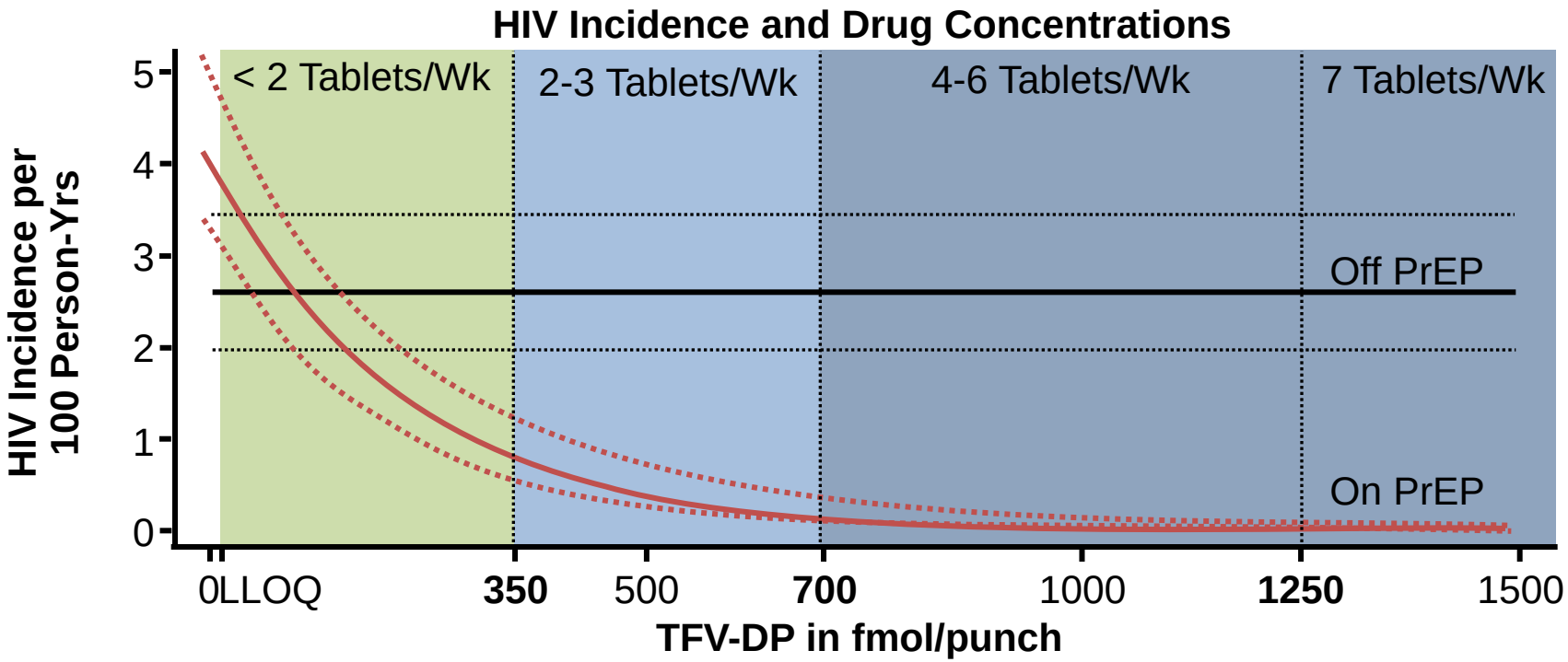
Ipergay : Event-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo) 24 hours later
- ✓ 1 tablet (TDF/FTC or placebo) 48 hours after first intake



86% reduction in HIV infections in PrEP arm

iPrEX OLE: 100% Adherence With Daily PrEP Not Required to Attain Full Benefit

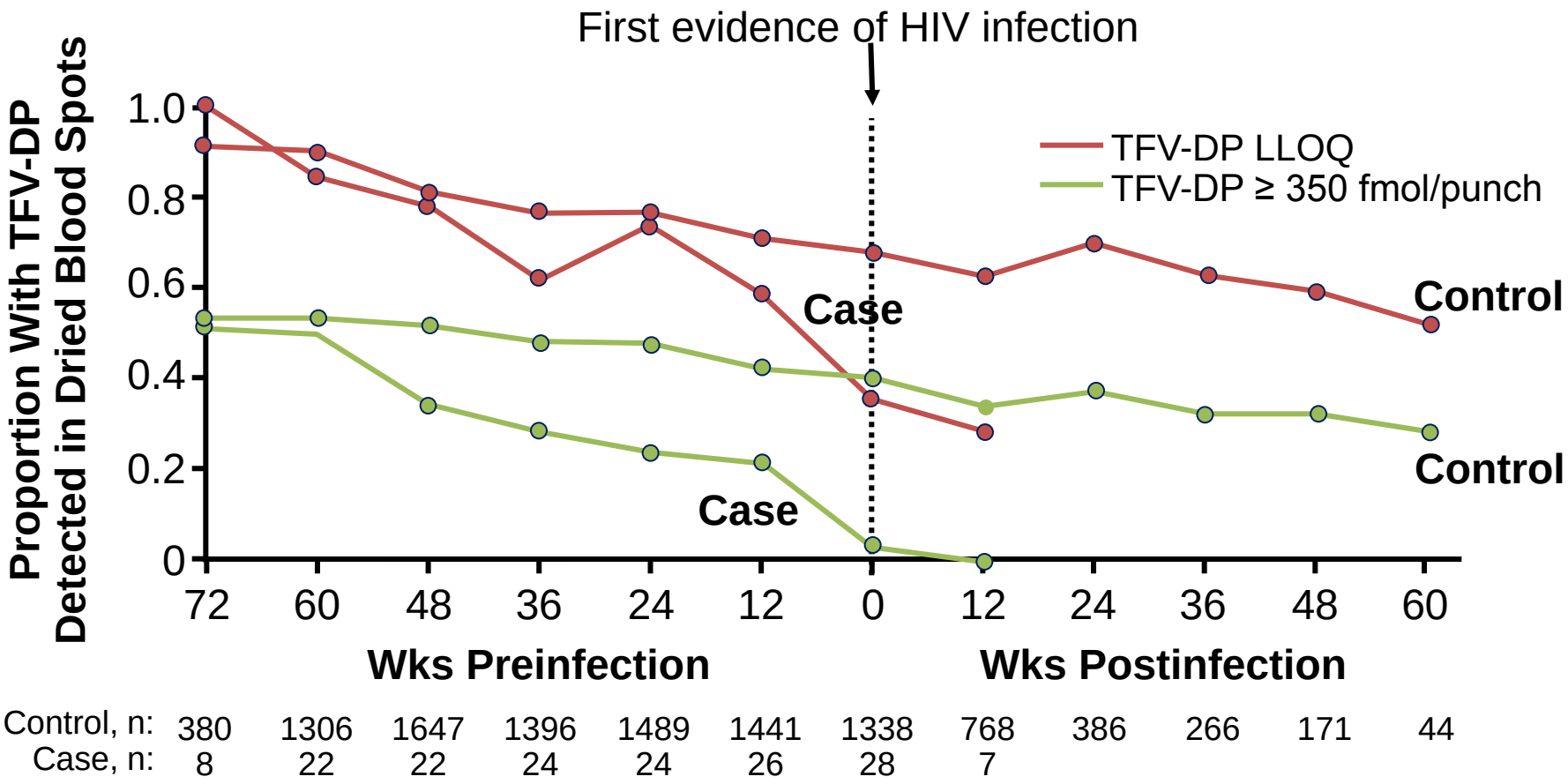


Follow-up,%	26	12	21	12
Risk Reduction,%	**44**	**84**	**100**	**100**
95% CI, %	-31 to 77	21 to 99	86 to 100 (combined)	

- TFV-DP: tenofovir diphosphate (measurable tenofovir in dried blood spots)

Grant R, et al. AIDS 2014. Abstract TUAC0105LB. Graphic used with permission.

iPrEX OLE: HIV Infection Occurred During Periods of Nonadherence



Grant R, et al. AIDS 2014. Abstract TUAC0105LB. Graphic used with permission.

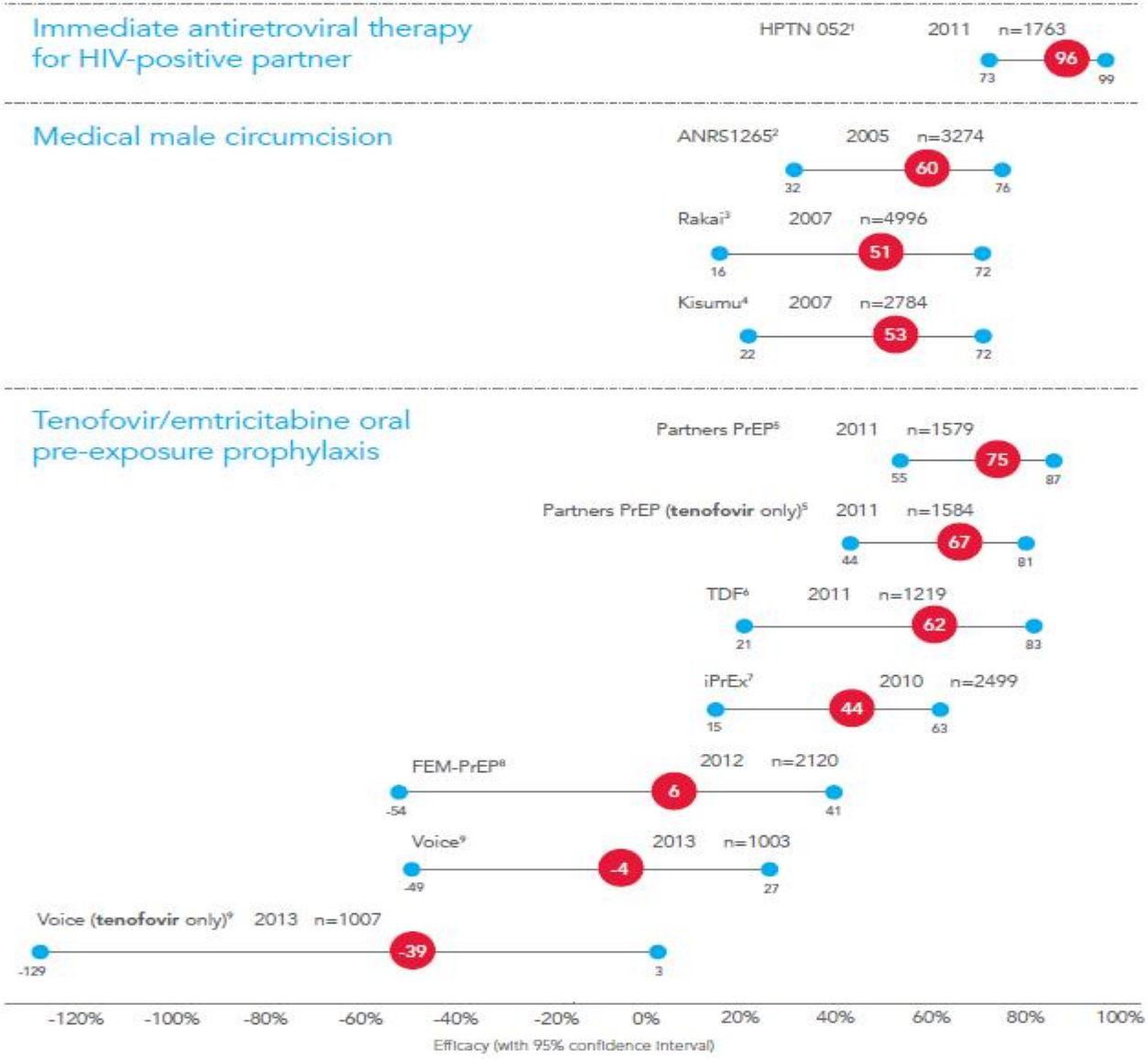
Case Report: Multiclass Resistant HIV Infection Despite High Adherence to PrEP

- 43-yr-old MSM acquired multiclass resistant HIV-1 infection following 24 mos of oral once-daily TDF/FTC PrEP
- Pharmacy records, blood concentration analyses, and clinical history support recent and long-term adherence to PrEP
- PrEP failure likely result of exposure to PrEP-resistant, multiclass resistant HIV-1 strain

Drug Class	Mutations Detected on Day 7 Following p24-Positive Test	Estimated Fold-Change in IC_{50} or Change in Response (Drug)
NRTI	41L, 67G, 69D, 70R, 184V, 215E	1.9x (ABC), 61x (3TC), 38x (FTC), 1.3x (TDF)
NNRTI	181C	43x (NVP)
PI	10I	No relevant change
INSTI	51Y, 92Q	Reduced (RAL), resistant (EVG), reduced (DTG)

Knox DC, et al. CROI 2016. Abstract 169aLB.

EFFICACY OF AVAILABLE BIO-MEDICAL PREVENTION INTERVENTIONS DERIVED FROM RANDOMIZED CLINICAL TRIALS. MODIFIED WITH PERMISSION FROM MARRAZZO ET AL, JAMA, IN PRESS, 2014.*



Sources: 1. Cohen M, Chen Y, McCauley M, Gamble T, Hosseinipour MC, et al. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med, 2011;365:493–505. DOI:10.1056/NEJMoa1105243 2. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. (2005)

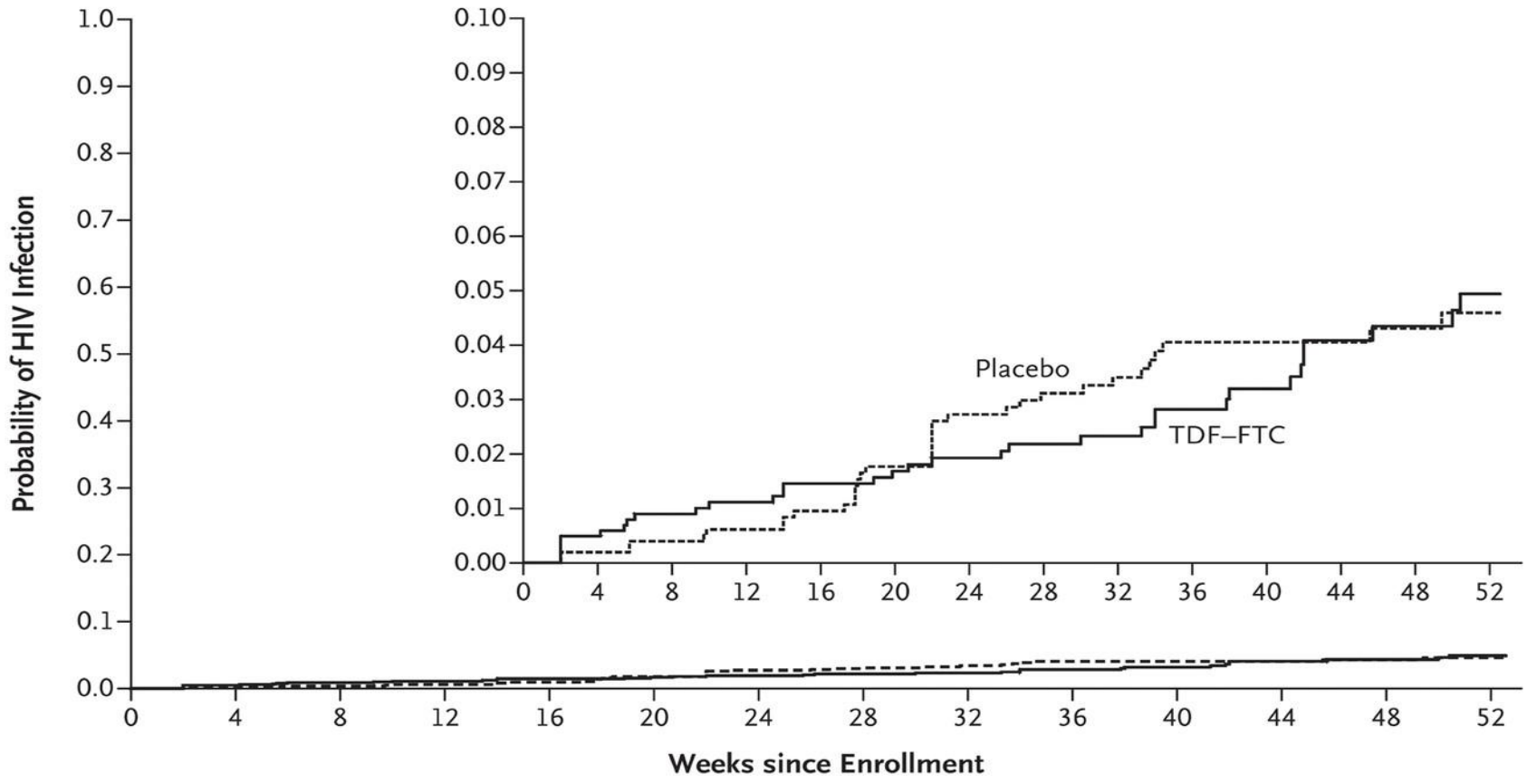
Has PrEP Been Shown to Be Effective?

Other studies have found PrEP ***not to be effective***

- ***FemPrEP*** study
  - Tested Truvada in Kenyan, Tanzanian, South African women at high risk for HIV
  - Stopped early – did not seem to help in preventing HIV transmission
- ***VOICE*** study
  - >5,000 women in South Africa, Zimbabwe, Uganda
  - Tested:

FemPrEP

Preexposure Prophylaxis for HIV Infection among African Women, randomised, double blind, placebo controlled trial, n= 2120 in Kenya, S Africa and Tanzania



No. at Risk

Placebo	1032	1019	963	917	864	841	799	736	659	565	491	420	360	229
TDF–FTC	1024	1008	953	904	860	844	811	733	663	569	486	418	356	212

Van Damme, et al. N Engl J Med 2012; 367:411-422

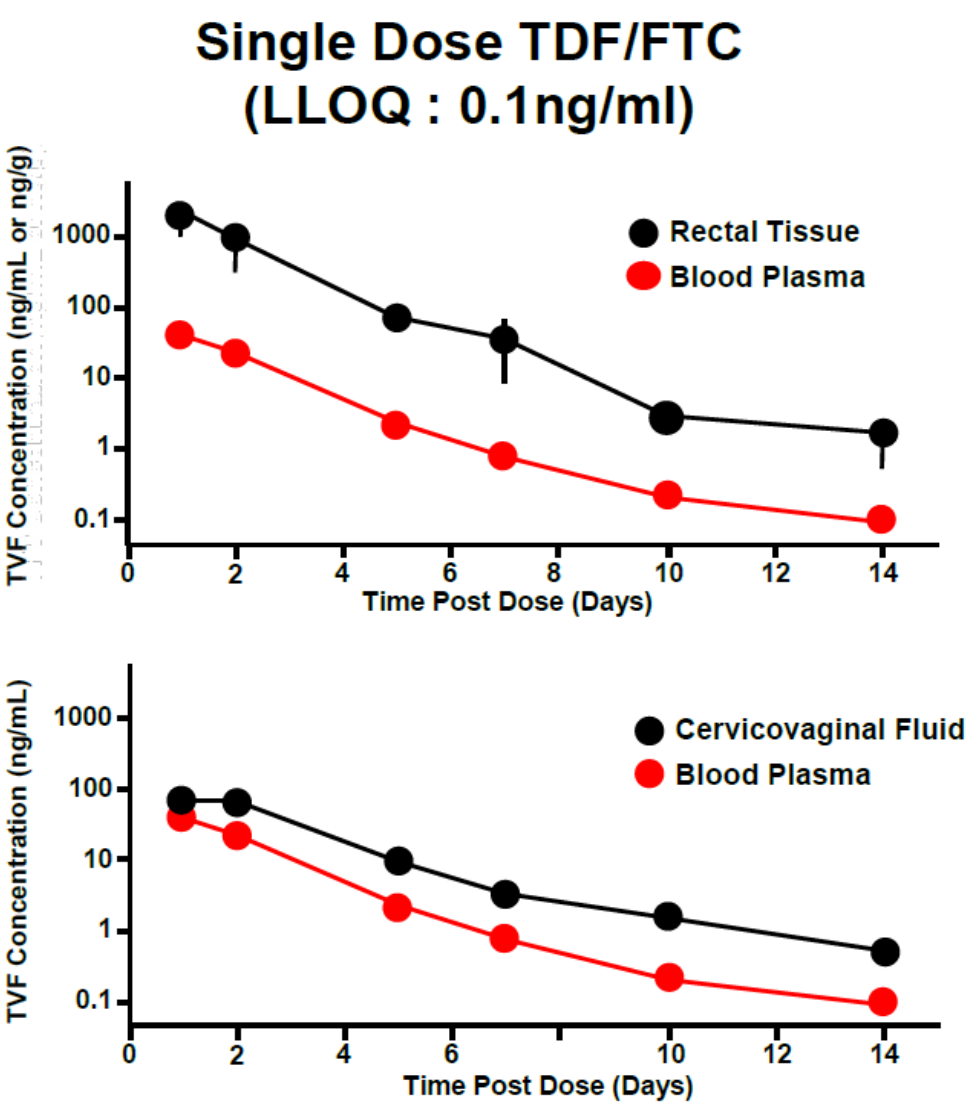
Adherence in women is the major limitation of oral PrEP

	VOICE	FemPrEP
Self-report	88-90%	95%
Product count	86%	88%
PK drug level*	25-30%	15-37%

*Tested at end of trial due to blinded trial

- VOICE: no detectable drug at any quarterly visit in approximately half of women tested (41-58%)

TDF/FTC PK in Blood and Mucosal Tissue

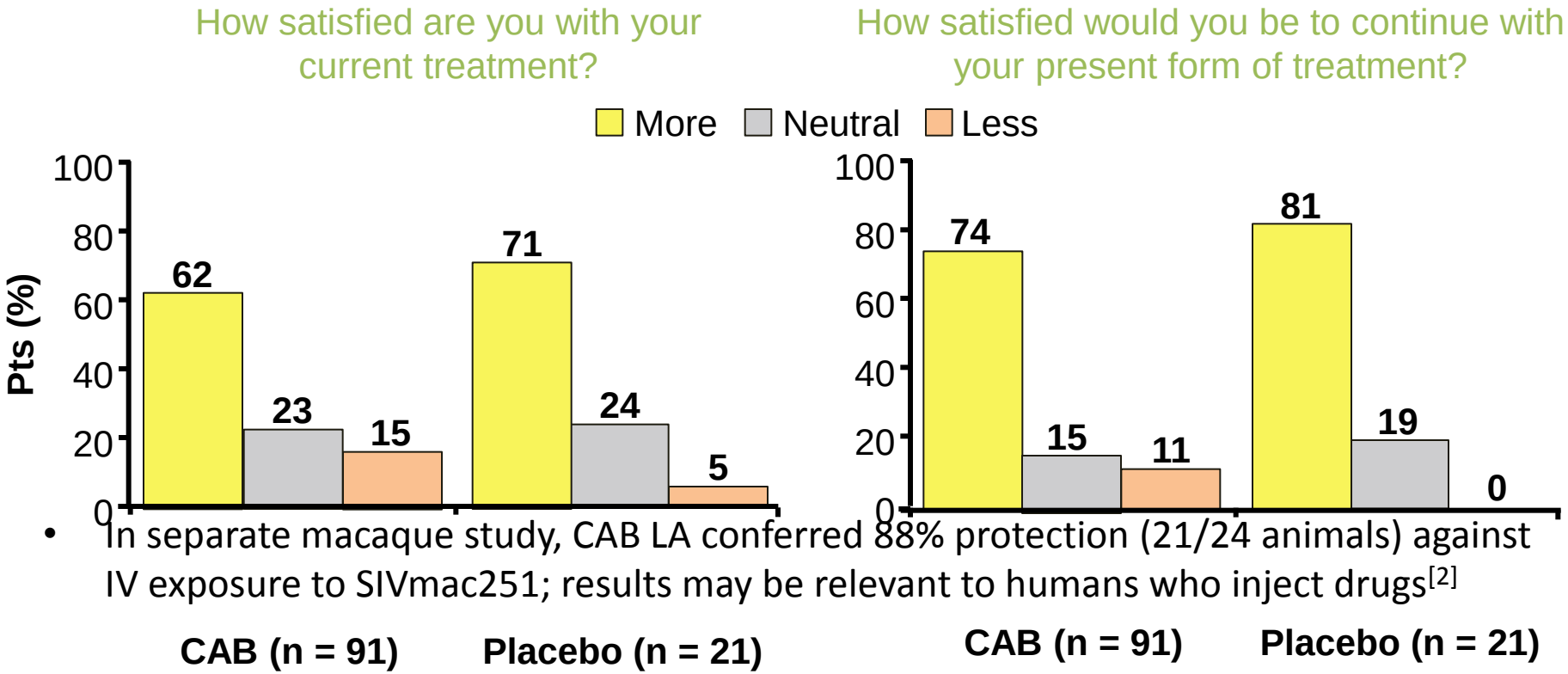


- 8 healthy men and 7 women
- Blood and tissue concentrations of TDF and FTC quantified up to 14 days
- Long half-lives : 47-49 hours
- Cumulative exposure of rectal tissue to TDF > 30-fold higher vs. blood, only 4-fold higher for FTC
- Cumulative exposure of cervical tissue to TDF 6-fold higher vs. blood, but > 40-fold higher for FTC

Patterson K, et al. Sci Transl Med 3, 2011, 112re4

ÉCLAIR: Patient Satisfaction With IM Therapy vs Oral Phase

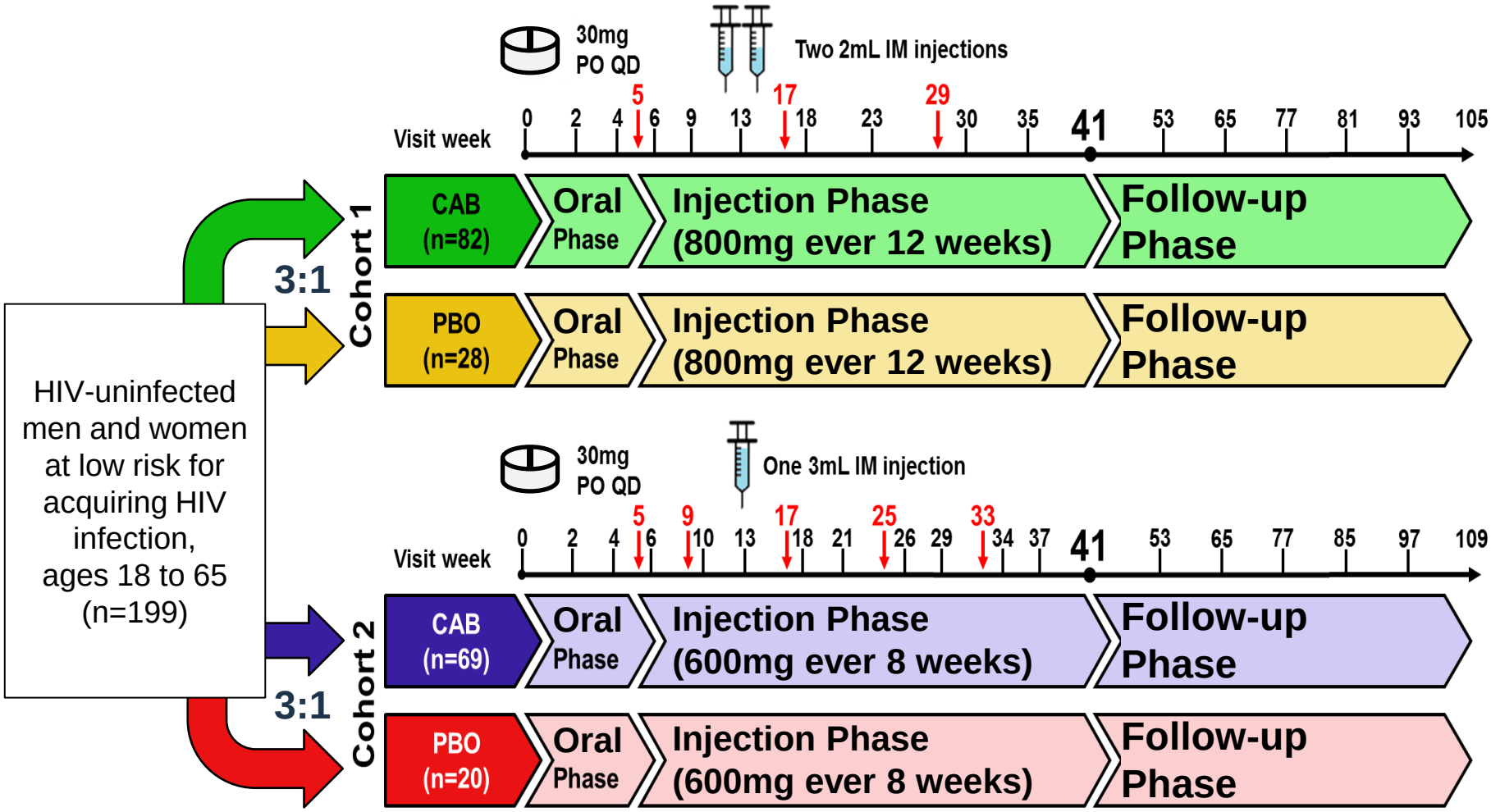
- Pt satisfaction assessed by questionnaire at Wk 18 of IM treatment; asked pts to compare satisfaction of current IM vs past oral therapy[1]



- In separate macaque study, CAB LA conferred 88% protection (21/24 animals) against IV exposure to SIVmac251; results may be relevant to humans who inject drugs[2]

1. Markowitz M, et al. CROI 2016. Abstract 106. 2. Andrews CD, et al. CROI 2016. Abstract 105.

HPTN 077 Study Design



HPTN 084: CAB LA 600mg

To Prevent HIV Acquisition in Women

Delaney-Moretlwe and Hosseinipour, *Protocol Chairs*

Step 1	**Daily oral CAB and TDF/FTC placebo**	**Oral TDF/FTC and oral CAB placebo**
Step 2	**CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter**	**Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter**
Step 3	**Open-label oral TDF/FTC to cover the PK tail**	**Open-label oral TDF/FTC to cover the PK tail**

HPTN 084
Long-acting Injectable For the Epidemic

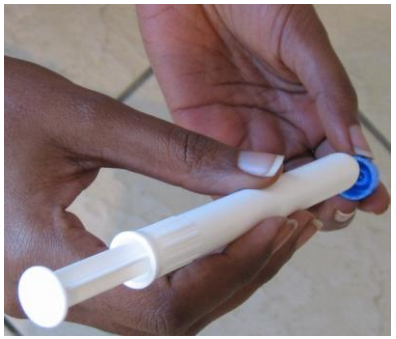
Primary Objective: Reduce HIV Incidence (superiority, double blind, double dummy design)

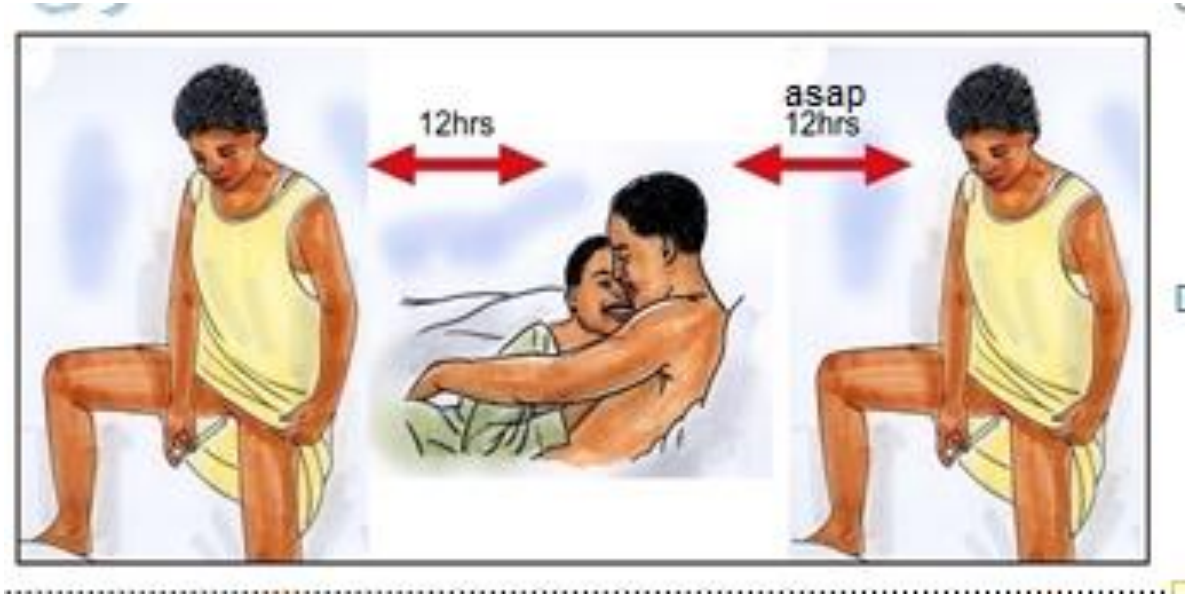
Study duration: Enrollment 24 months; follow-up up to 4.5 years

N=3200

CAPRISA & FACTS: **on-demand** topical PrEP

- BAT 24 on-demand topical PrEP
  - Insert 1 gel up to 12 hours **B**efore sex,
  - Insert 1 gel as soon as possible within 12 hours **A**fter sex,
  - No more than **T**wo doses in **24** hours





CAPRISA & FACTS: **on-demand** topical PrEP

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  - Insert 1 gel up to 12 hours **B**efore sex,

FACTS: no gel used in approximately half of all sex acts (40-50%)

Vaginal bacteria do affect blood and tissue concentrations of tenofovir in microbicide use

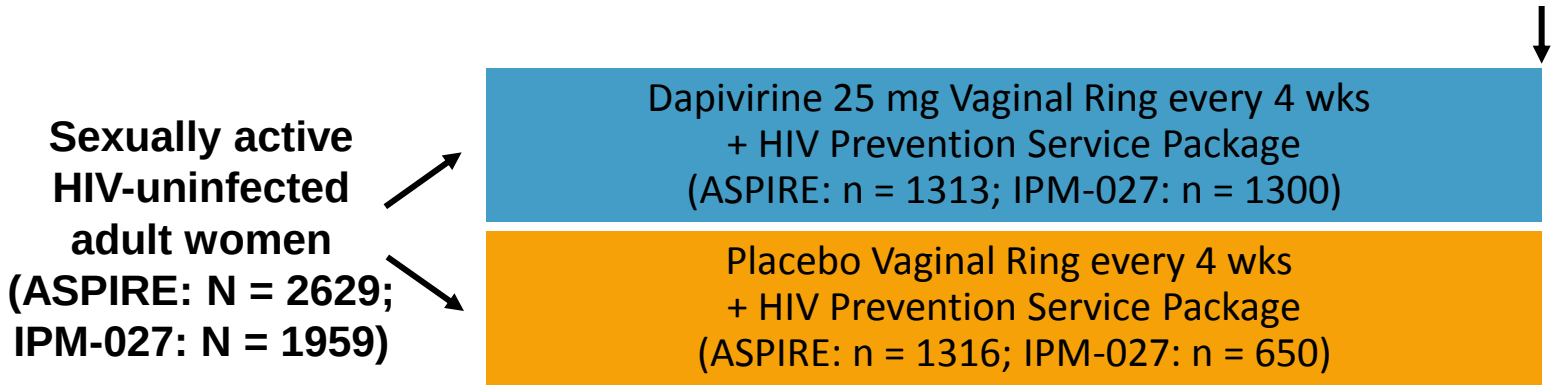
RESULTS:

N=41

- In vaginal fluid there was a significant correlation between higher levels of non-*Lactobacillus* bacteria and lower tenofovir levels, minor correlation blood
- Much stronger positive correlation between *Lactobacillus* bacteria and tenofovir levels in both vaginal fluid and blood samples.
- Women with no *Lactobacillus* were more likely to have undetectable levels of tenofovir
- Similarly strong relationships were found after a single dose in the laboratory
- Possible mechanism: the inflammation caused by BV bacteria may be turning tenofovir into adenine, the non-active 'base' compound it is designed to imitate.
- BUT it does not directly prove that these impact on the efficacy of topical PrEP

MTN-020/ASPIRE & IPM-027: Dapivirine Vaginal Ring for HIV Prevention in Women

- Silicone elastomer vaginal matrix ring containing NNRTI dapivirine 25 mg; ring replaced every 4 wks
- Randomized, double-blind phase III trials
  - MTN-020/ASPIRE[1,2]: Malawi, South Africa, Uganda, Zimbabwe
  - IPM-027 (The Ring Study)[3]: South Africa, Uganda
  - Primary endpoints: efficacy and safety



1. Baeten JM, et al. CROI 2016. Abstract 109LB.
2. Baeten JM, et al. N Engl J Med. 2016;[Epub ahead of print].
3. Nel A, et al. CROI 2016. Abstract 110LB.

MTN-020/ASPIRE & IPM-027: Efficacy and Safety of Dapivirine Vaginal Ring

- Efficacy for HIV prevention similar in both studies
- No clinically relevant safety differences between arms

Outcome	ASPIRE[1,2]: 15 Sites		ASPIRE[1,2]: 13 Sites*		The Ring Study[3]	
	Dapivirine (n = 1308)	Placebo (n = 1306)	Dapivirine (n = 1198)	Placebo (n = 1197)	Dapivirine (n = 1300)	Placebo (n = 650)
HIV infections, n	71	97	54	85	77	56
HIV incidence (per 100 PYs)	3.3	4.5	2.8	4.4	4.1	6.1
HIV protection efficacy, %	**27 (*P* = .046)**		**37 (*P* = .007)**		**31 (*P* = .040)**	
▪ **Among women older than 21 yrs**	-		**56 (*P* < .001)**		**37 (*P* = .10)**	

*Excludes 2 sites with low adherence.

1. Baeten JM, et al. CROI 2016. Abstract 109LB.
2. Baeten JM, et al. N Engl J Med. 2016;[Epub ahead of print].
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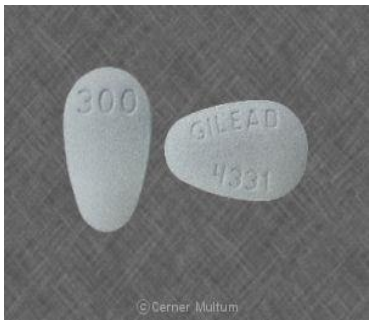
MDP 401 Program

A pragmatic randomized open-label wait-listed trial to evaluate the effectiveness of tenofovir (PrEP) to reduce the risk of HIV acquisition among women at high risk of HIV in Mozambique, Rwanda, Tanzania and Uganda

- Conduct an intensive **PREPARATORY STUDY** to inform which of three tenofovir products to test in the clinical trial.
- Followed by an open-label wait-listed randomised **CLINICAL TRIAL** designed to evaluate the preferred tenofovir product whereby women are randomised to receive the product immediately or after a deferred period of 12 months.

1. Tenofovir on-demand gel
   - Efficacy, acceptability, HSV2 protection
2. Tenofovir on-demand oral tablet
   - Cheaper, less drug, less resistance
3. Tenofovir vaginal ring
   - Three-monthly, longer half-life than Dapivirine



Imbokodo (HVTN 705/HPX2008) vaccine trial

HIV VACCINE
TRIALS NETWORK

- Mosaic technology combines immune-stimulating proteins from different HIV strains, representing different types of virus from around the world aiming for a global HIV vaccine for use in any geographic region
- Collaboration between Pharma and HIV organisations
- “Imbokodo” is the Zulu word for “rock” which is part of a well-known proverb in South Africa that refers to the strength of women and their importance in the community
- Aims to enroll 2,600 sexually-active women aged 18-35 in five southern African countries, starting in South Africa, then Malawi, Mozambique, Zambia and Zimbabwe
- Ad26 will be combined with a protein, Clade C gp140, which is similar to a protein found on the surface of HIV, and also helps to develop an immune response to the virus, and mixed with booster Aluminum Phosphate

Is PrEP acceptable?

- PrEP publications 2016/17 mainly on willingness to take PrEP
  - Transgender women Argentina
  - Black MSM Chicago
    - Apart from a small group who believe in a conspiracy theory
  - MSM China
    - On demand but not daily
  - ChemSex MSM US
    - On demand prior to chems use, but not daily
  - Long Acting Injectible PrEP
    - Acceptable if efficacious

Limited awareness of pre-exposure prophylaxis among black men who have sex with men and transgender women in New York city

- STAR Study, which recruited black MSM/TGW in New York City for HIV testing and linked HIV-infected individuals into care from July 2012 to April 2015
- 1673 participants
  - median age was 43 years
  - 25% were under age 30
  - 85.8% reported having insufficient income for basic necessities at least occasionally
  - 54.8% were homeless
  - 71.3% were unemployed

Garnett M[1], Hirsch-Moverman Y[1,2], Franks J[1], Hayes-Larson E[1,2], El-Sadr WM[1,2], Mannheimer S[1,2,3]. AIDS Care. 2017 Aug 9:1-9

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- Awareness of PrEP was reported among **18.2%** of participants
- PrEP awareness was associated with
  - younger age (adjusted odds ratio [aOR] 0.87, per 5 years)
  - gay identity (aOR 2.46)
  - higher education (aOR 1.70)
  - more frequent past HIV testing (aOR 3.18)
  - less HIV stigma (aOR 0.61)
  - less hazardous/harmful alcohol use (aOR 0.61)
  - more sexual partners (aOR 1.04, per additional partner in past 30 days)

Garnett M[1], Hirsch-Moverman Y[1,2], Franks J[1], Hayes-Larson E[1,2], El-Sadr WM[1,2], Mannheimer S[1,2,3]. AIDS Care. 2017 Aug 9:1-9

How Much Do We Know about Drug Resistance Due to PrEP Use?

- Will widespread use of PrEP outside well controlled trial conditions result in increased drug resistance?
- A survey of expert virologists with questions about biological assumptions regarding drug resistance due to PrEP use
- For comparability, 50% PrEP-coverage of and 90% per-act efficacy of PrEP in preventing HIV acquisition are assumed in all simulation

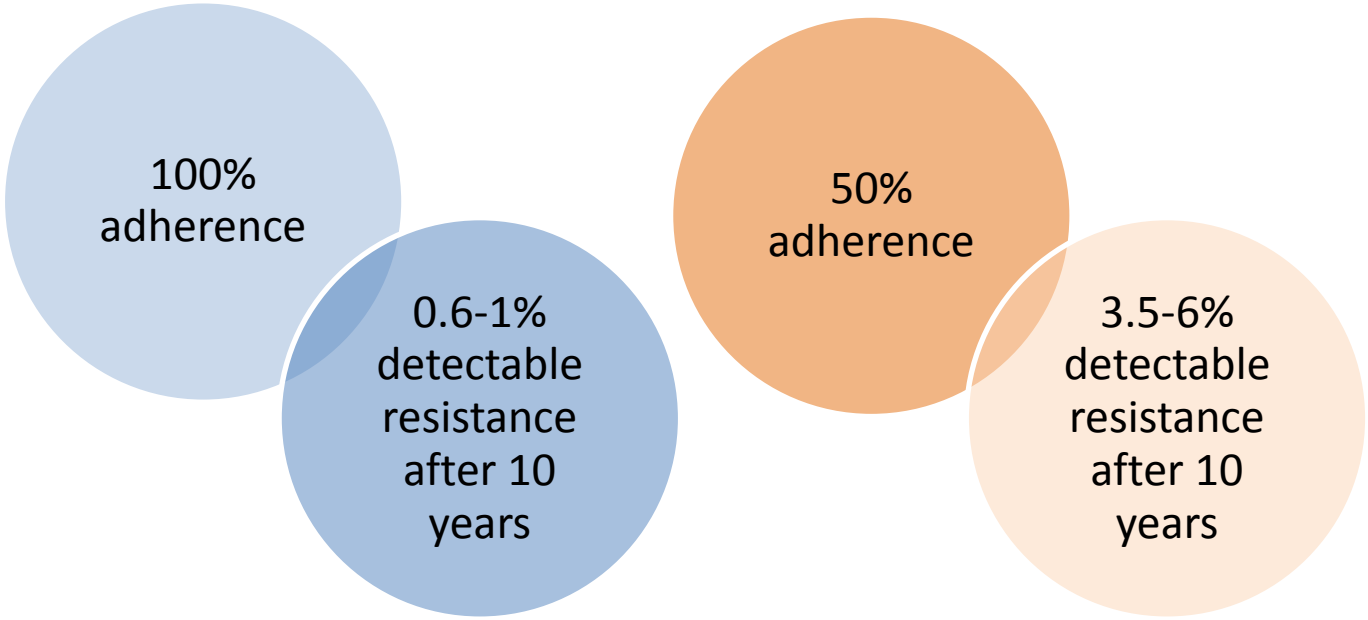
Dimitrov DT, Boily MC, Hallett TB, Albert J, Boucher C, Mellors JW, Pillay D, van de Vijver DAMC. PLoS One 2016;11(7):e0158620

Virologists disagreed!

20-180 days — Time until resistance emergence in infected PrEP users with breakthrough HIV infections

25-90% — The efficacy of PrEP against drug-resistant HIV

10-75% — The likelihood of resistance acquisition upon transmission



KEY POINT

- 17–23% infected individuals could virologically fail treatment as a result of past PrEP use or transmitted resistance to PrEP with moderate adherence

EACS PrEP Guidelines

- PrEP can be used in adults at high-risk of acquiring HIV infection.
- Recommended in HIV-negative men who have sex with men (MSM) and transgender individuals who are inconsistent in their use of condoms with casual partners or with HIV-positive partners who are not on treatment
- A recent STD or use of post-exposure prophylaxis may be markers of increased risk for HIV acquisition.
- May be considered in HIV-negative heterosexual women and men who are inconsistent in their use of condoms and likely to have HIV positive partners who are not on treatment
- PrEP is a medical intervention that may not provide full protection against acquiring HIV, does not protect against other STDs and should be used in combination with other preventive interventions, including the use of condoms.
- PrEP should be supervised by a doctor, experienced with sexual health and use of HIV medicines, possibly as part of a shared care arrangement.
- The following procedures are recommended:
- Documented negative fourth generation HIV test prior to starting PrEP.
- During PrEP, this test should be repeated every 3 months, and PrEP should be stopped immediately in case of early clinical signs of HIV seroconversion or a positive HIV diagnostic test and the person referred for evaluation to an HIV unit.

EACS PrEP Guidelines

- Before PrEP is initiated, HBV serology status should be documented.
- If HBsAg positive see Clinlical Management and Treatment of HBV and HCV Co-infection in HIV-positive Persons.
- Counsel that PrEP does not prevent other types of STD; screen for STD (including HCV) when starting PrEP and regularly during use of PrEP.
- Counsel that PrEP may impact renal and bone health
- Check renal function and bone mineral density according to guidelines on TDF use.
- Counsel that PrEP, like other prevention methods, only works when it is taken. Adherence counselling is recommended.
- Counsel that PrEP can be prescribed long term but that each consecutive PrEP prescription should be for a period of maximum 3 months (90 tablets) to ensure appropriate monitoring.
- 3. PrEP regimen
- TDF/FTC 300*/200 mg 1 tablet qd. For MSM with high-risk sexual behavior PrEP may be dosed ‘on demand’ (double dose of drug 2-24 hours before each sexual intercourse, followed by two single doses of drug, 24 and 48 hours after the first drug intake). If dosed ‘on demand’, the total dose per week should not exceed 7 tablets.
- In certain countries TDF is labelled as 245 mg rather than 300 mg to reflect the amount of the prodrug (tenofovir disoproxil) rather than the fumarate salt (tenofovir disoproxil fumarate).

EACS online PrEP teaching within HIV course

Summary HIV Prevention Strategies

- TasP is key
- PEP and PrEP are highly effective
- Assessment of risk
- Part of risk reduction strategy
- Regimens well tolerated
- Newer agents/methodologies being needed for PrEP
- Studies ongoing in heterosexual populations, particularly women
- Clear guidelines on management and follow-up
- Essential part of HIV and Sexual Health Care