PrEP and Women: (Some)Facts and Figures

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Swift

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

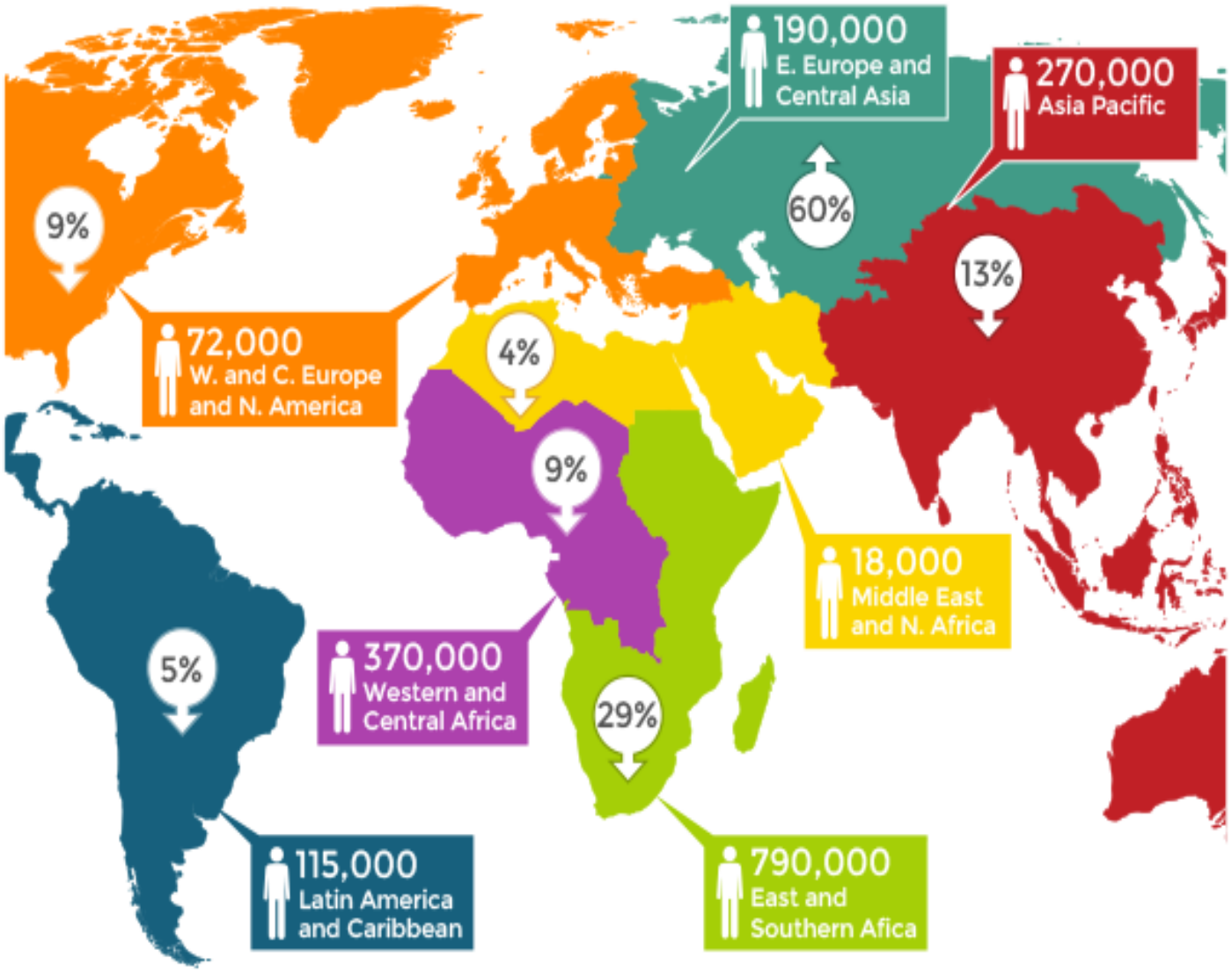
World Health Organization

Number of new HIV infections in 2016 and change since 2010

1.8 million people newly infected in 2016 globally

Decrease in number of new infections across the global population each year since 2010

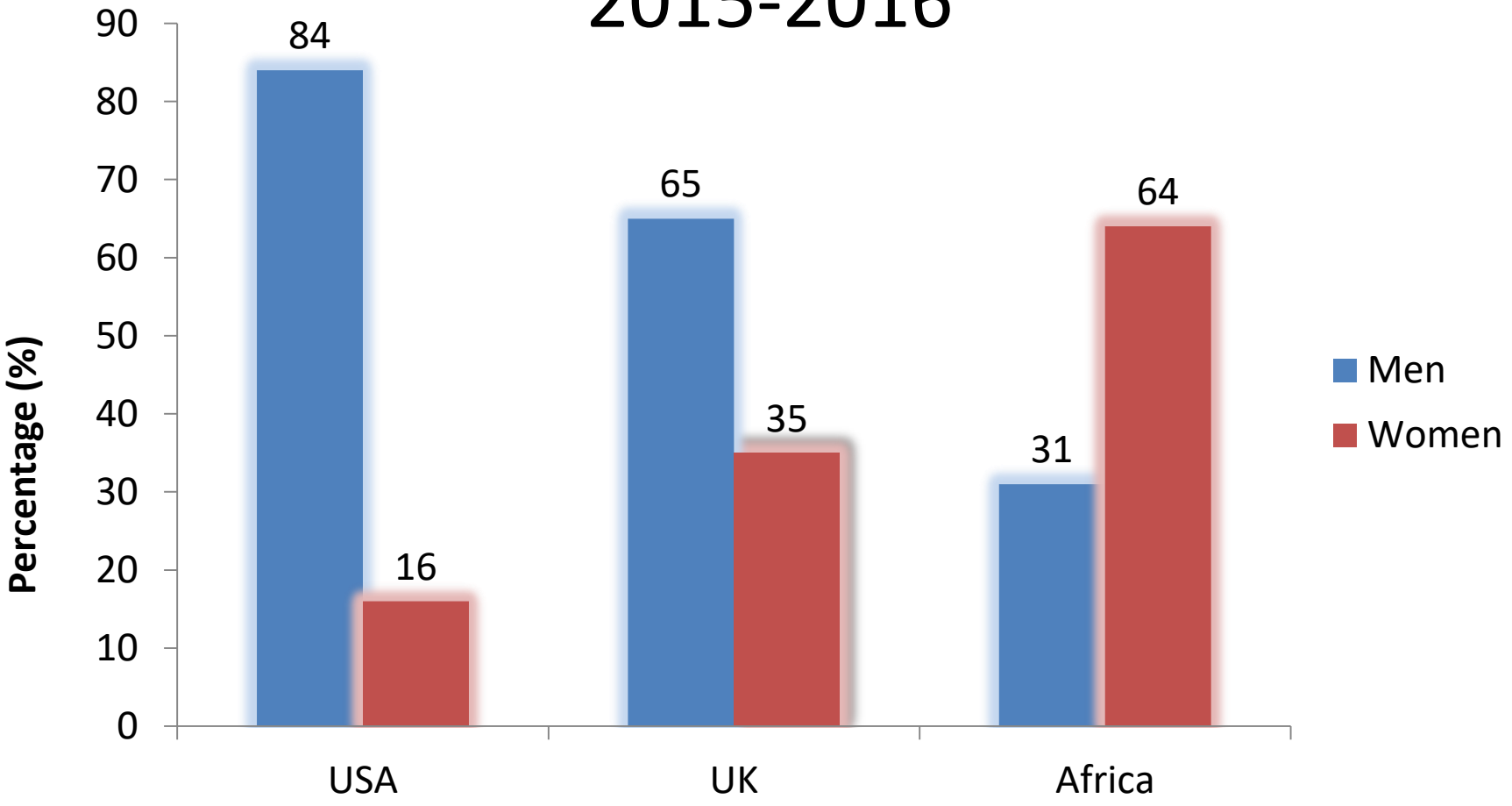
16%



AVERT.org

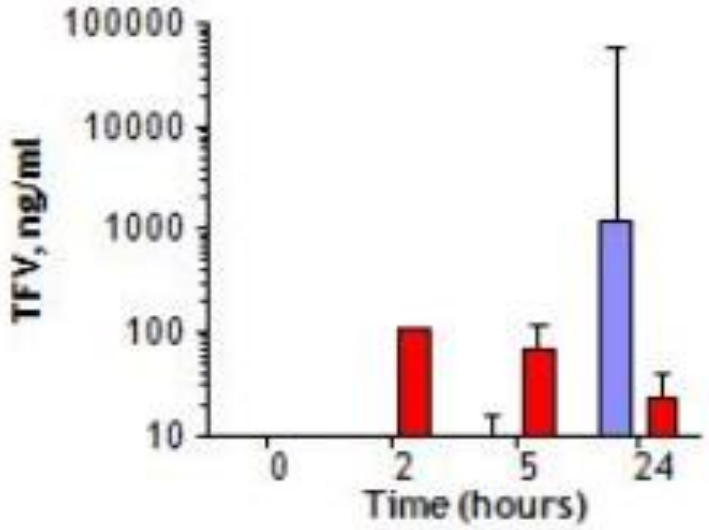
Source: UNAIDS Data 2017

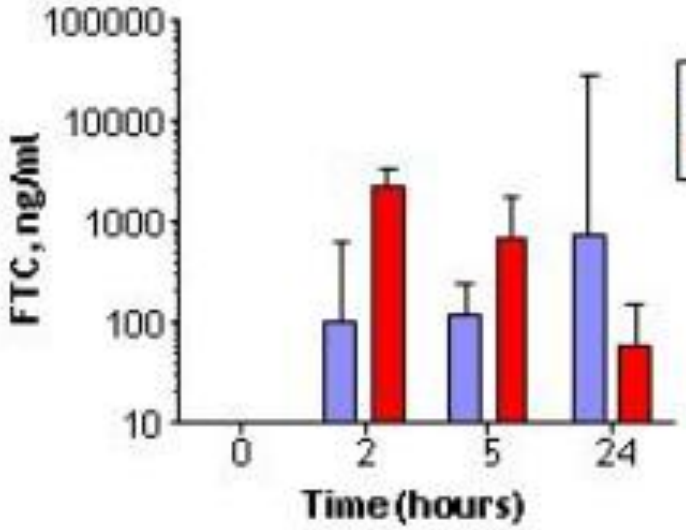
New HIV Diagnoses by Gender 2015-2016

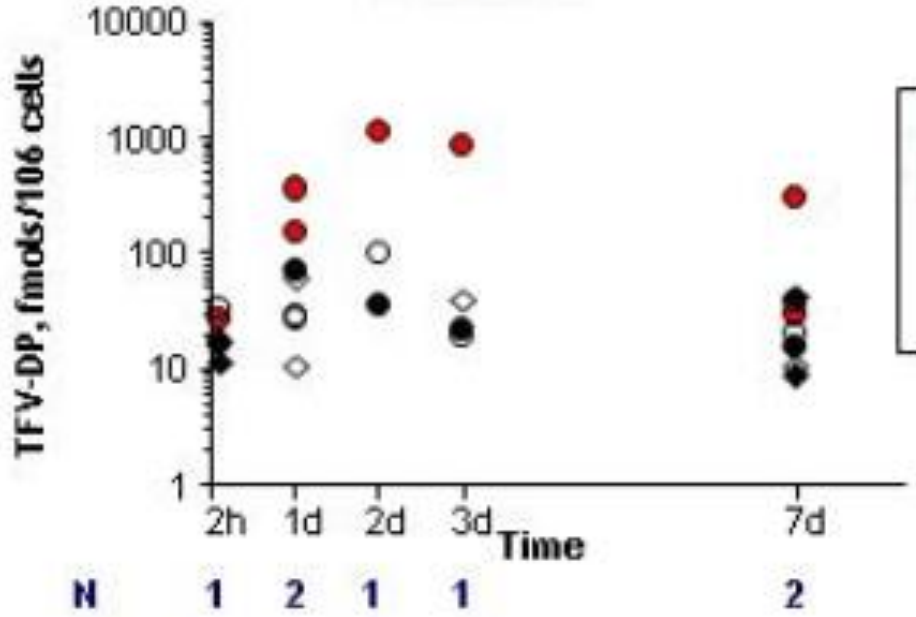


- Young African women are especially at risk, with 59% of new infections among young people aged 15-24 occurring among this group
- There is much more that needs to be done to improve knowledge of HIV and HIV testing among adolescents and young adults

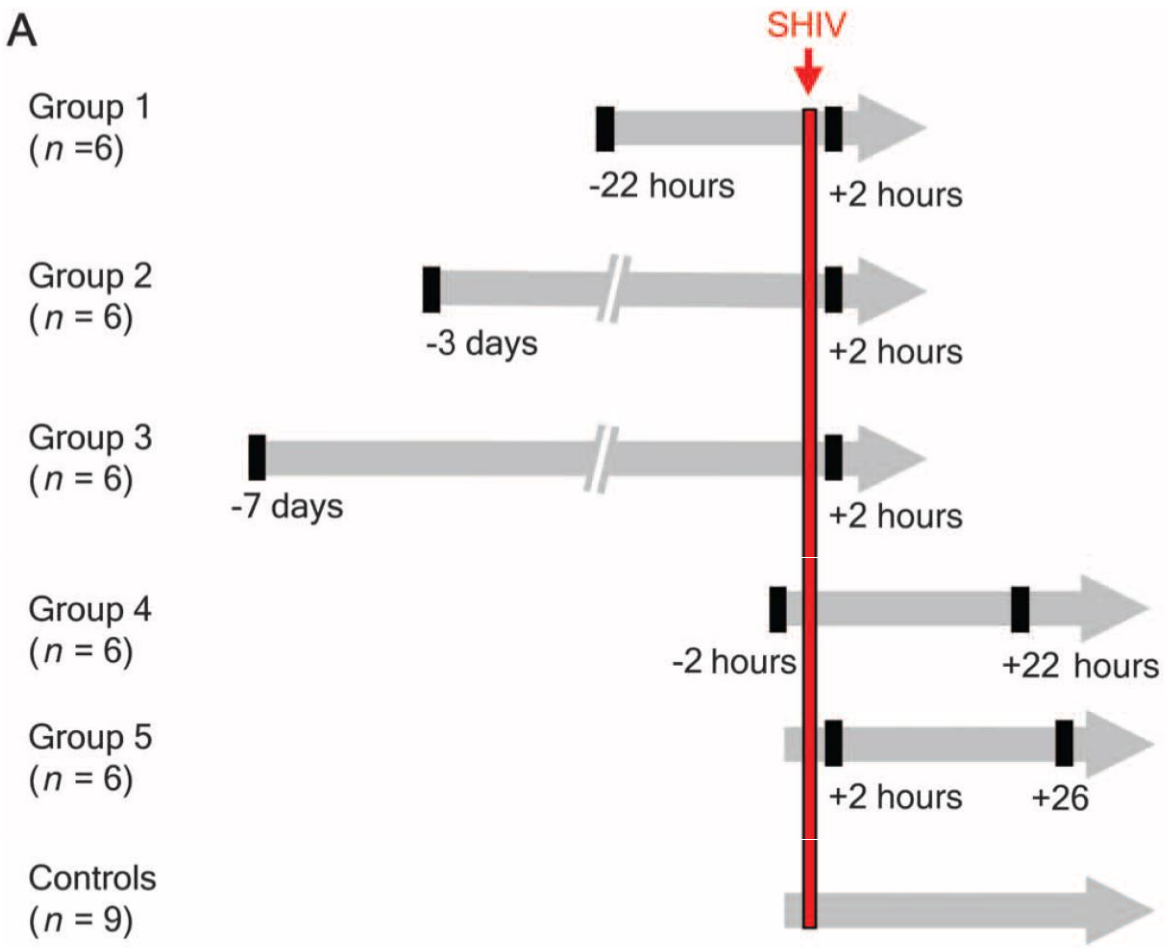
Local and systemic drug concentrations after oral administration of Truvada







Efficacy of intermittent rectal 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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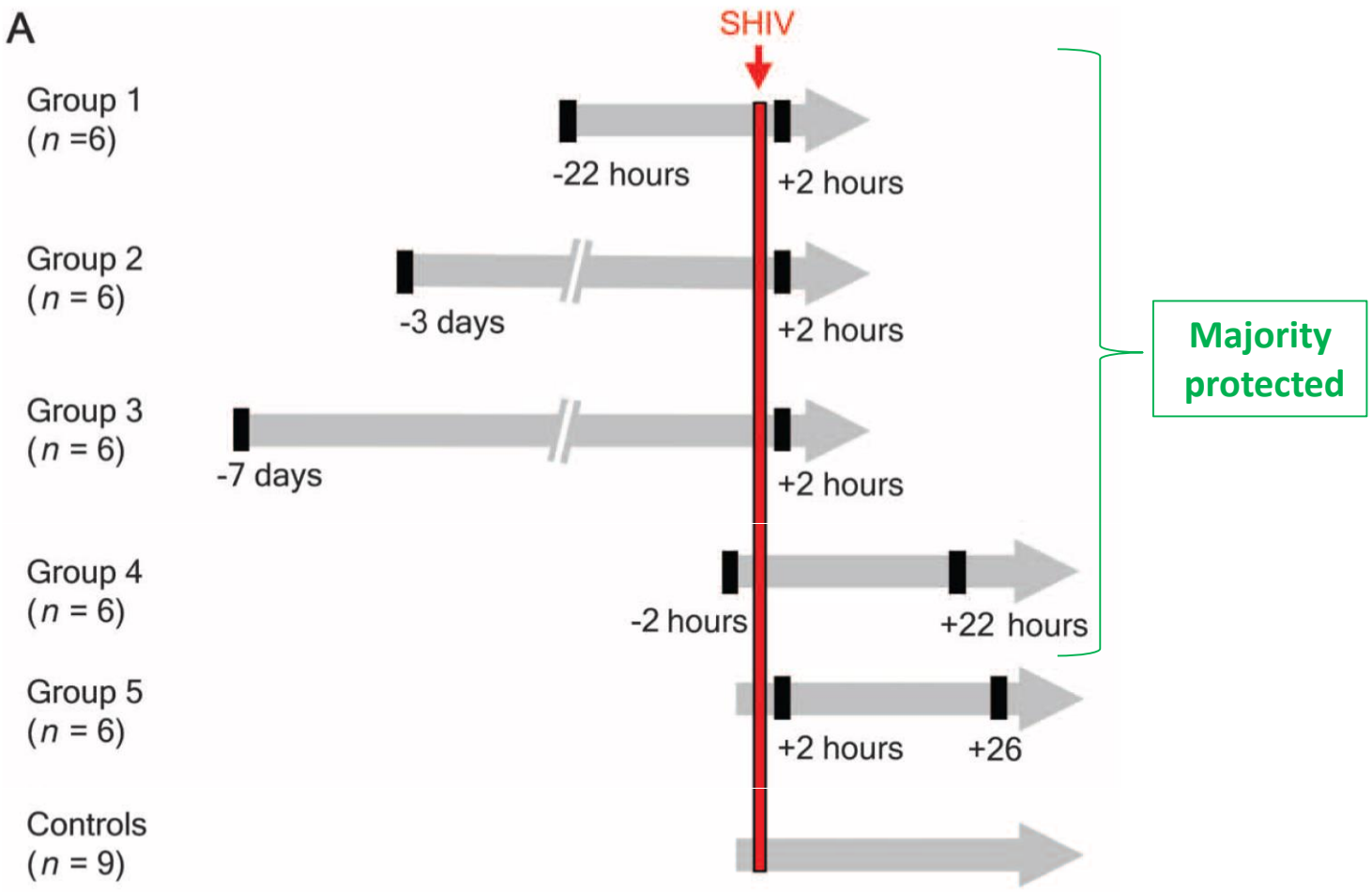

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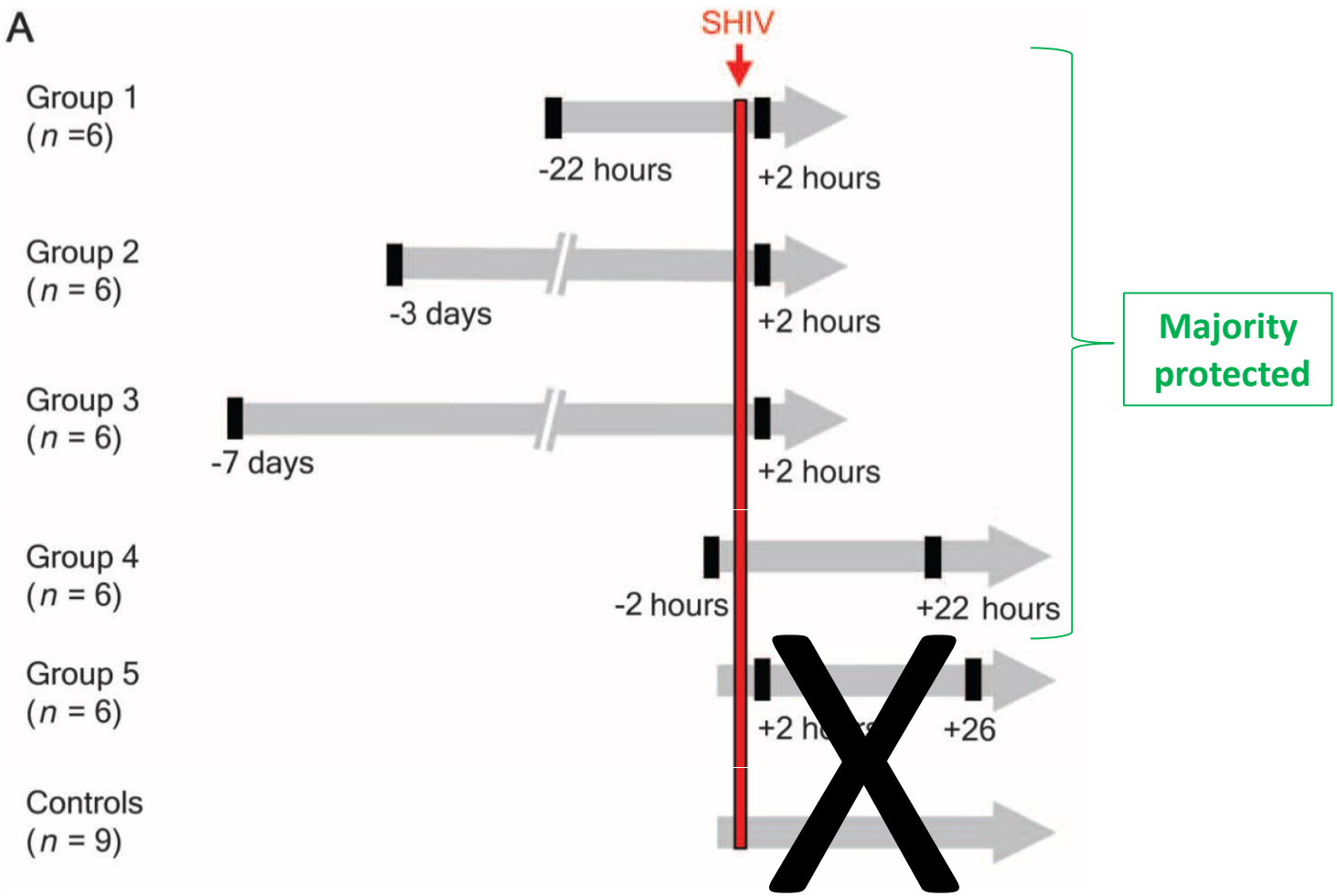


Slides courtesy of Gerardo Garcia-Lerma*1 CROI 2010 Paper # 83

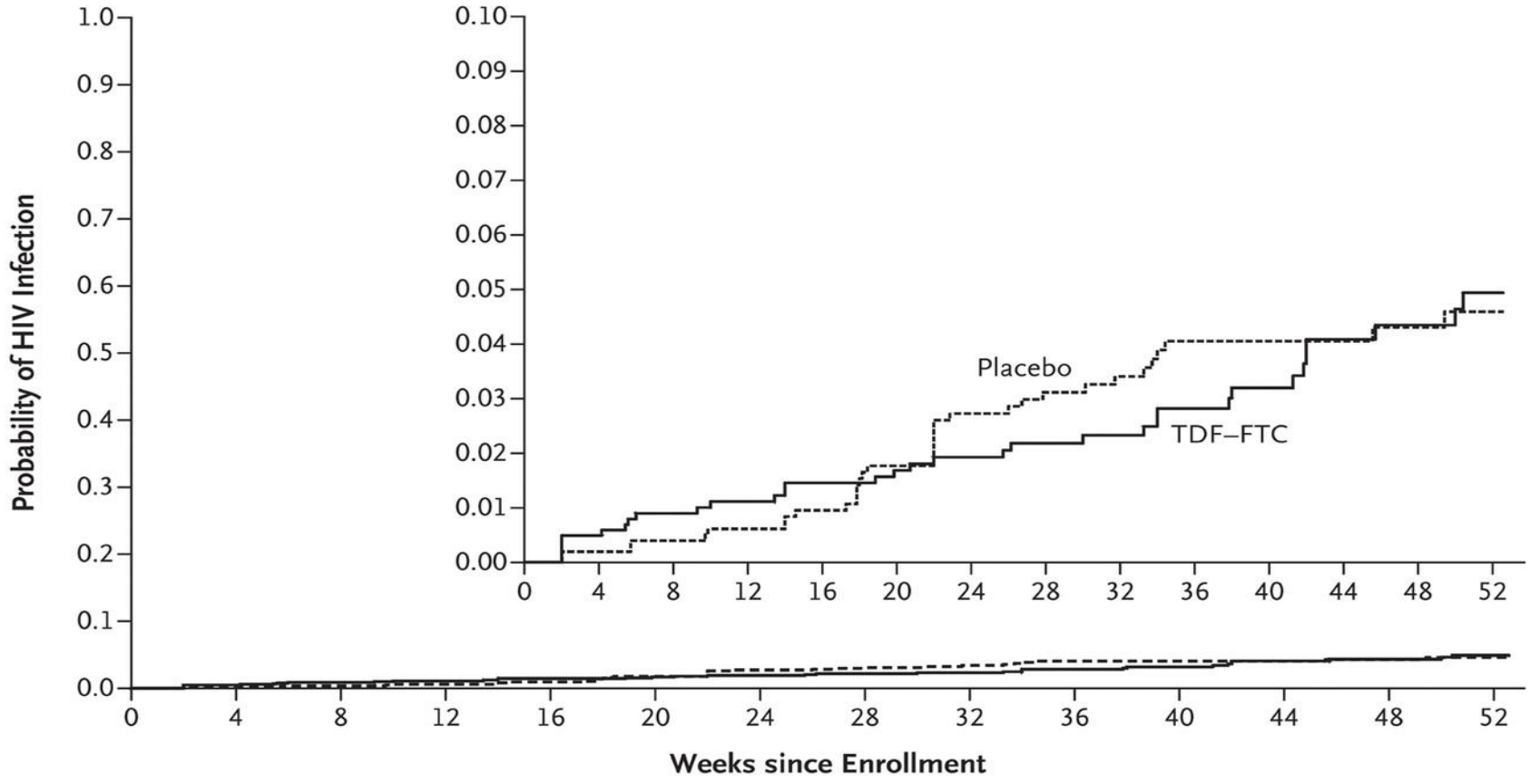
Summary clinical trials of daily oral PrEP in women

Trial	Population (average FU)	Proportion of women	Intervention	Overall efficacy (95%CI)	Efficacy among women	Adherence (- vs +)	Efficacy based on adherence
iPrEX	2499 MSM and TGW (median 1.2yrs)	339 (14%) transgender women	Daily oral TDF/FTC vs placebo	44% (95% CI: 15–63%)	11 infections in TDF/FTC vs 10 in placebo groups (HR: 1.1, 95% CI: 0.5–2.7)	No detectable drug among transgender women who acquired HIV	95% risk reduction with detectable study drug
Partners PrEP (Uganda & Kenya)	4758 HIV-SDC, seropositive partner not eligible for ART (24m)	1785 (52%) women	Daily oral TDF vs TDF/FTC vs placebo	67% (CI 44–81%) for TDF; 75% (CI 55–87%) for TDF/FTC 17 new diagnoses in TDF vs 13 in TDF/FTC vs 52 in placebo group (0.65 vs 0.50 vs 1.99/100 PY)	No difference between men & women **71%** for TDF **vs 66%** for TDF/FTC Efficacy consistent (64–84%) among HR women	Detectable plasma tenfovir levels in 83% who did not acquire HIV vs 31% who acquired HIV	86% risk reduction for TDF and 90% for TDF/FTC with detectable tenofovir level
TDF2 (Botswana)	1219 heterosexual men & women (median 1.1 yrs)	557 (45.7%) women	Daily oral TDF/FTC vs placebo	62.2% (21.5–83.4%) 9 new diagnoses in TDF/FTC group vs 24 in placebo (1.2 vs 3.1/100 PY)	Efficacy among women **49%**	Detectable plasma tenofovir levels in 80% who did not acquire HIV vs 50% who acquired HIV	HIV acquisition associated with lower plasma concentrations of tenofovir and emtricitabine
BTS (Thailand)	2413 men & women IDU (average 4 yrs)	489 (20%) women	Daily oral TDF vs placebo	48.9% (9.6–72.2%) 17 new diagnoses in TDF vs 33 in placebo group (0.35 vs 0.68/100 PY)	Efficacy among women **78.6%**	Detectable plasma tenofovir levels in 66% overall	70% risk reduction with detectable tenofovir level

Adapted from Gandhi et al. J Virus Erad. 2016 Jul; 2(3): 149–155.

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

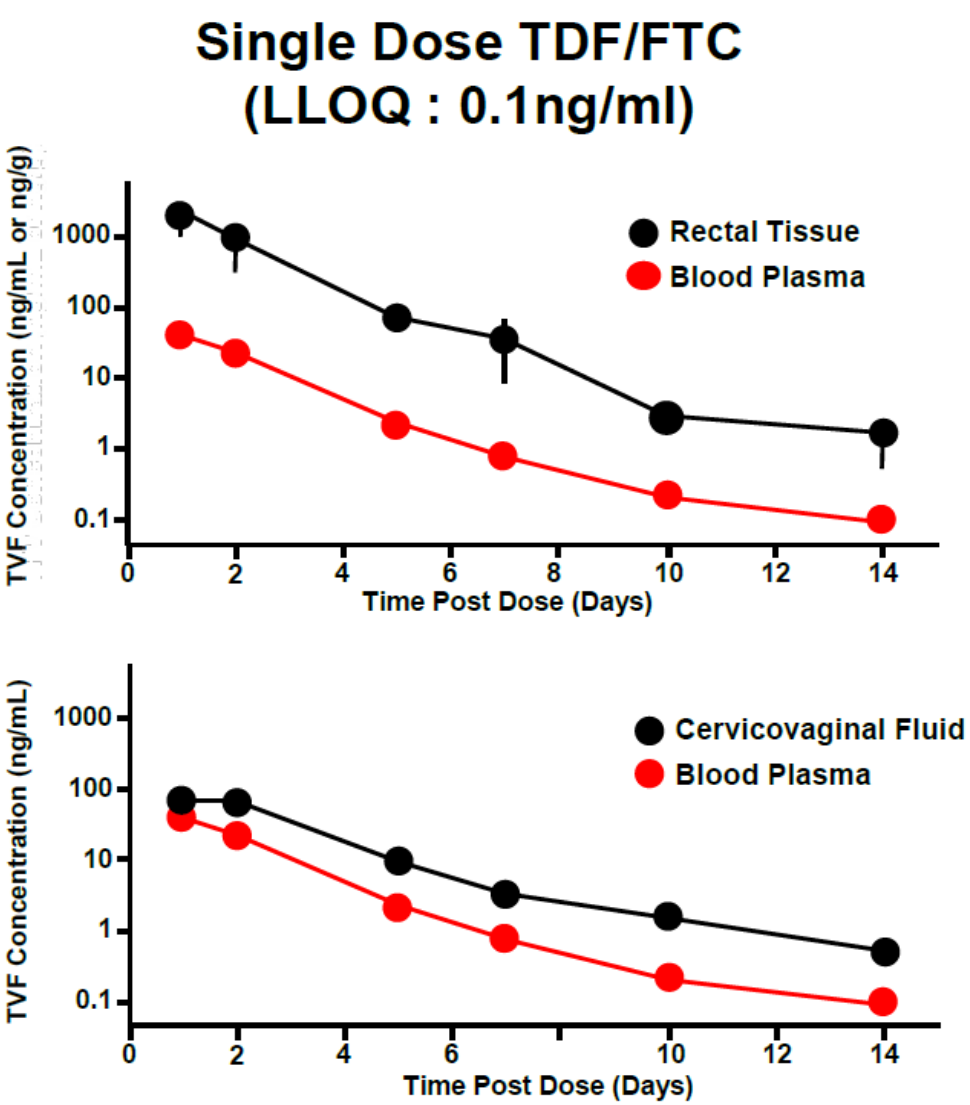
Adherence in women is the major limitation of oral PrEP

	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

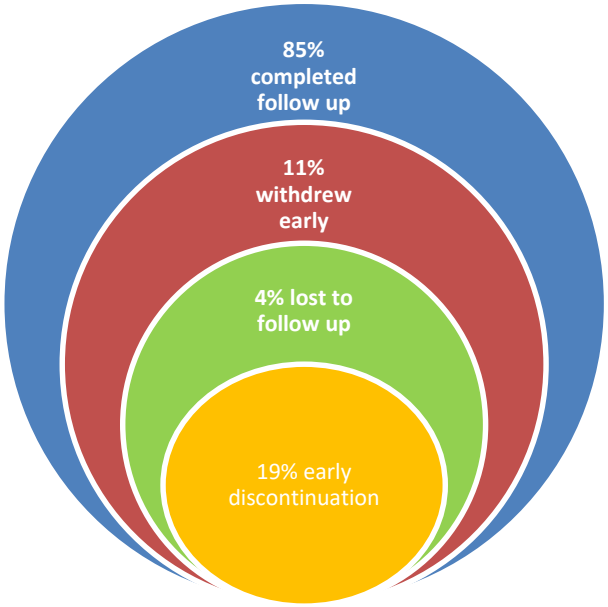
Patterson K, et al. Sci Transl Med 3, 2011, 112re4

Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Women: A Phase 2 Randomized Trial, n= 188

- To assess the safety and tolerability of MVC-containing PrEP over 48 weeks in U.S. women at risk for HIV infection.
- Phase 2 randomized, controlled, double-blinded study of 4 antiretroviral regimens used as PrEP
- 12 clinical research sites of the HIV Prevention Trials Network and AIDS Clinical Trials Group.
- HIV-uninfected women reporting condomless vaginal or anal intercourse with at least 1 man with HIV infection or unknown serostatus within 90 days

MVC only	MVC-emtricitabine (FTC)	MVC-tenofovir disoproxil fumarate (TDF)	TDF-FTC (control)

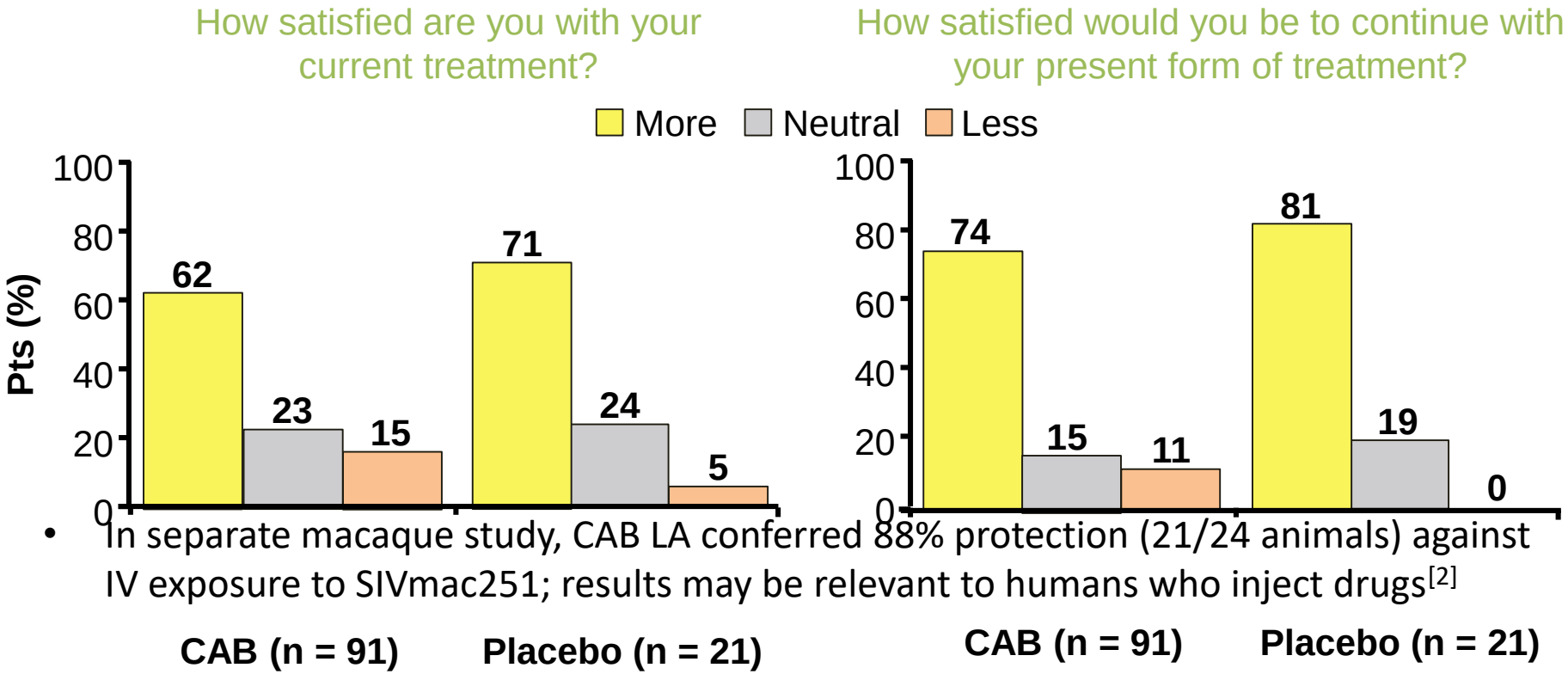
- Grade 3 or 4 adverse events occurred in 5 (MVC), 13 (MVC-FTC), 9 (MVC-TDF), and 8 (TDF-FTC) participants; rates did not differ among regimens. Of available plasma samples at week 48 (n = 126), 60% showed detectable drug concentrations. No new HIV infections occurred
- **Limitations:**
- Participants were not necessarily at high risk for HIV infection. The regimen comprised 3 pills taken daily. The study was not powered for efficacy



Gulick RM, et al. Ann Intern Med 2017 Sep 19;167(6):384-393

ÉCLAIR: Patient Satisfaction With IM Therapy vs Oral Phase

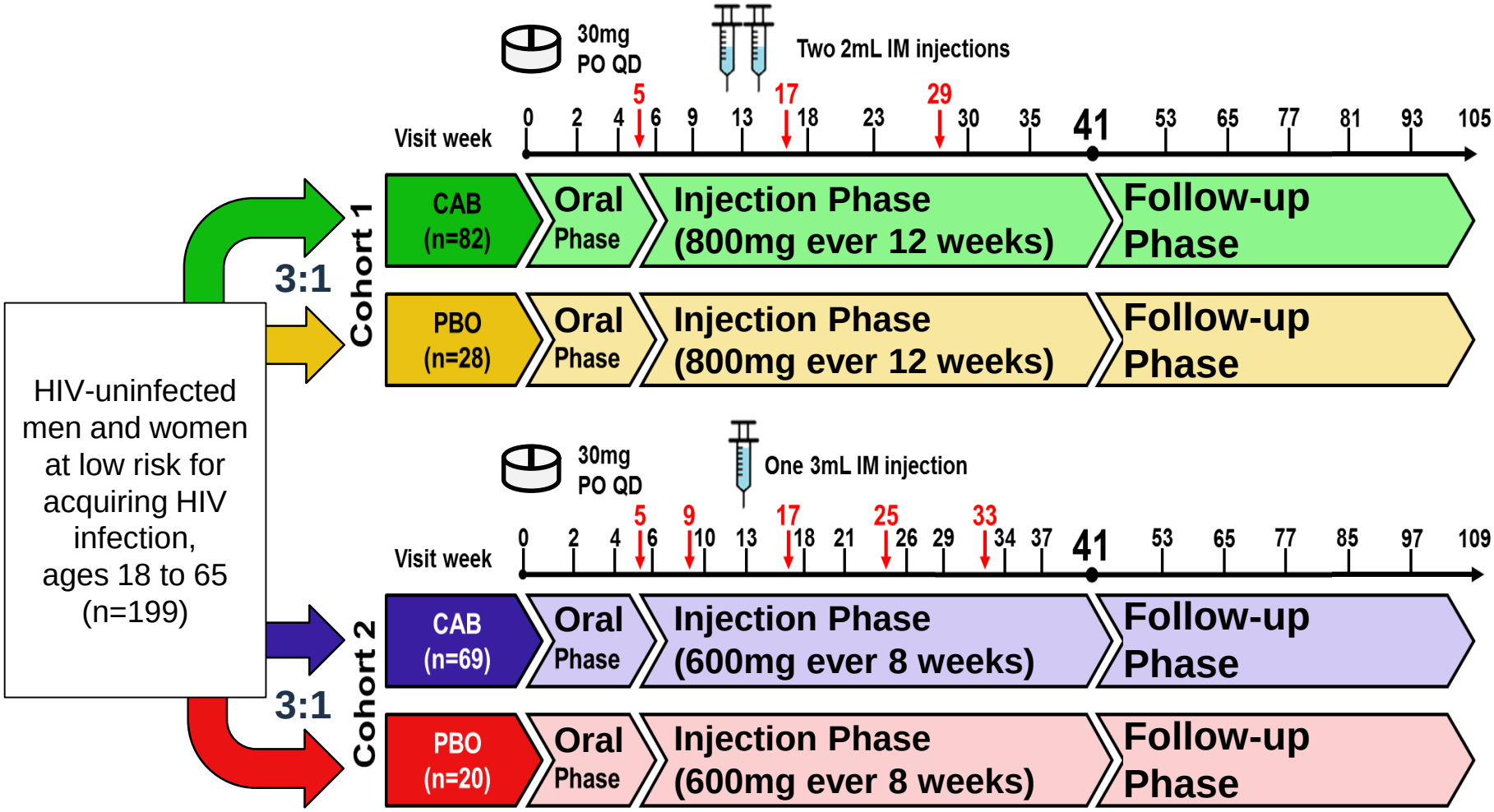
- Pt satisfaction assessed by questionnaire at Wk 18 of IM treatment; asked pts to compare satisfaction of current IM vs past oral therapy[1]



- 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

ImPREP: Same-Day PrEP With TDF/FTC for High-Risk 5019 MSM (94%) and TGW 335 TGW (6%)in Brazil, Mexico, and Peru 30-day supply of TDF/FTC

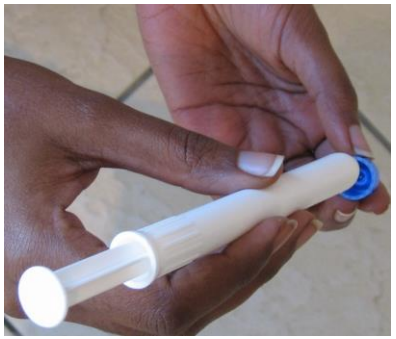
- Primary outcomes
  - **PrEP early continuation:** attendance to the first 2 follow-up visits within 120 days of PrEP initiation
  - **PrEP adherence:** ≥ 16 days of PrEP medication filled per 30-day period (medication possession ratio ≥ 0.53)

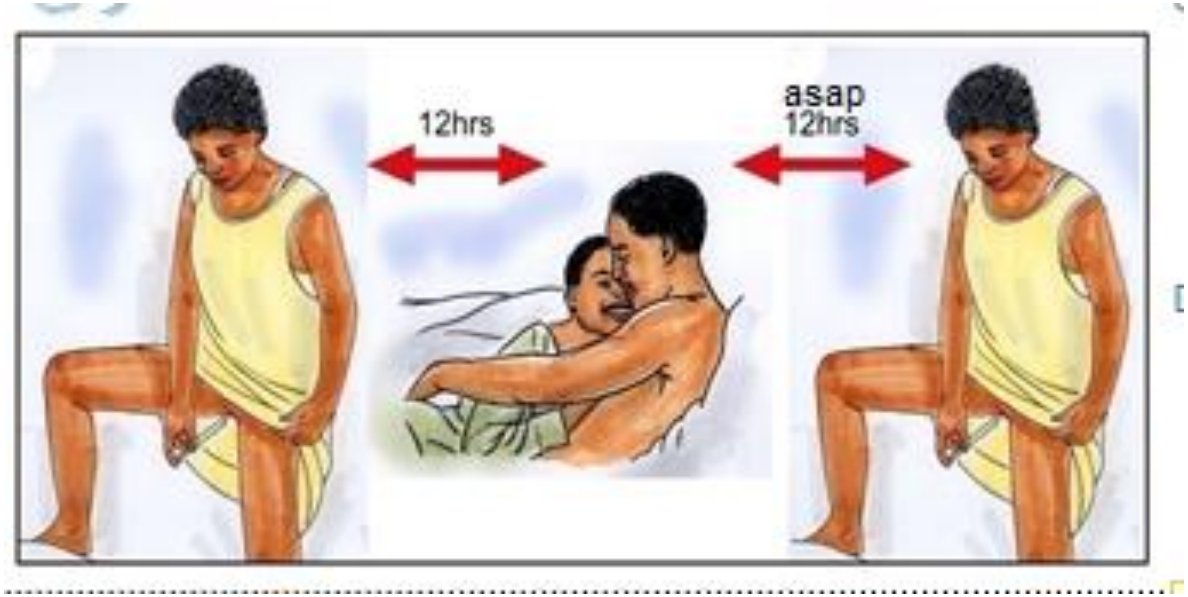
Population	Early Continuation, %	Medication Possession Ratio ≥ 0.53, %	Follow-up, PY	HIV Incidence per 100 PY (95% CI)
Brazil	85.4	98.7	1438.6	0.2 (0.1-0.6)
Mexico	84.0	98.0	344.0	0.6 (0.2-2.3)
Peru	52.7	91.0	286.4	2.4 (1.2-5.1)
Overall ▪ TGW	79.6 55.7	97.2 88.7	2069.0 --	0.6 (0.3-1.0) --

Veloso. IAS 2019. Abstr TUAC0404LB.

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

- BAT 24 on-demand topical PrEP
  - 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

BACKGROUND: Caprisa 004 microbicide study presented at IAS 2016

- Tenofovir gel was barely effective (39% fewer infections in women using it versus placebo)
- *Lactobacillus* dominant = 61% effectiveness which was highly significant
- Non-*Lactobacillus* types dominant = 18% effective
- BUT women with BV tend to have more sex

AIM: Whether BV bacteria really do affect drug concentrations in the vaginal mucous membrane (epithelium)

METHODS: A secondary analysis of FAME-04, a phase 1 safety study comparing vaginal film and gel formulations of tenofovir

N=41, mean age 28yo, 71% were white women

Tenofovir levels were compared between women with BV species and not

- after seven days of microbicide gel or film use at home
- after a single application at the trial centre

Hillier S, et al. CROI 2017

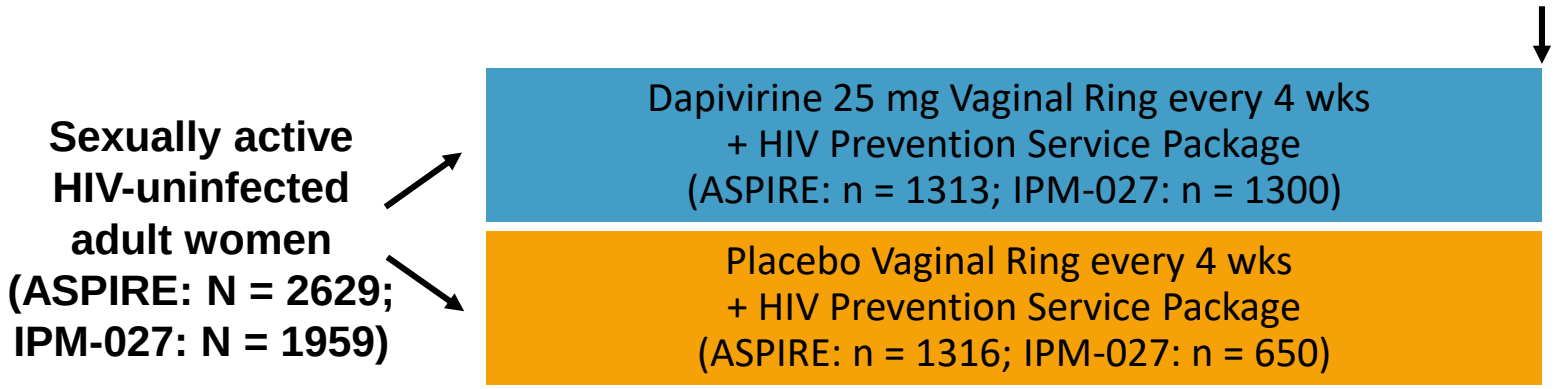
VAGINAL BACTERIA DO AFFECT BLOOD AND TISSUE CONCENTRATIONS OF TENOFOVIR IN MICROBICIDE USE

RESULTS:

- 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.

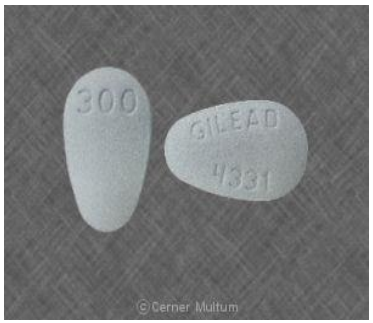
1. Baeten JM, et al. CROI 2016. Abstract 109LB.
2. Baeten JM, et al. N Engl J Med. 2016;[Epub ahead of print].
3. Nel A, et al. CROI 2016. Abstract 110LB.

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

Sophia

Women and PrEP

Sophia Forum and our partners cliniQ, Forum Link and ATHENA Initiative are delighted to share a new web resource on PrEP for women.

Women and PrEP was developed by a small group of volunteers, who are passionate about HIV prevention for women, and wanted to create a resource by women and for women.

The website is designed to answer all the questions a woman might have about PrEP, including how it works and how to access it as well as HIV prevention and testing more broadly. It also includes space for women to share their own views and experiences about PrEP.

Please share the website with your networks – women need and deserve full, accurate and accessible information about PrEP!

We are very grateful to colleagues from United4PrEP who provided invaluable feedback and guidance to shape and improve the website.

We need more Facts and Figures!

Thank you

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