PrEP focus

AWACC 2017

Michelle Moorhouse

08 Sep 2017

University of the Witwatersrand
WITS RHI

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

Disclosures

Dr Moorhouse has received speaker fees and honoraria from Gilead Sciences, AbbVie, Cipla, Mylan and Janssen, and has received conference sponsorship from BD, Gilead, Merck, Cipla and Mylan.

Wits RHI is part of optimisation collaborations – grants to improve testing, new drug regimens, linkage to care and has received drug donations for studies

HIV in South Africa, 2016

South Africa (2016)

7.1 million people living with HIV

18.9% adult HIV prevalence

270,000 new HIV infections

110,000 AIDS-related deaths

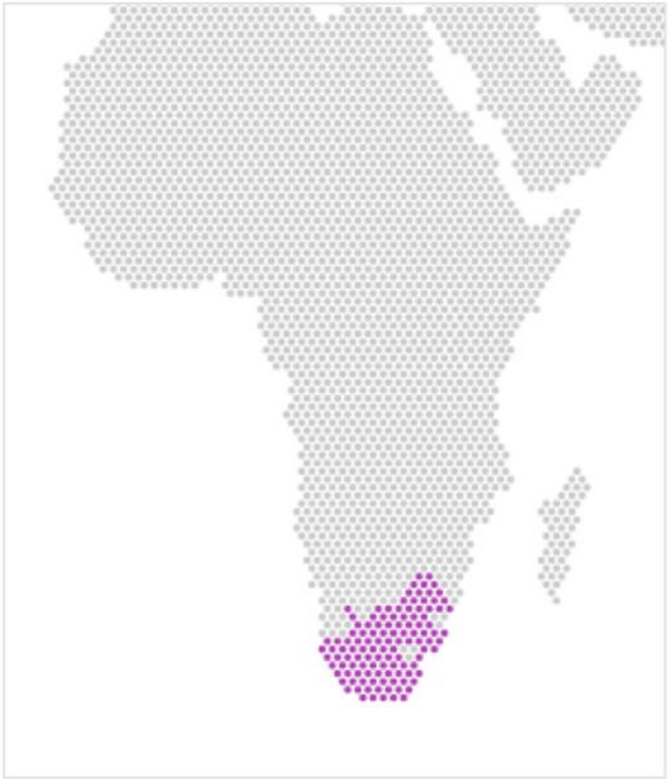
56% adults on antiretroviral treatment

55% children on antiretroviral treatment

Source: UNAIDS Data 2017

UNAIDS data 2017

HIV in South Africa, 2016



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270,000 new HIV infections

110,000 AIDS-related deaths

56% adults on antiretroviral treatment

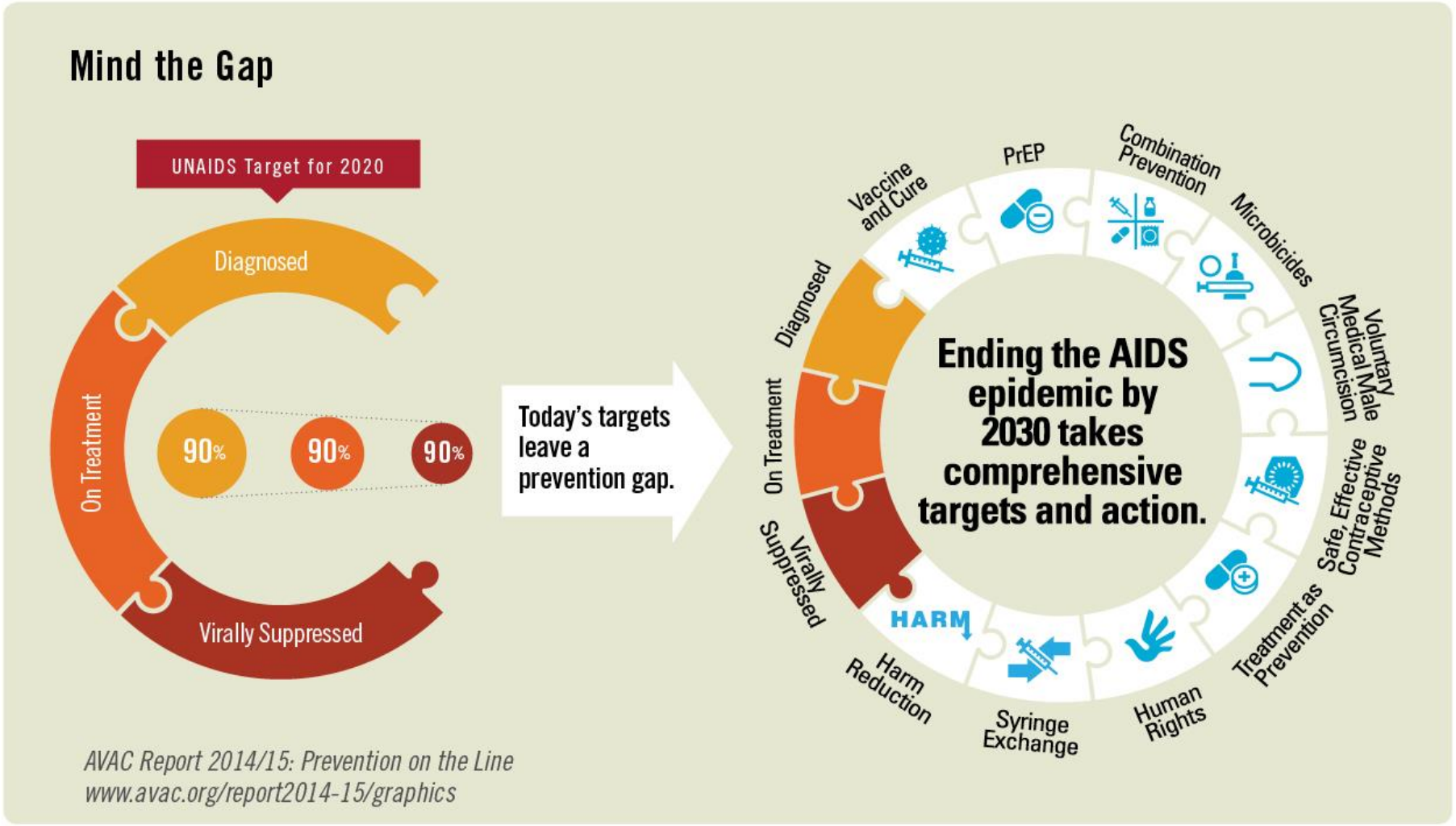
55% children on antiretroviral treatment

Source: UNAIDS Data 2017

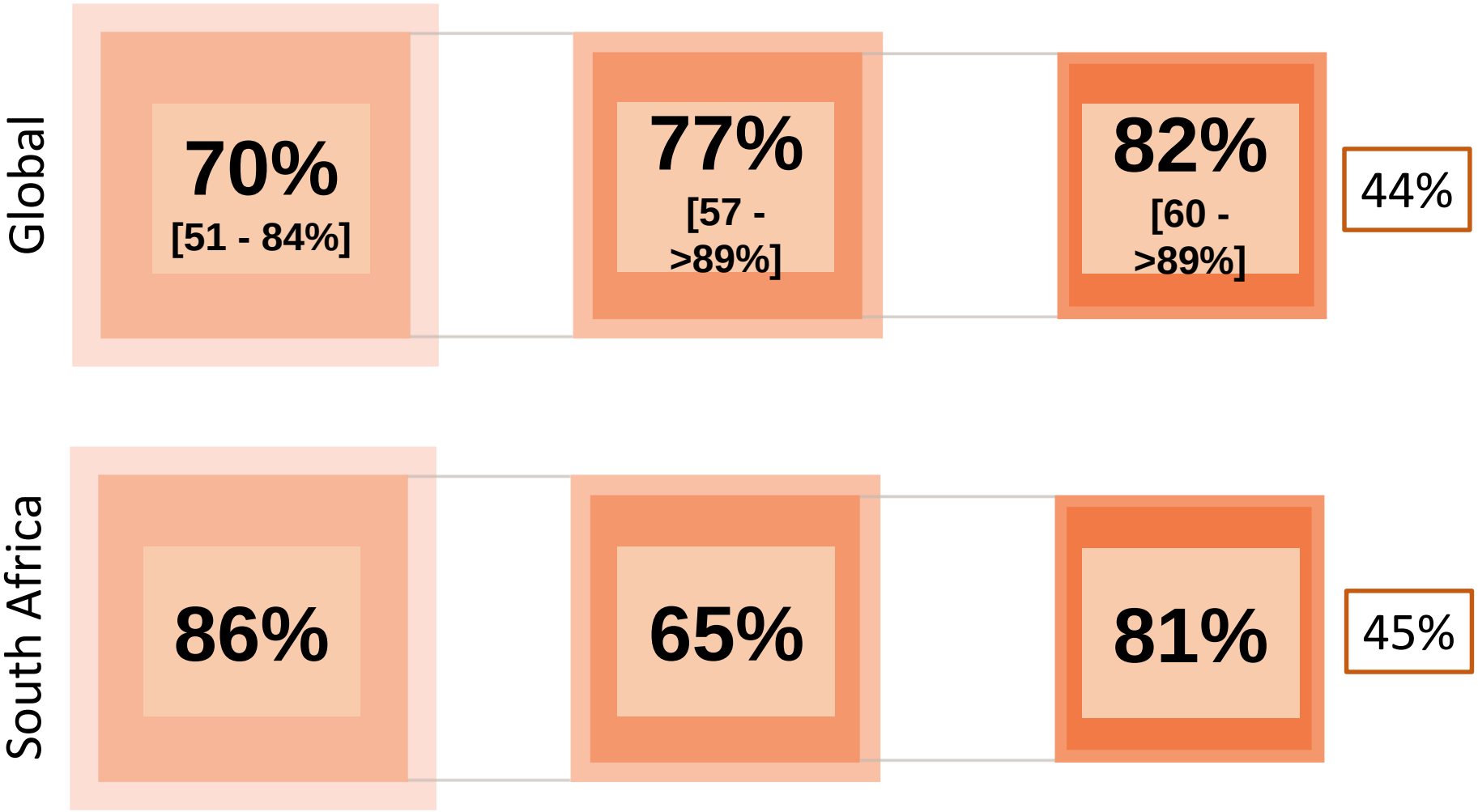
One third of new infections in Eastern and Southern Africa

UNAIDS data 2017

Will 90-90-90 do it?

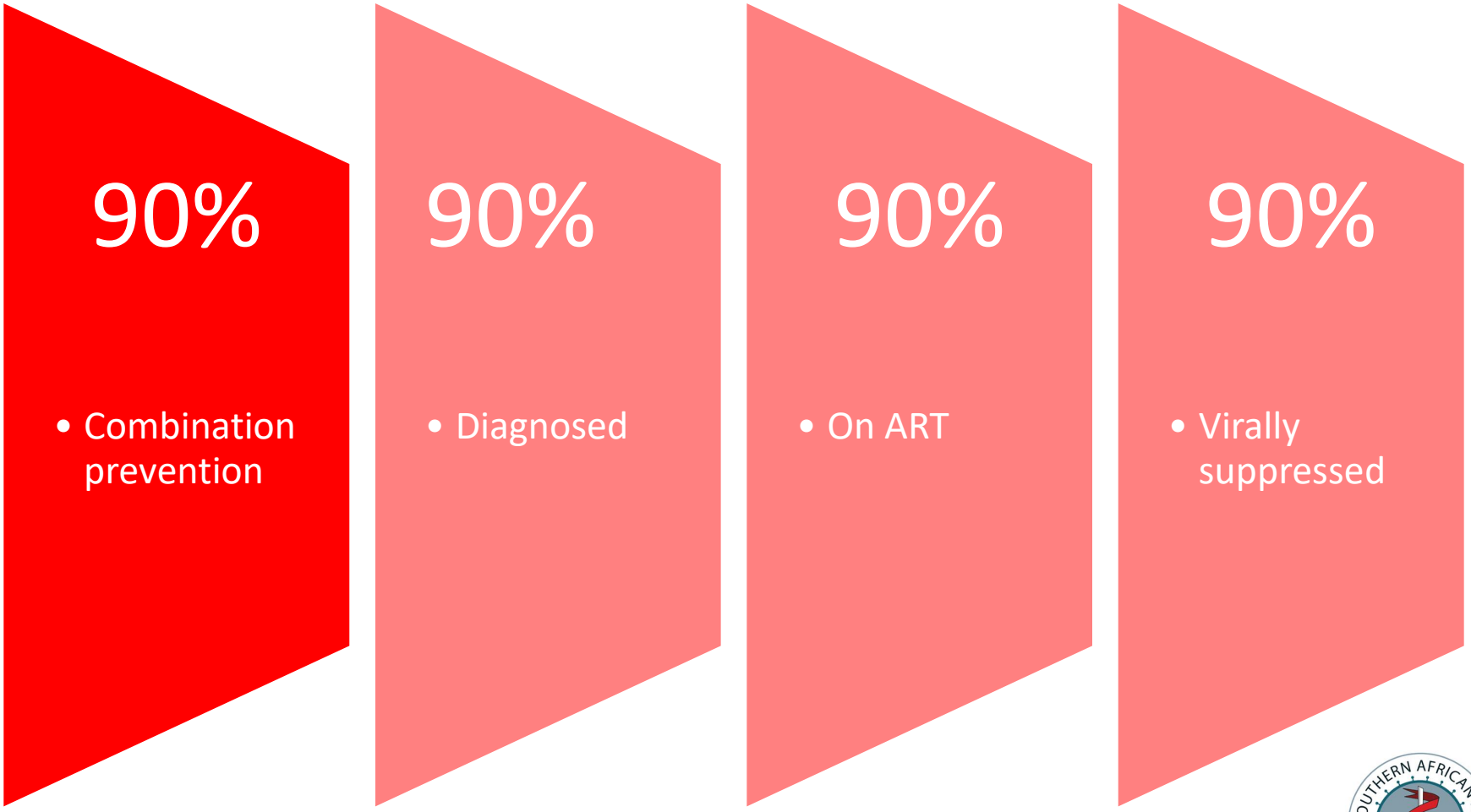


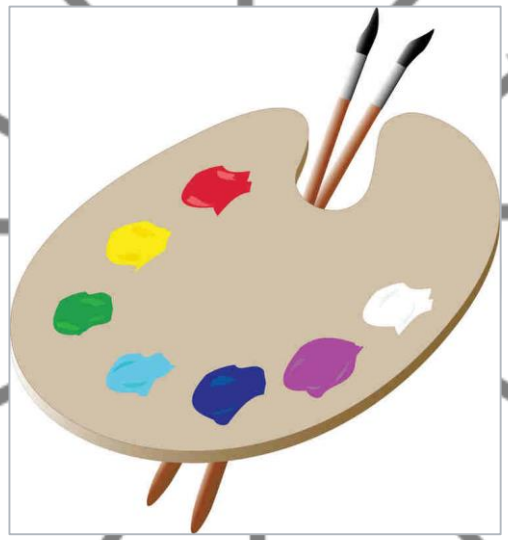
Are we on target?



UNAIDS data 2017

Will 90-90-90 do it?





Microbicides for women

Abdool Karim Q, Science 2010

Male circumcision

Auvert B, PloS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007

Treatment of STIs

Grosskurth H, Lancet 2000

Treatment for prevention

Donnell D, Lancet 2010
Cohen M, NEJM 2011

Female Condoms

Male Condoms

Behavioural positive prevention

Fisher J, JAIDS 2004

HIV Counselling and Testing

Coates T, Lancet 2000

Oral pre-exposure prophylaxis

Grant R, NEJM 2010 (MSM)
Baeten J , 2011 (Couples)
Paxton L, 2011 (Heterosexuals)

Behavioural Intervention

- Abstinence
- Be Faithful

Post Exposure prophylaxis (PEP)

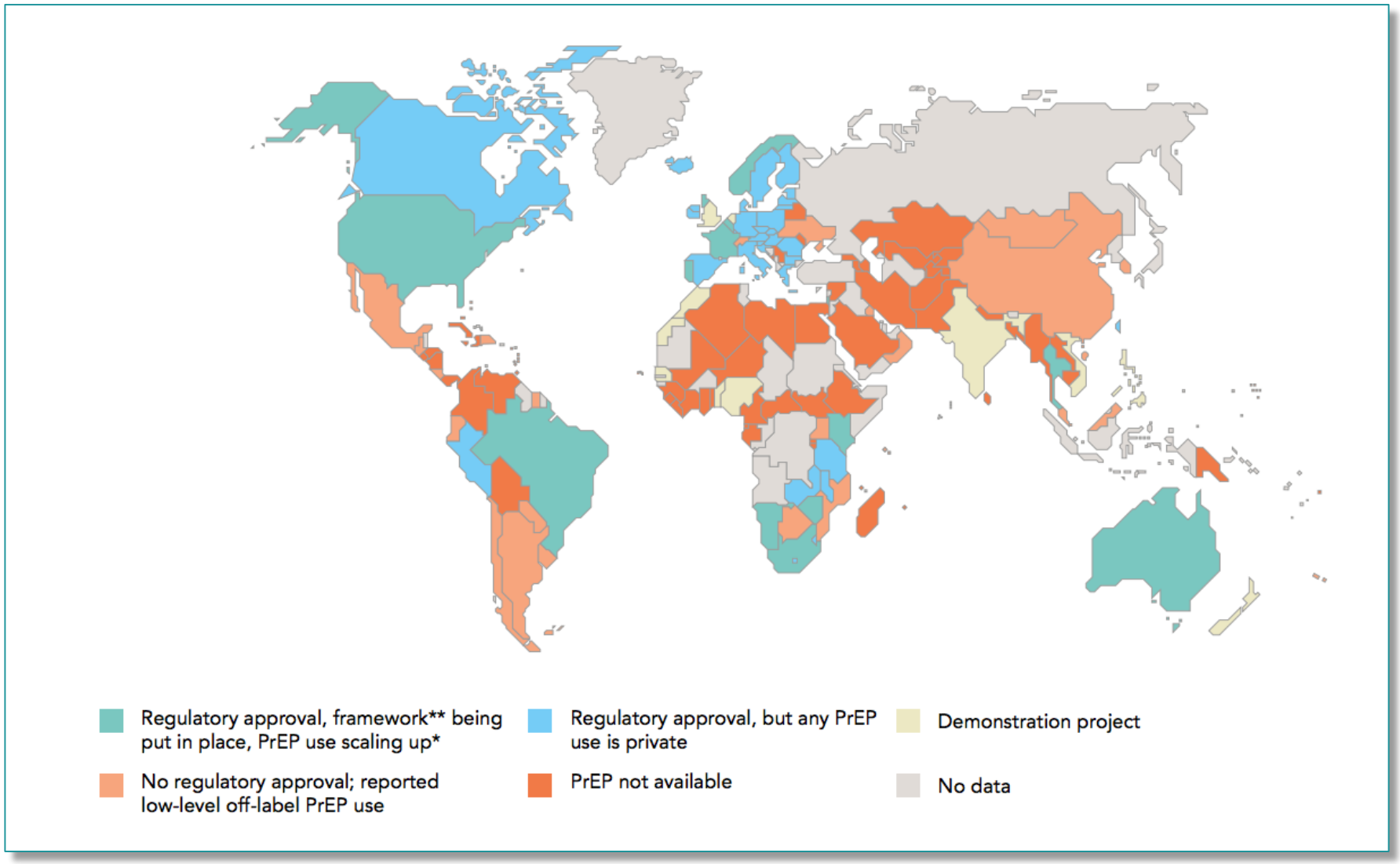
Scheckter M, 2002

Vaccines

Rerks-Ngarm S, NEJM 2009

Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission

PrEP availability still limited

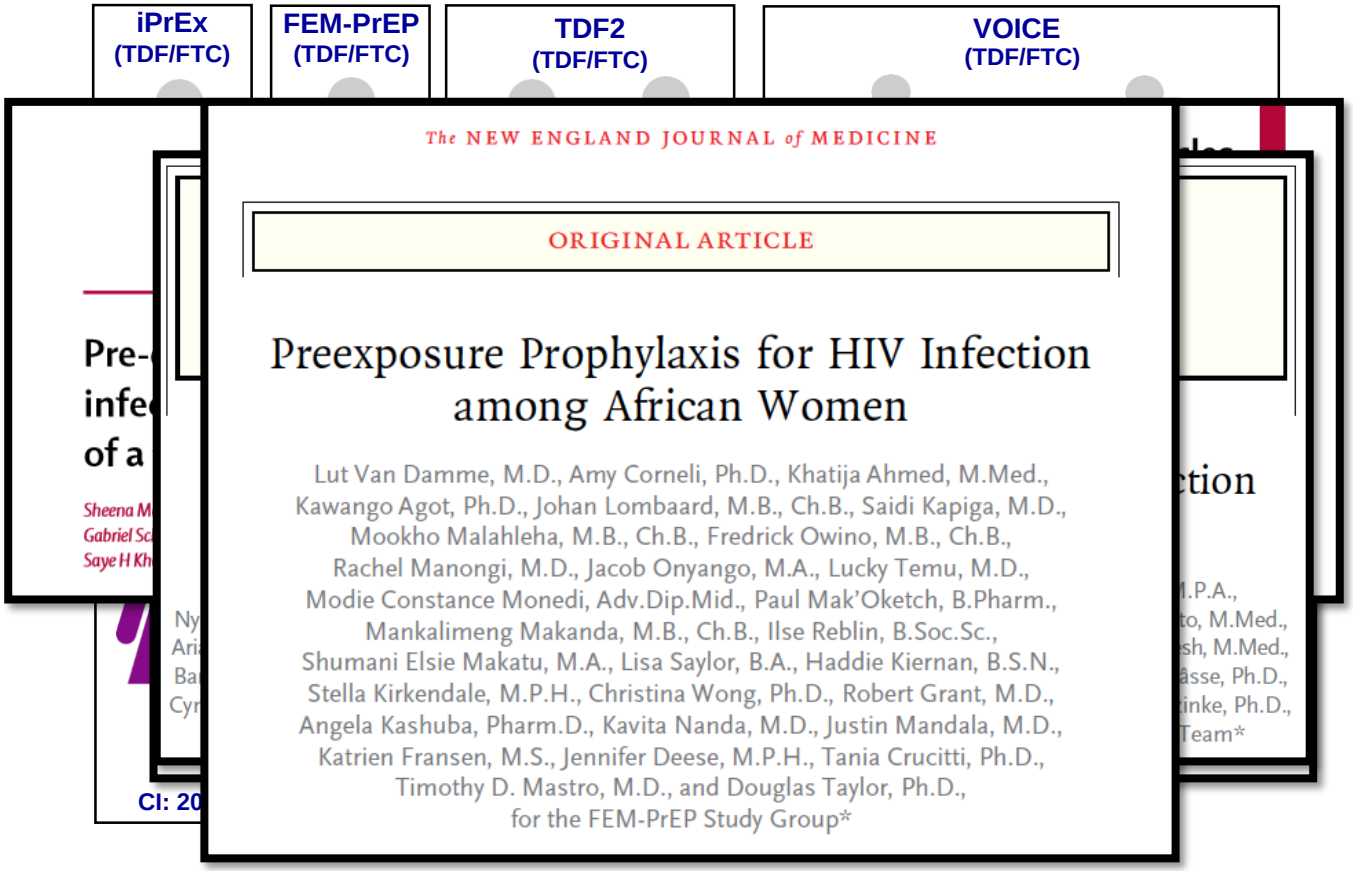


UNAIDS data 2017

What is PrEP?

- PrEP involves taking a pharmaceutical agent prior to an exposure to prevent an outcome
  - (e.g. infection by a microbe, such as malaria)
- HIV: ARV medications to prevent HIV infection
- TDF/FTC as FDC recommended

Effectiveness of daily TDF/FTC in clinical trials



Efficacy results from clinical trials

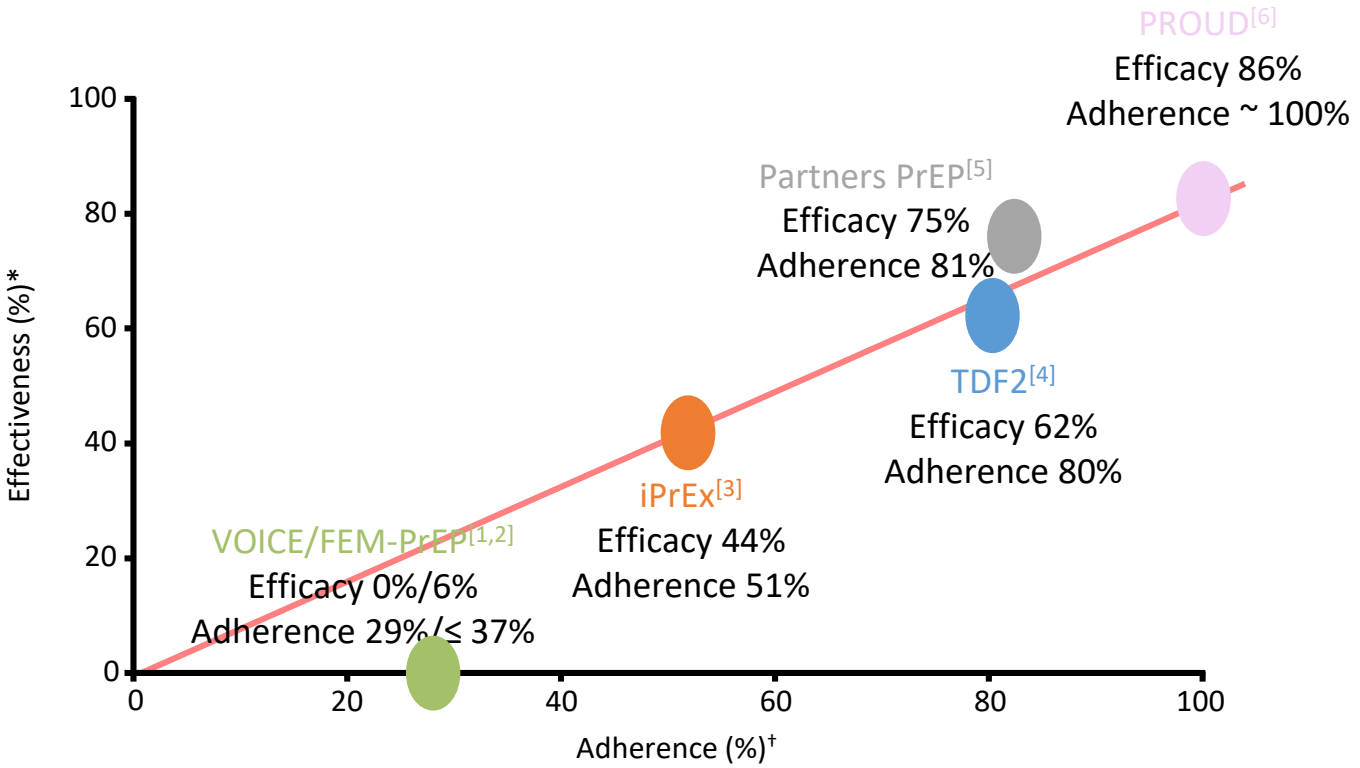
Clinical trial	Participants	Number	Drug	mITT [a] efficacy of % reduction in acquisition of HIV infection [b]		Adherence-adjusted efficacy based on TDF detection in blood [c]	
				%	(95% CI)	%	(95% CI)
iPrEx	Men who have sex with men (MSM)	2499	TDF/FTC	42	(18-60)	**92**	(40-99)
Partners PrEP	HIV discordant couples	4747	TDF	67	(44-81)	**86**	(67-94)
			TDF/FTC	75	(55-87)	**90**	(58-98)
TDF 2	Heterosexually active men and women	1200	TDF/FTC	62	(22-83)	**84**	NS
Bangkok Tenofovir Study	IDU	2413	TDF	49	(10-72)	**74**	(2-91)
PROUD	MSM	500	TDF/FTC	86	(58-96)	-----	-----
IPERGAY	MSM	400	On demand TDF/FTC	86	(40-99)	-----	-----
Fem-PrEP	Heterosexually active women	1951	TDF/FTC	NS	-----	**< 40%**	-----
VOICE	Heterosexually active women	5029	TDF/FTC	NS	-----	**<30%**	-----

a. Modified Intent to Treat
b. Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
c. The percentage of reduction in HIV incidence among those with TFV detected in blood, compared with those without detectable TFV

On-demand" regimen constitutes: FTC/TDF or 2 placebo < 24 hrs prior to sexual intercourse exposure 1 FTC/TDF or placebo dose 24 hrs after; and a final dose 48 hrs after sexual intercourse

Molin, J. et al. CROI 2015; Seattle, WA. #23LB
McCormack S, et al. CROI 2015; Seattle, WA. #22LB
US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014. http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf.

Select daily oral TDF/FTC PrEP trials: Effectiveness improves with adherence



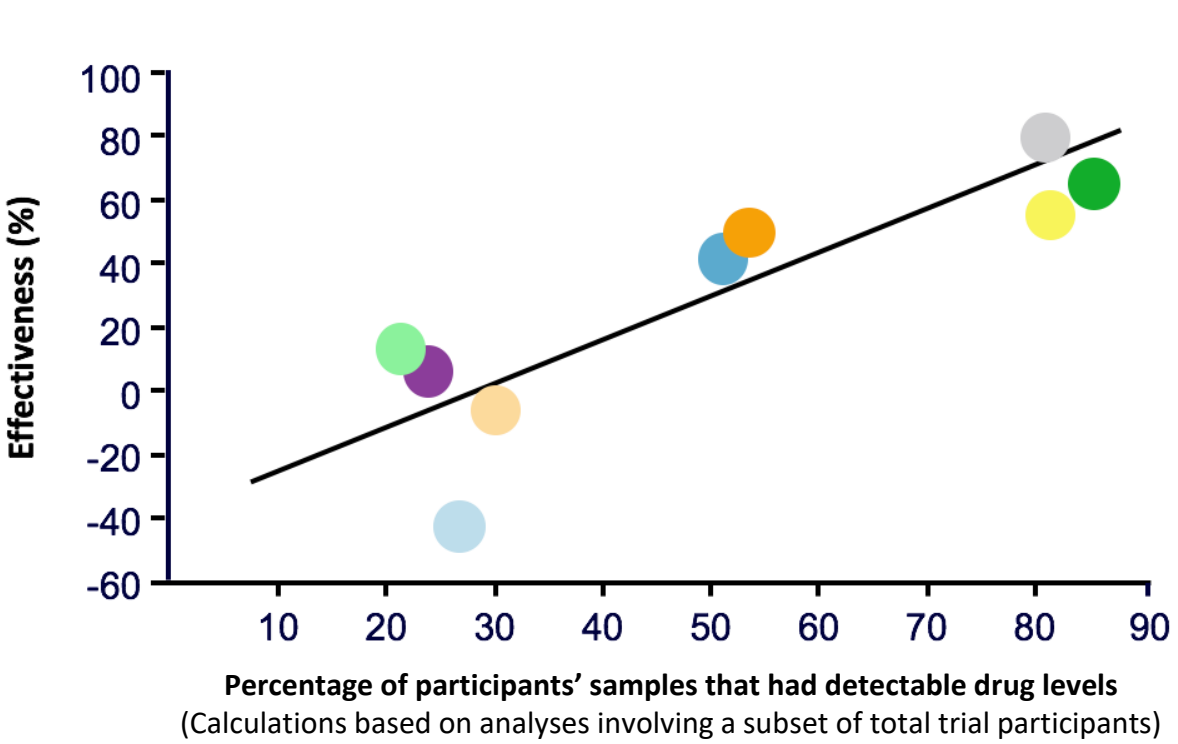
*Reduction in HIV incidence vs control.

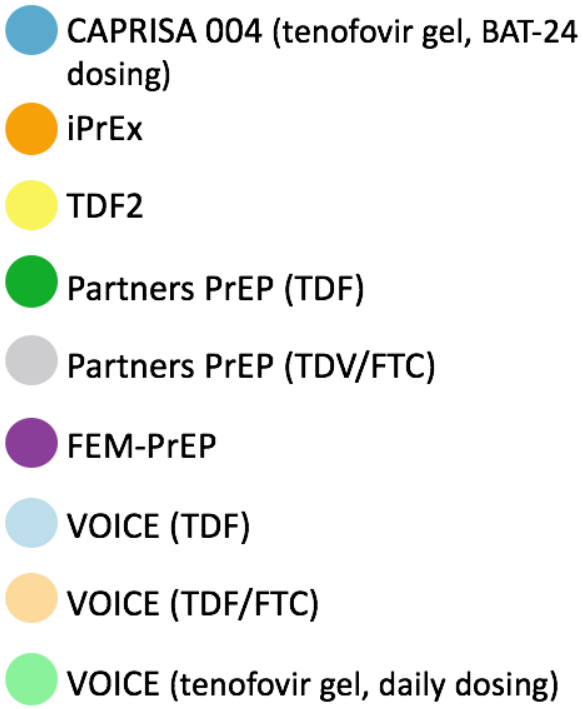
†Based on pill counts or the detection of study drug in plasma.

Slide credit: clinicaloptions.com

References in slide notes.

Effectiveness and adherence of oral and topical TDF-based prevention

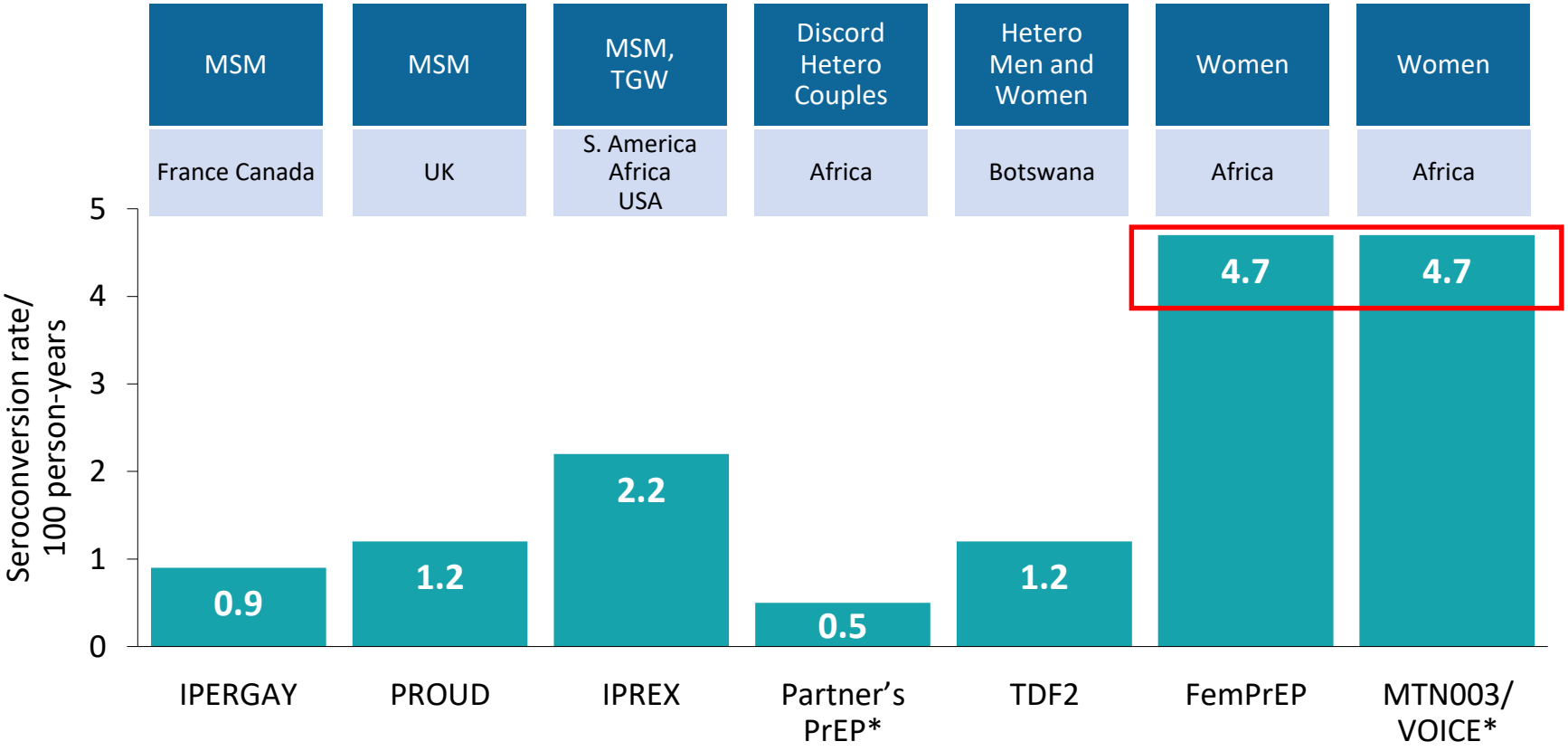




Higher adherence associated with greater protection

Seroconversion rates in PrEP clinical studies

- HIV-1 seroconversion rates for participants on TDF/FTC for PrEP are variable in clinical studies (0.5 to 4.7 per 100 person-years exposure)



*TDF/FTC only
TGW, transgender women

Mera, R. AIDS 2016. Durban, South Africa. Oral #TUAX0105LB; Molina NEJM 2015;373:2237-46; McCormack Lancet 2016;387:53-60; Grant NEJM 2010;363:2587-99; Baeten NEJM 2012;367:399-410; Thigpen NEJM 2012;367:423-34; Peterson PLoS Clin Trials 2007;2:e27; Marrazzo NEJM 2015;372:509-18.

Luecke EH et al. *Journal of the International AIDS Society* 2016, **19**:20875
http://www.jiasociety.org/index.php/jias/article/view/20875 | http://dx.doi.org/10.7448/IAS.19.1.20875

JIAS Journal of the International AIDS Society

Research article

Stated product formulation preferences for HIV pre-exposure prophylaxis among women in the VOICE-D (MTN-003D) study

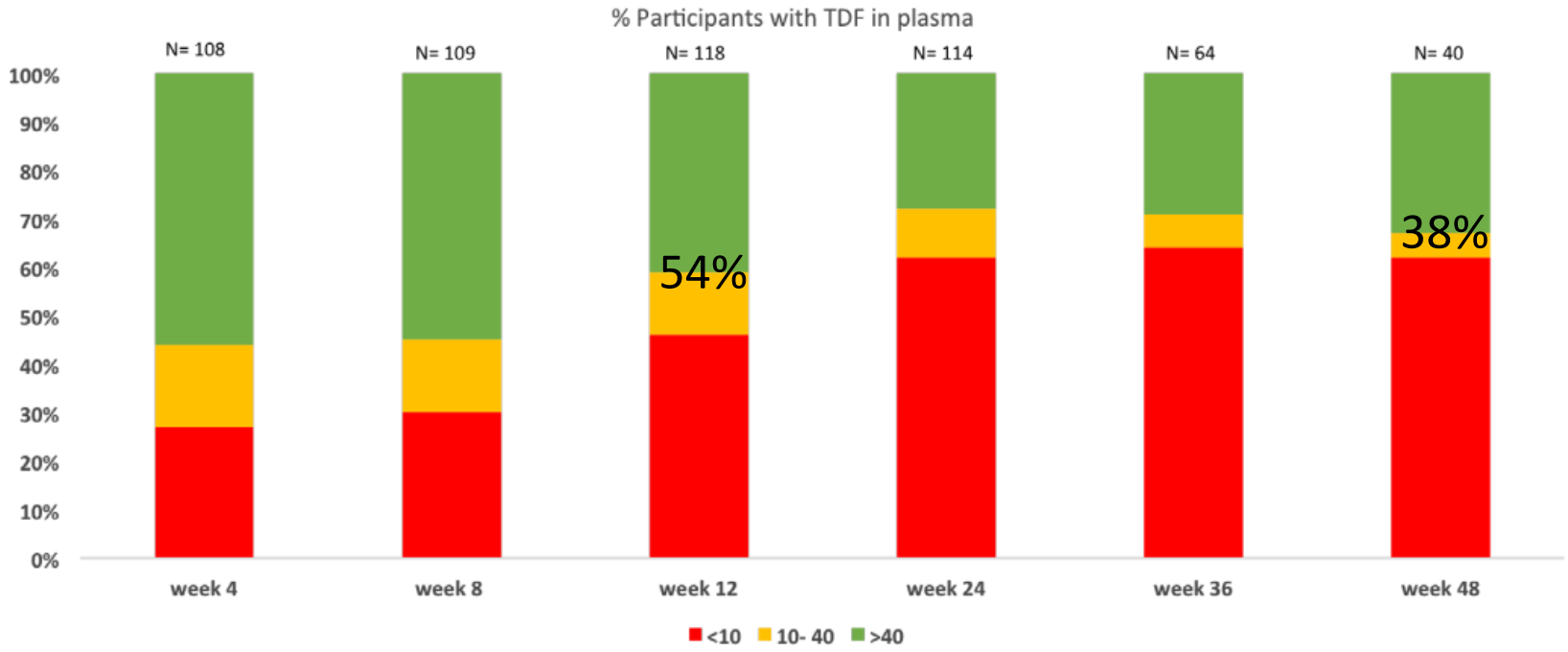
Ellen H Luecke[§,1], Helen Cheng[1], Kubashni Woeber[2], Teopista Nakyanzi[3], Imelda C Mudekunye-Mahaka[4] and Ariane van der Straten[1,5] on behalf of the MTN-003D Study Team

[§]**Corresponding author:** Ellen H Luecke, 351 California Street, Suite 500, San Francisco, CA 94104, USA. Tel: +(415) 848 1392. (eluecke@rti.org)

Pluspills study

Open label demonstration study of TDF/FTC PO daily PLUS support for HIV prevention in uninfected, sexually active adolescents 15-19 years in South Africa (n=244)

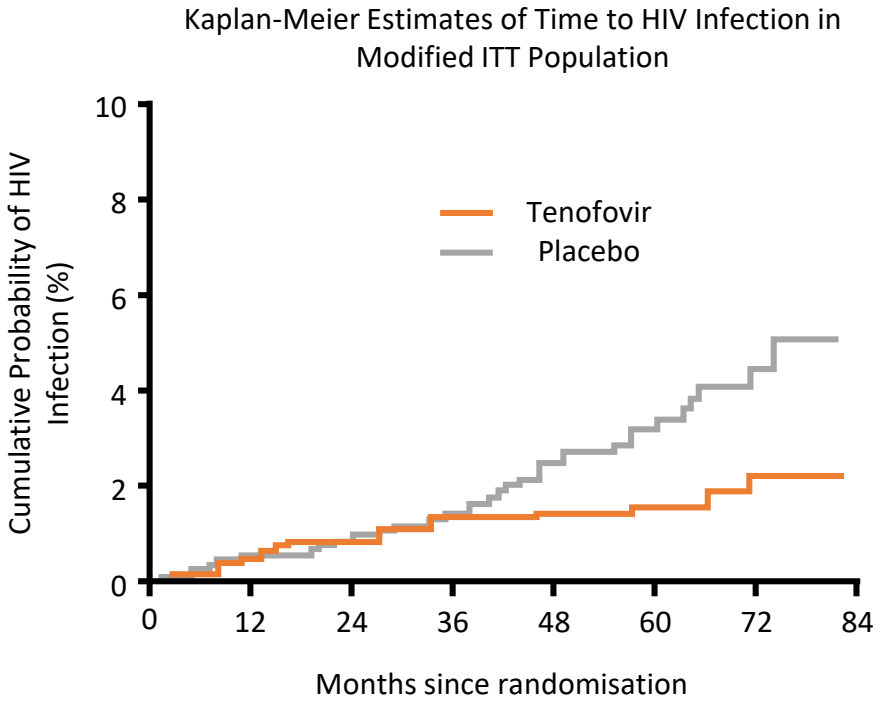
- Adherence decreased over time and with less frequent study visits



Gill K, et all. IAS 2017. Abstract TUAC0207LB

Bangkok Tenofovir Study: PrEP efficacy in IDUs

- HIV-negative adults aged 20-60 years reporting IDU in previous year randomised to PrEP with TDF QD (n = 1204) or PBO (n = 1209); pts could choose DOT or monthly visits

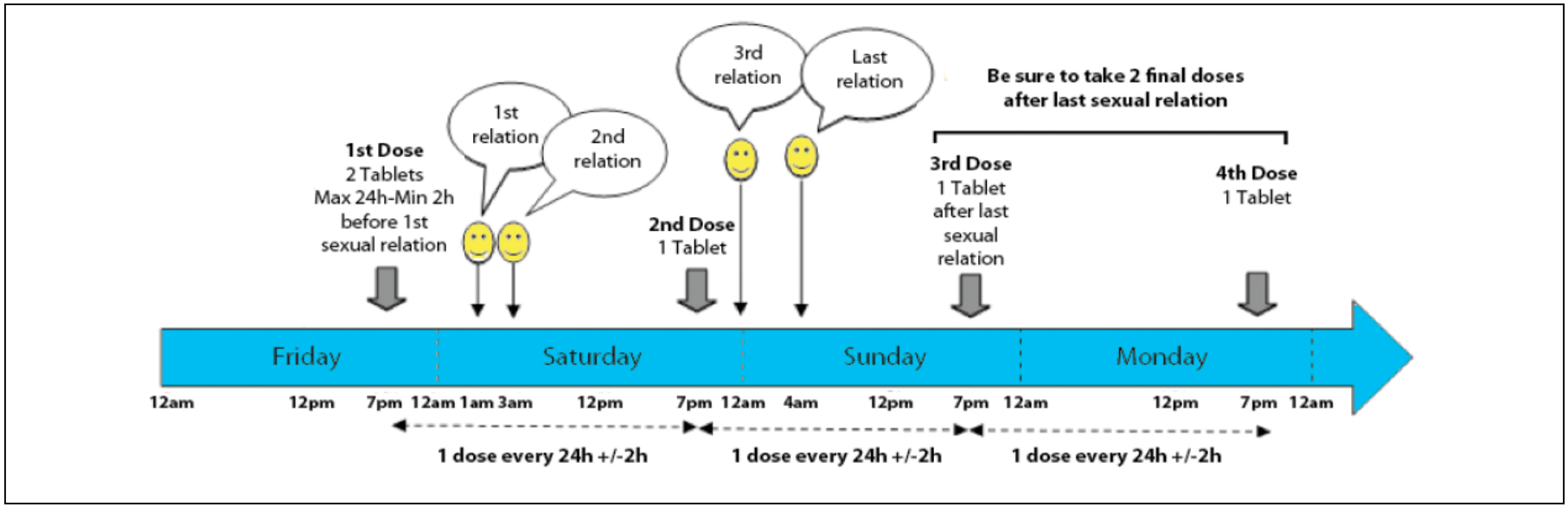


- Risk of infection significantly decreased with TDF PrEP (48.9%; p = 0.01)
- For pts who became infected and met adherence criteria (took study drug > 71% of days with < 2 consecutive days off study drug, n = 17), TDF PrEP reduced risk of infection 55.9% (-18.8% to 86.0%; p = 0.11)
- In pts with detectable TDF: 73.5% (16.6% to 94.0%; p = 0.03)

Slide credit: clinicaloptions.com

Choopanya K, et al. Lancet. 2013;381:2083-2090.

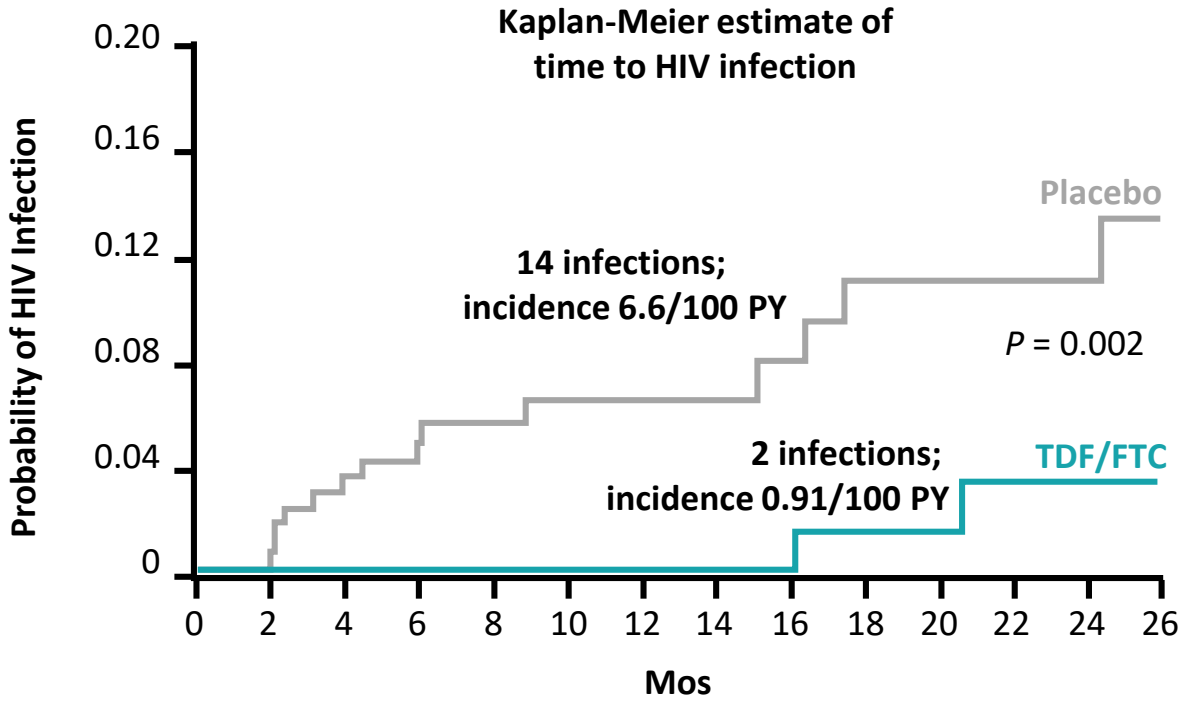
Can we use less than daily dosing?



Association
Nous sommes PrEP
Communiqué de presse

IPERGAY: Efficacy

86% risk reduction seen in PrEP arm
(95% CI: 40% to 98%; P = 0.002)



Pts at risk, n					
Placebo	201	141	74	55	41
TDF/FTC	199	141	82	58	43

*Event-driven PrEP strategy not FDA approved.

Slide credit: clinicaloptions.com

Molina JM, *et al*. N Engl J Med. 2015;373:2237-2246.

IPERGAY: Efficacy

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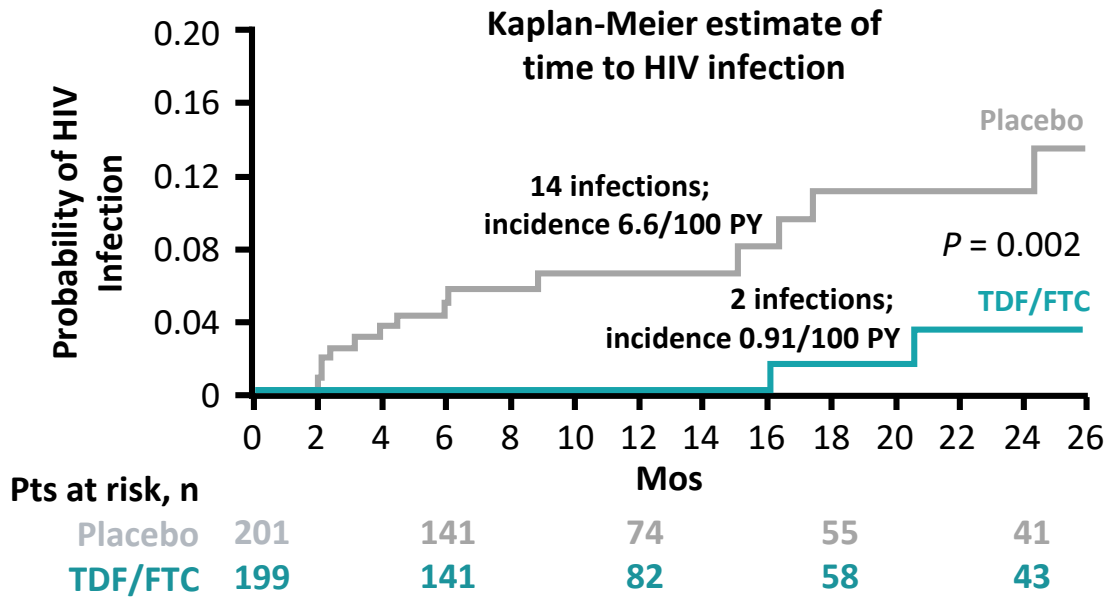
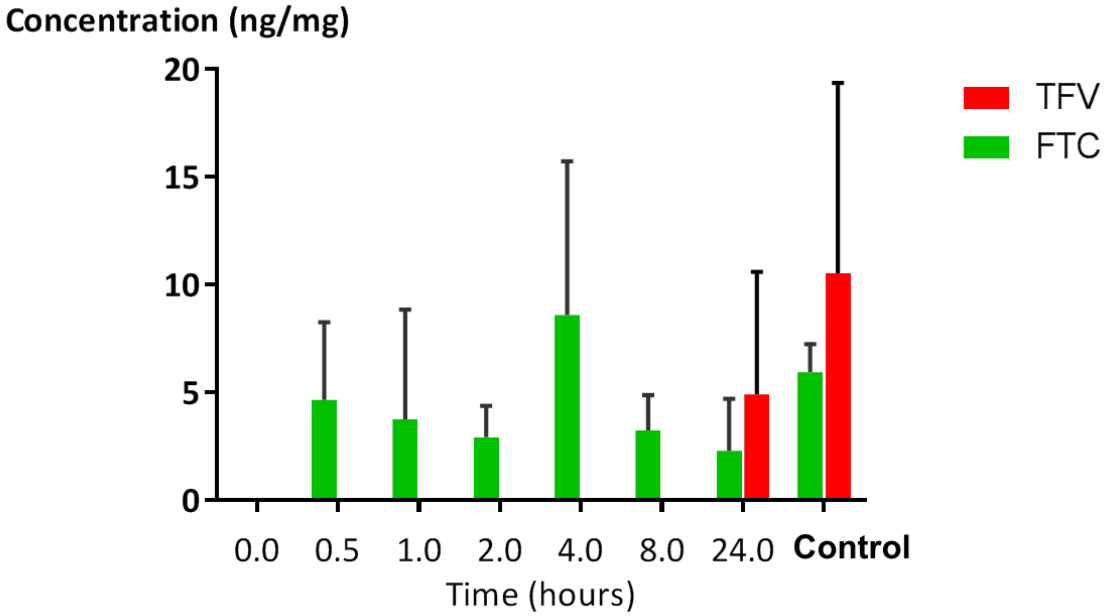


Substudy of 269 pts using ≤ 15 pills/month with reported PrEP use systematically/often during intercourse:

- HIV incidence/100 PY, FTC/TDF vs placebo groups 0 vs 9.3 (P = 0.013)

Molina JM, *et al*. N Engl J Med. 2015;373:2237-2246.
Antoni G, *et al.* IAS 2017. Abstract TUAC0102.

TFV and FTC concentration in rectal tissue

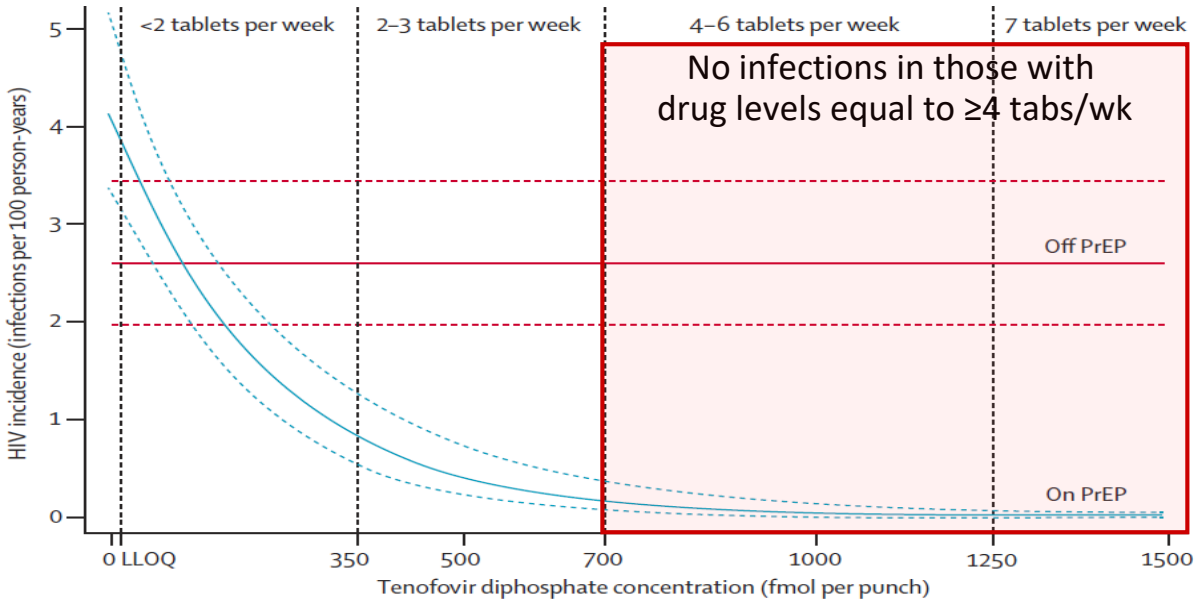


- Early detection of FTC in rectal tissue at high concentrations similar to HIV-infected patients on ART
- TFV is only detectable at 24 hours post drug intake at high concentrations

Molina JM, IAS 2015, Abstract MOSY0102

HIV incidence and drug concentrations in MSM

Modelling data from subjects in randomised placebo-controlled iPrEx, ATN 089, or US PrEP safety trials who were enrolled in the 72-week open label extension (iPrEx OLE)

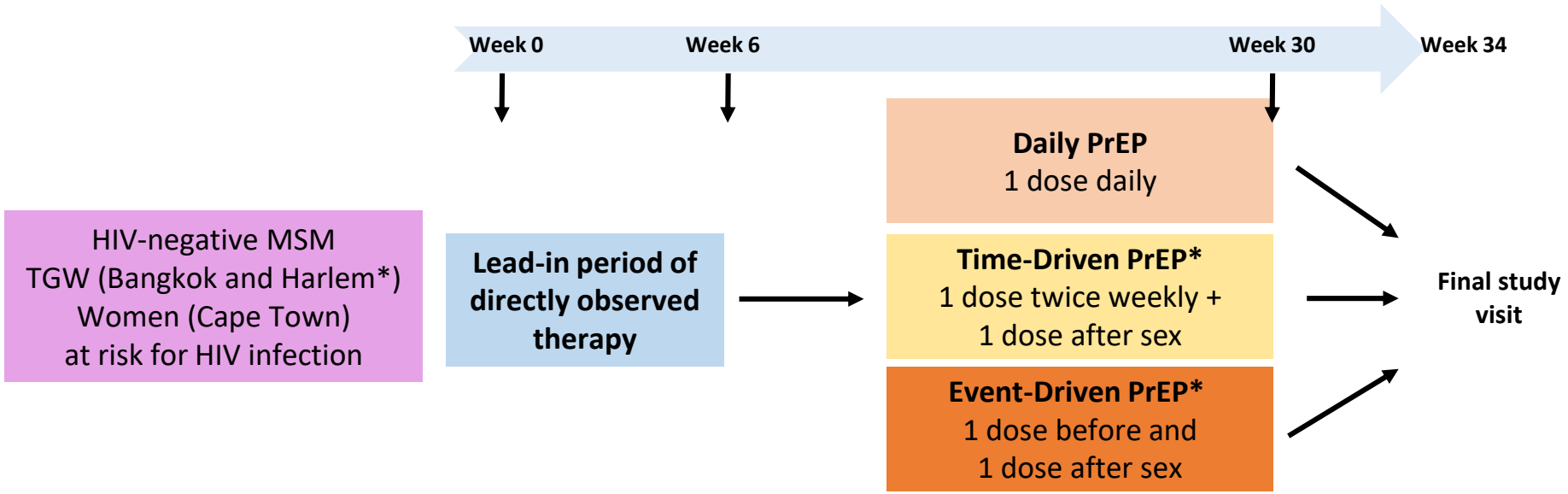


Drug Concentration	none	< 2 pills/week	2-3 pills/week	≥ 4 pills/week	7 pills/week
HIV Incidence per 100 PY (95%CI)	4.7 (2.99-7.76)	2.25 (1.19-4.79)	0.56 (0.00-2.50)	0	0
Risk Reduction (95%CI)		44% (-31-77)	84% (21-99)	100% (86-100)	

Buchbinder S, et al. Lancet ID 2014;14(6):468-475

HPTN 067/ADAPT: PrEP strategies

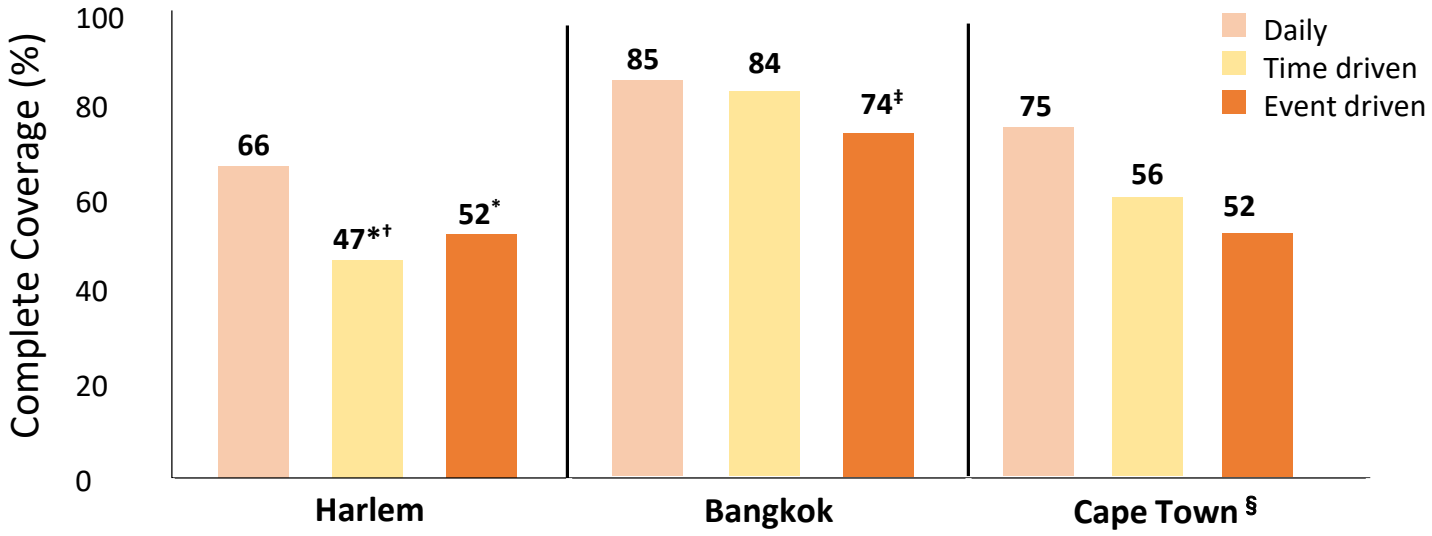
International, randomised, open-label phase II trial; results reported from Harlem (N = 179), Bangkok (N = 178), and Cape Town (N = 179) cohorts



TDF/FTC PrEP given at standard dose.
*Participants instructed to take no more than 2 doses/day or 7 doses/week.

Mannheimer S, *et al*. IAS 2015. Abstract MOAC0305LB. Holtz TH, *et al*. IAS 2015. Abstract MOAC0306LB. Bekker L, *et al.* CROI 2015. Abstract 978LB.

HPTN 067/ADAPT: Coverage of sex acts according to PrEP strategy

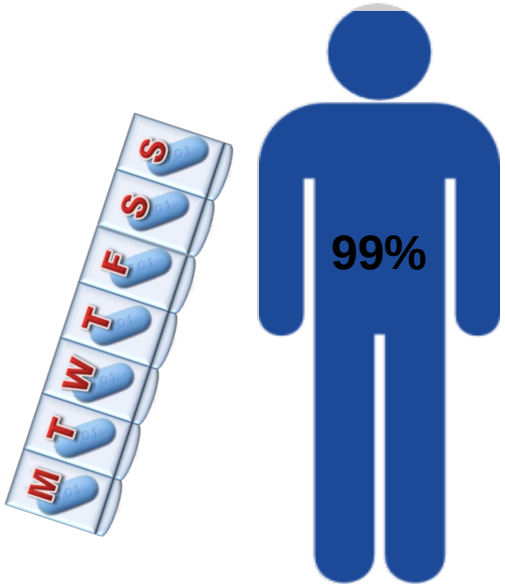


*P = 0.001 vs daily.
†P = 0.47 vs event driven.
‡P = 0.02 vs daily arm, P = 0.04 vs time-driven arm.
§ P < 0.001 comparing 3 arms.
Complete coverage: taking ≥ 1 PrEP dose within 4 days before sex and ≥ 1 dose within 24 hours after sex.

Mannheimer S, *et al*. IAS 2015. Abstract MOAC0305LB. Holtz TH, *et al*. IAS 2015. Abstract MOAC0306LB. Bekker L, *et al.* CROI 2015. Abstract 978LB.

Does PrEP have to be daily?

TDF/FTC (7x/week)

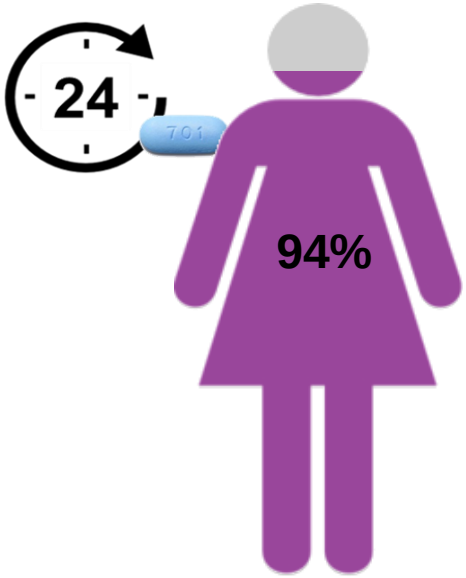


CI: 96 - 99

Some adherence forgiveness with retained protection

Anderson P *et al,* Sci Transl Med. 2012.

TDF/FTC (~1x/24)



CI: -17 - 100

6-7 doses per week likely required

Donnell D *et al,* JAIDS. 2014.
Cottrell ML *et al*, JID, 2016.

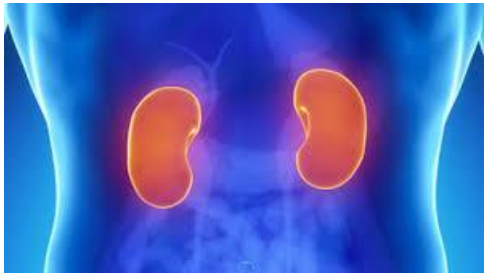
Risks and side effects

GI effects

ARV resistance

HBV management

Renal



BMD

Risk compensation

PrEP and ARV resistance

Resistance from PrEP was very rare, with only a small number who had acute infection at the time they were started on PrEP

	# of HIV seroconverters assigned PrEP with HIV resistance	
	HIV infected after enrollment	**Seronegative acute HIV infection at enrollment**
6 studies*	5/533 [6/533; 2%]	6/44 [8/44; 18%]

* Incl Partners PrEP, iPrEx, TDF2

Additional HIV infections showed resistance unrelated to PrEP

Resistance = K65R (TDF) or M184V/I (FTC) mutations

Case reports: HIV infection despite high adherence to PrEP

Pt	PrEP adherence	Seroconversion	Likely cause of PrEP failure
43-yr-old MSM[1]	24 months, supported by pharmacy records, blood concentration analyses, and clinical history	Acquired MDR HIV infection	Exposure to PrEP-resistant, multiclass-resistant HIV strain
MSM in his 20s[2]	Excellent by self-report, supported by blood and hair concentration analyses	Acquired MDR HIV infection after 2 instances of condomless insertive anal intercourse with 2 different partners within 11 weeks before diagnosis	Exposure to PrEP-resistant, multiclass-resistant HIV strain
50-yr-old MSM[3]	Excellent by self report, supported by blood analyses	Acquired wild-type HIV infection after 2-5 median condomless anal sex partners per day in each month following PrEP initiation	Chronic rectal inflammation ± trauma

PrEP is not 100% effective but is highly protective, so to optimise protection and decrease STDs, condoms can be helpful

1. Knox DC, et al. N Engl J Med 2017;376:501-502.
2. Grossman H, et al. HIVR4P 2016. Abstract OA03.06LB.
3. Hoornenborg E, et al. CROI 2017. Abstract 953.

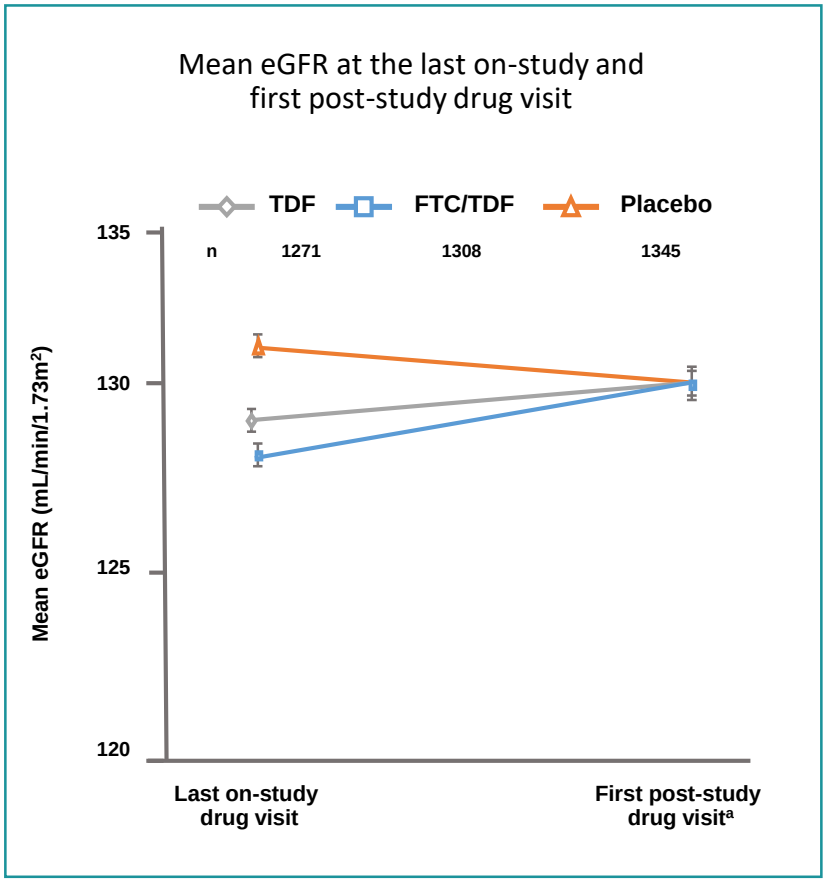
The safety of PrEP in the presence of hepatitis B infection

- Most studies to date excluded HBV-positive individuals
  - Concern about “flares” if stop TDF/FTC
- HBV is common in countries that don’t vaccinate
- 20% of incident infections become chronic
- TDF/FTC suppresses HBV and thus acts as treatment

The safety of PrEP in the presence of hepatitis B infection

- Substudy of HBV-positive participants in iPrEx
- 13/2499 (0.5%) chronic HBV
- 6/13 were in the group assigned TDF/FTC
- 0/6 experienced “flares” after stopping PrEP
- 2 participants had evidence of acute HBV and started PrEP → severe elevated LFTs (as expected in acute infection) which settled and both cleared virus and became immune

Decline in eGFR resolves within weeks of discontinuing TDF-based PrEP



- Partners PrEP: Phase 3, randomised trial of daily oral TDF PrEP vs. TDF/FTC PrEP vs. PBO among African HIV-negative men and women (N=4747) with normal baseline renal parameters
  - Serum creatinine was assessed quarterly while on study medication, and at 2 monthly visits after d/c
  - eGFR was calculated using CKD-EPIa
- Mean eGFR was 2-3 mL/min lower on PrEP vs. PBO (P<0.01) at first post-study drug visit
- >96% of participants had >75% eGFR reversion to baseline levels by 8 weeks of study drug discontinuation

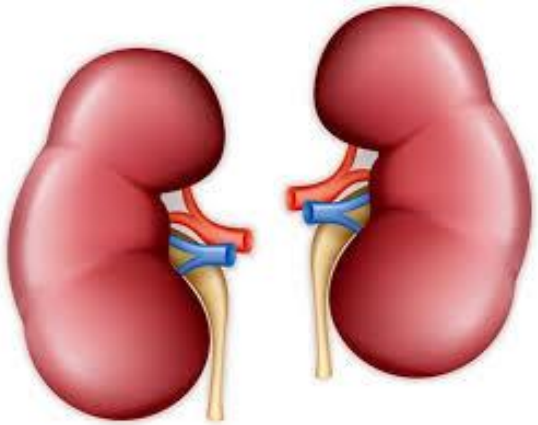
[a] Chronic Kidney Disease Epidemiology Collaboration Equation.
[b] Median time from the last on-study drug visit to the first post-study drug visit was 4 weeks (IQR: 3 - 5), which was similar across treatment groups.

Mugwanya, K. CROI 2015

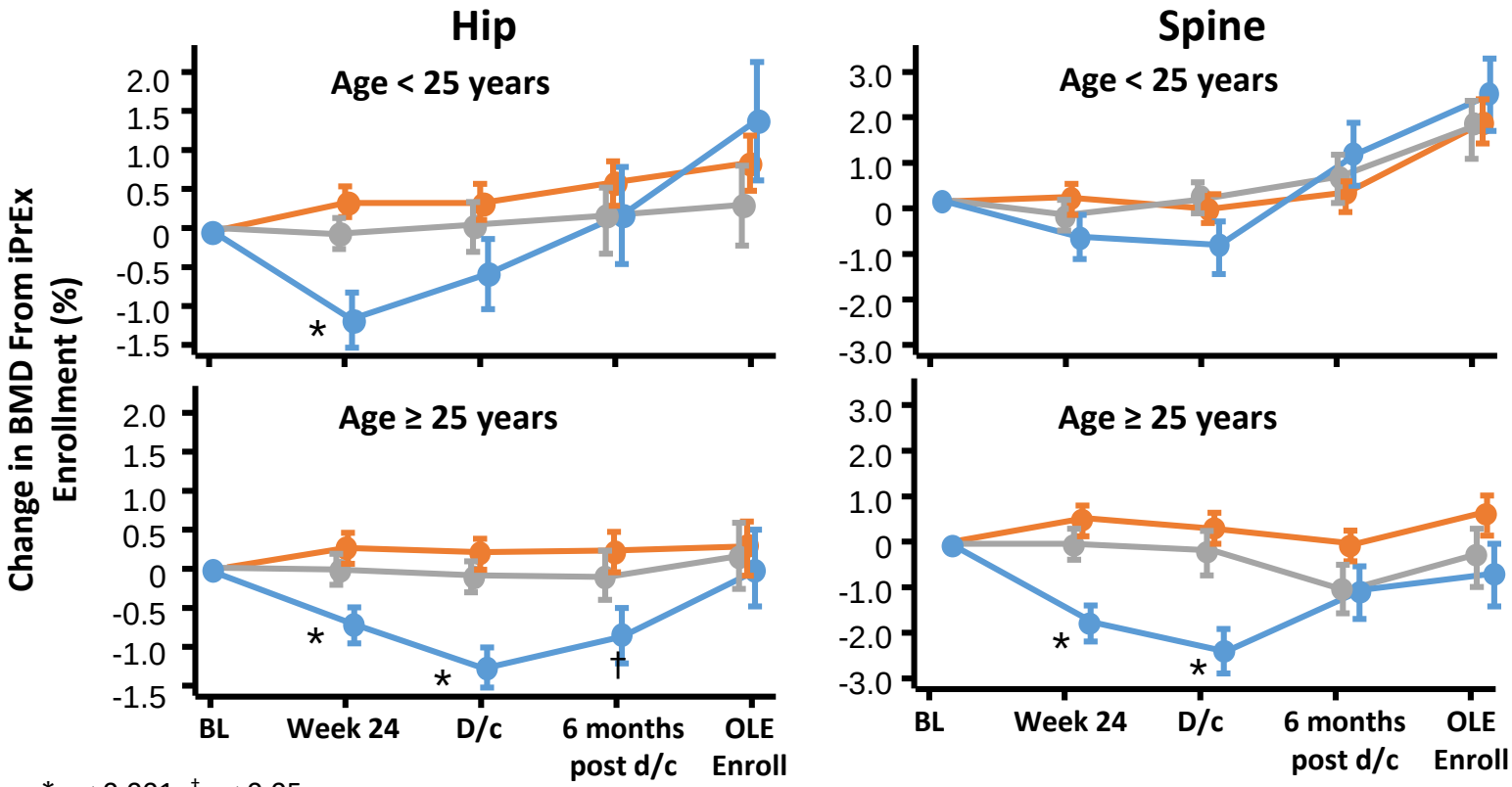
Exclude the usual suspects

Don’t forget:

- Hypertension
- Check glucose
- Nephrotoxic agents (e.g. no NSAIDs)
- Family history
- Urine dipstix (no proteinuria)



iPrEx BMD substudy: BMD recovery after TDF/FTC discontinuation



*p < 0.001; †p < 0.05

- Data compared for TFV-DP < or ≥ 16 fmol/M viable PBMC, concentration associated with 90% reduction in HIV infection risk in MSM/TGW

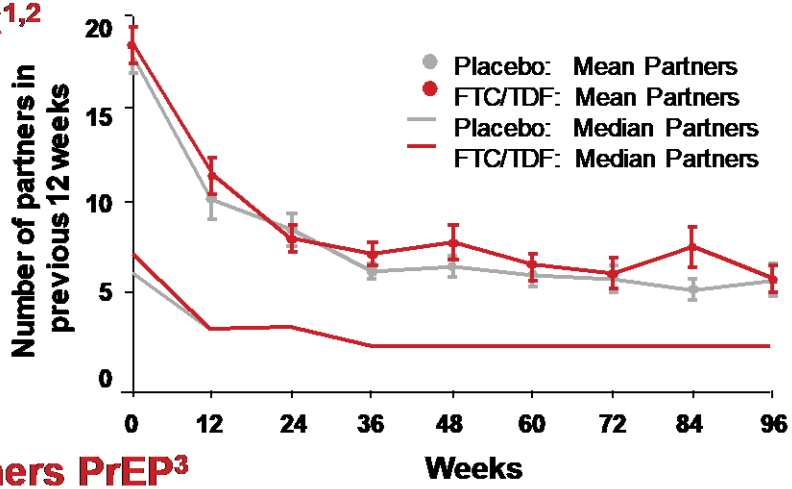
Placebo
W24 TFV-DP <16
W24 TFV-DP ≥16

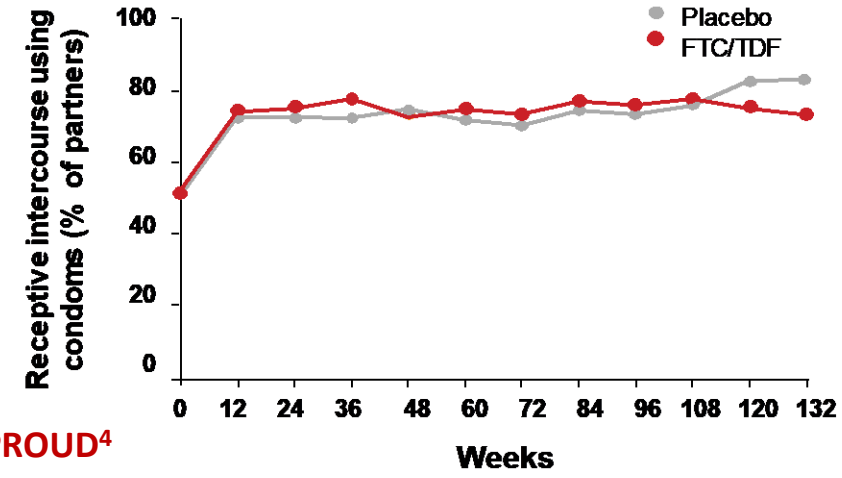
Slide credit: clinicaloptions.com

Grant R, *et al*. CROI 2016. Abstract 48LB.

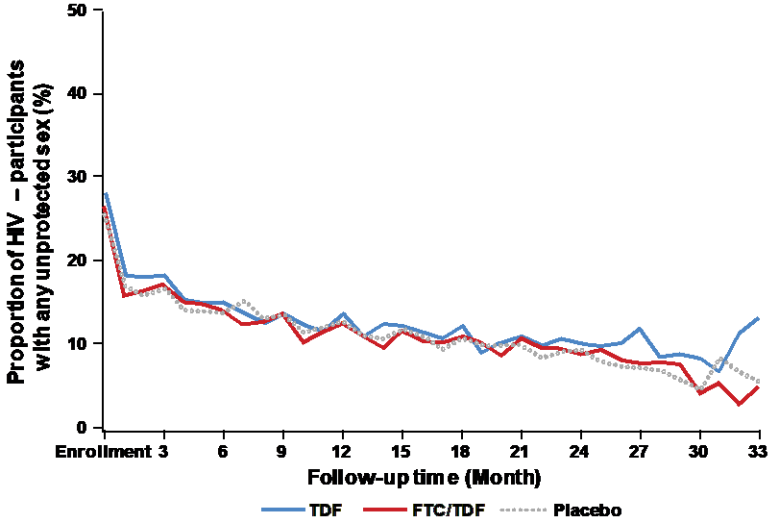
Risk compensation in PrEP clinical trials

iPrEx[1,2]

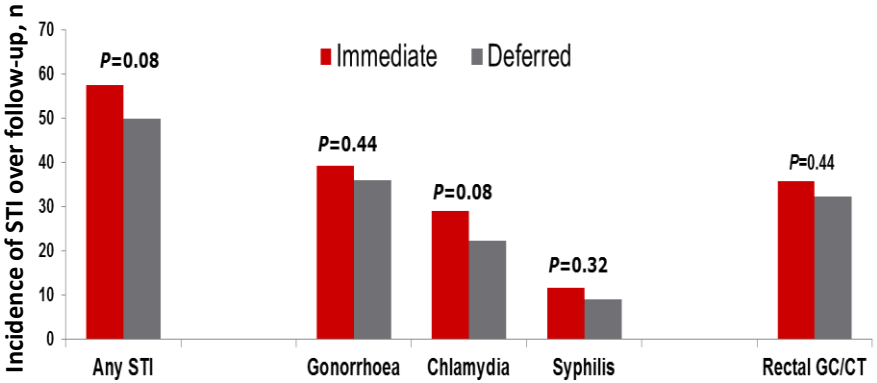




Partners PrEP[3]



PROUD[4]



There was no risk compensation seen in iPrEX, Partners PrEP, or PROUD

1. Grant R, et al. CROI 2011. Boston #92; 2. Grant R, et al. N Engl J Med 2010;30:2587-9; 3. Baeten J, et al. IAS 2011; Rome. #MOAX0106; 4. McCormack S, et al. CROI 2015; Seattle, WA. #22LB

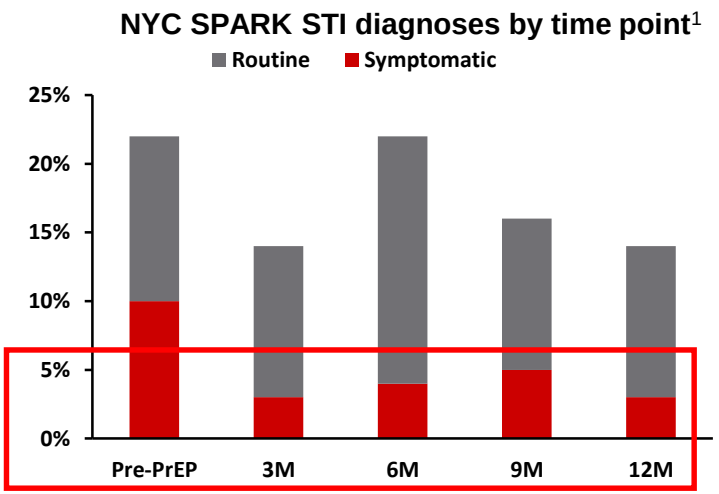
STI data from community-based PrEP implementation

Retrospective record review in SPARK (NYC);
prospective cohort analysis in The Demo Project (SF, DC, Miami)

	NYC SPARK (n=280)[1]	The Demo Project (n=557)[2]
STIs pre-PrEP	21%	>25%
STIs on PrEP	13-21% quarterly	18-25% quarterly
STIs that CDC guidelines* would have missed (asymptomatic at 3M and 9M)	77% at 3M; 68% at 9M	34% GC; 40% CT; 20% syphilis
Extragenital STIs	71-100% quarterly	83% GC; 76% CT

*Current CDC guidelines recommend STI screening q6mo and asking about symptoms quarterly

- In The Demo Project, transmission modeling suggested that q3mo screening prevented a median of 3 partners from being exposed to an STI via condomless anal sex
- **Data from both projects indicate that not screening extra-genital sites and only following the CDC's current STI screening guidelines would miss or delay many STI diagnoses**



1. Golub S, et al. CROI 2016. Boston, MA. #869
2. Cohen S, et al. CROI 2016. Boston, MA #870

Time to achieving protection on PrEP

- The time from initiation of daily doses of TDF/FTC to maximal protection against HIV infection is unknown
- No scientific consensus on what intracellular concentrations are protective for either drug or the protective contribution of each drug in specific body tissues

Daily oral PrEP: Time to maximum intracellular concentrations of TFV-DP in different tissues	
Rectal tissue	~7 days
Blood	~20 days
Cervicovaginal tissues	~20 days
Penile tissues	No data available

TFV-DP, tenofovir diphosphate

US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014. http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf. Accessed June 13, 2014.

What about pregnancy and breastfeeding?

- Risk of seroconversion during conception and pregnancy
  - biological susceptibility and behavioural exposure
- Limited data regarding safety of PrEP for foetus
  - RCTs excluded pregnant women
  - Demonstration projects will provide some data
  - Most data will come from real world use
- APR: no evidence adverse outcomes in infants exposed to TDF/FTC ART

Birth defects with TDF or FTC

HIV+ Women on ART	Any FTC-containing regimen[1]	Any TDF-containing regimen[1]
Pregnancies enrolled, n		
First trimester	1728	2478
Second trimester	525	670
Third trimester	206	351
Defects/live births, n/N (%)		
First trimester exposure	35/1543 (2.3%)	47/2141 (2.2%)
Second/third trimester exposure	15/729 (2.1%)	21/1021 (2.1%)

Among pregnant women in the US reference population, the background rate of birth defects is 2.7%. There was no association between FTC or TDF and overall birth defects observed in the APR[1,2]

Risk versus benefit?

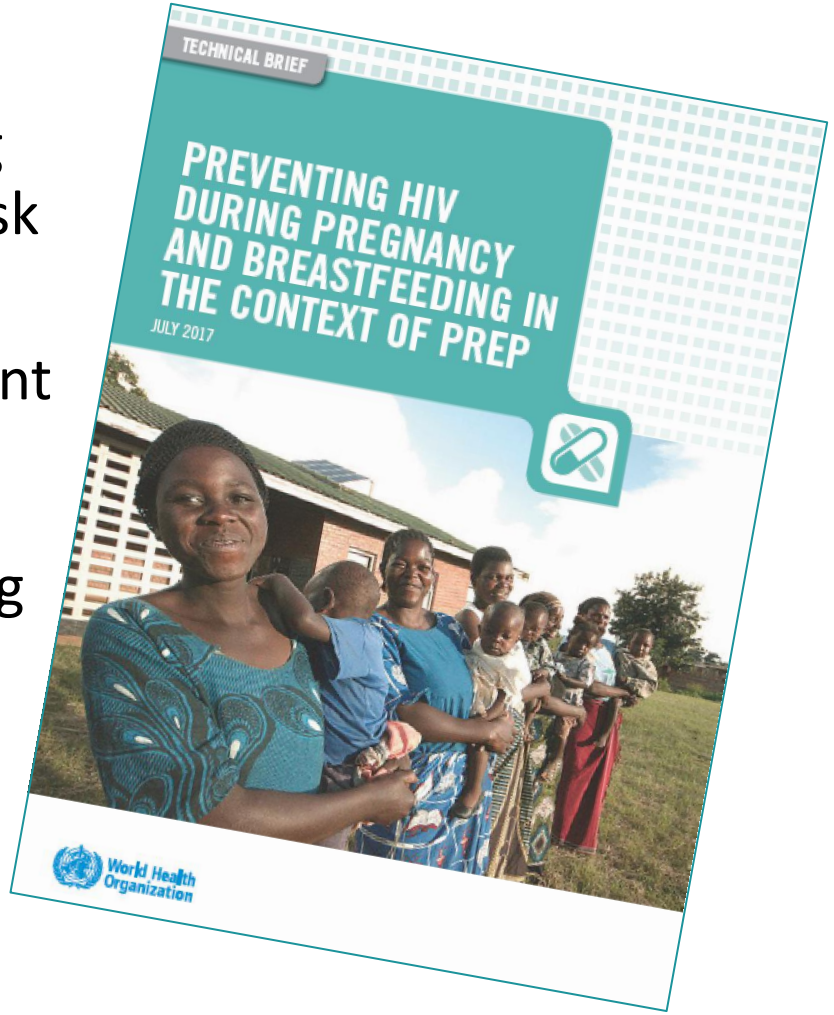
	Stop PrEP	Continue PrEP
Mother	Ongoing HIV risk to mom (5% incidence in some studies)	Protects mom
Baby	Minimises TFV-related risk to baby But high risk if mom gets infected	Risk of bone abnormalities but insufficient data

"There are no adequate and well-controlled studies of TDF/FTC for PrEP in pregnant women"

WHO recommendations

PrEP can be offered to an HIV-negative woman who is trying to conceive if her partner is HIV-positive and not virally suppressed or she does not know his HIV status.

- Existing safety data support use of PrEP in pregnant and breastfeeding women at continuing substantial risk of HIV infection.
- WHO systematic review: no apparent safety-related rationale for disallowing or discontinuing PrEP during pregnancy and breastfeeding for HIV-negative women at continuing risk of HIV acquisition.



PEP to PrEP transition

- Data-free zone – no guidelines
  - Guidelines often “disallow” simple transition
- The concern: Could PEP “fail”, i.e. patient is actually HIV-infected, suppressed and antibody response attenuated from PEP (3 drugs) – and now transition to PrEP (2 drugs) will lead to viral resistance
- Any hiatus in PrEP/PEP in a high-risk individual is a window for HIV acquisition.
- No perfect way to rule out HIV acquisition
- Perform Ag/Ab test at Week 4 of PEP (while still on PEP) and then transition to PrEP?

TFV and TFV-DP in female mucosal tissues (single dose)

	TAF 25mg, Tissue samples BLQ, %		*n*	TDF 300mg Tissue samples BLQ, %		*n*
	TFV	**TFV-DP**		**TFV**	**TFV-DP**	
Cervicovaginal fluid	58	n/a	40	23	n/a	95
Genital tissue	6	75	16	0	25	16
Rectal tissue	0	63	8	0	0	8

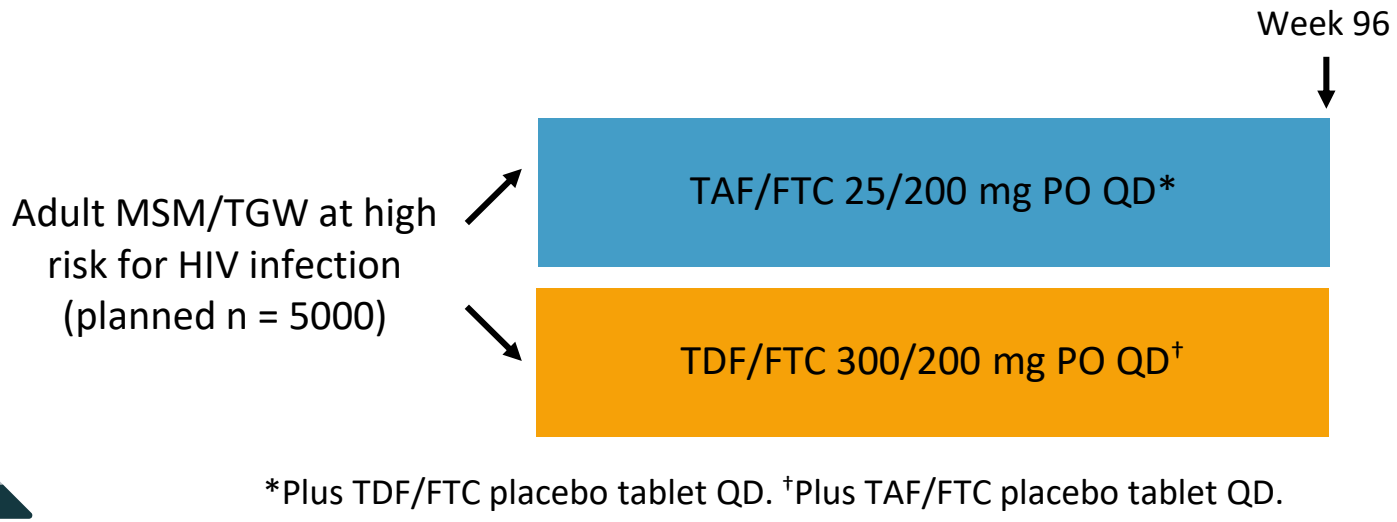
Compared with TDF, TAF administration results in a **higher percentage of tissue samples with undetectable levels of TFV and TFV-DP**:
clinical relevance?
Best correlate of protection against HIV infection has yet to be determined.

BLQ=below the level of quantification. 0=all the samples had detectable TFV (none were BLQ)

Garrett K, et al. CROI 2016. Boston, MA. #102LB

TAF/FTC for HIV prevention

- TAF may offer improved bone/renal safety vs TDF[1]
- TAF: TFV prodrug
  - TAF/FTC approved in combination with other ARVs for HIV treatment[2]; **not currently approved for PrEP**
  - Systemic TFV levels reduced 90% with TAF 25 mg vs TDF 300 mg[3]
- Randomised phase 3 PrEP trial now under way[4] (DISCOVER)



*Plus TDF/FTC placebo tablet QD. †Plus TAF/FTC placebo tablet QD.

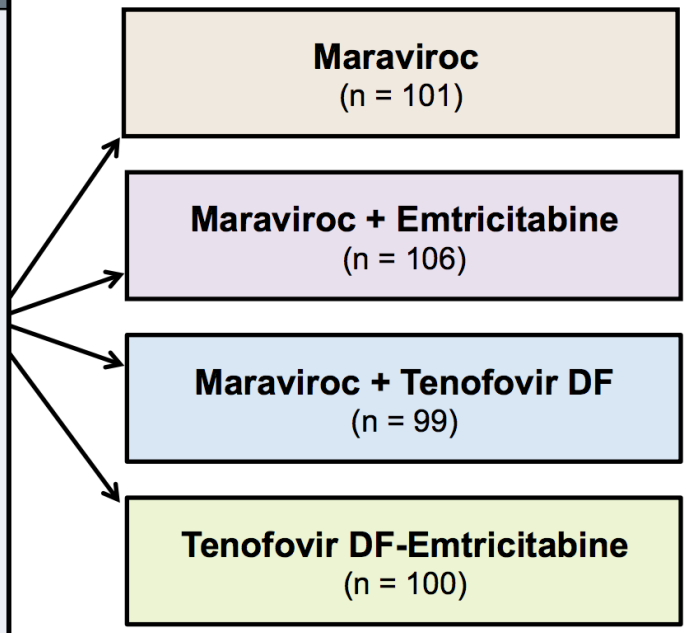
Slide credit: clinicaloptions.com

References in slide notes.

HPTN 069: Maraviroc as PrEP

Study Design: HPTN 069/ACTG 5305

- **Background**: Phase 2b, randomized, double-blind study of the safety and tolerability of maraviroc (alone or combined with FTC or TDF) for preexposure prophylaxis (PrEP), as compared to TDF-FTC, for at-risk men and transgender women
- **Inclusion Criteria (n = 406)**
  - Men and transgender women who have sex with men who self-reported condomless anal sex with at least one man within last 90 days
  - Creatinine clearance ≥70 mL/min
  - Negative HIV Ag/Ab and RNA
  - Negative hepatitis B surface Ag
  - No reported injection-drug use



- MVC-containing regimens were safe and well tolerated compared with TDF and FTC; this study was not powered for efficacy.
- Among those acquiring HIV infection, drug concentrations were absent, low, or variable.

Gulick RM et al. J Infect Dis. 2017;215(2):238-246.

Give PrEP a Shot

Weighing up injectables

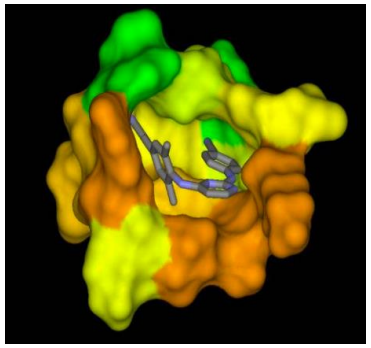
Pros

- Injection every 1-3 months could address adherence issues
- Different drug, not used heavily for treatment - less concern for resistance/cross-resistance

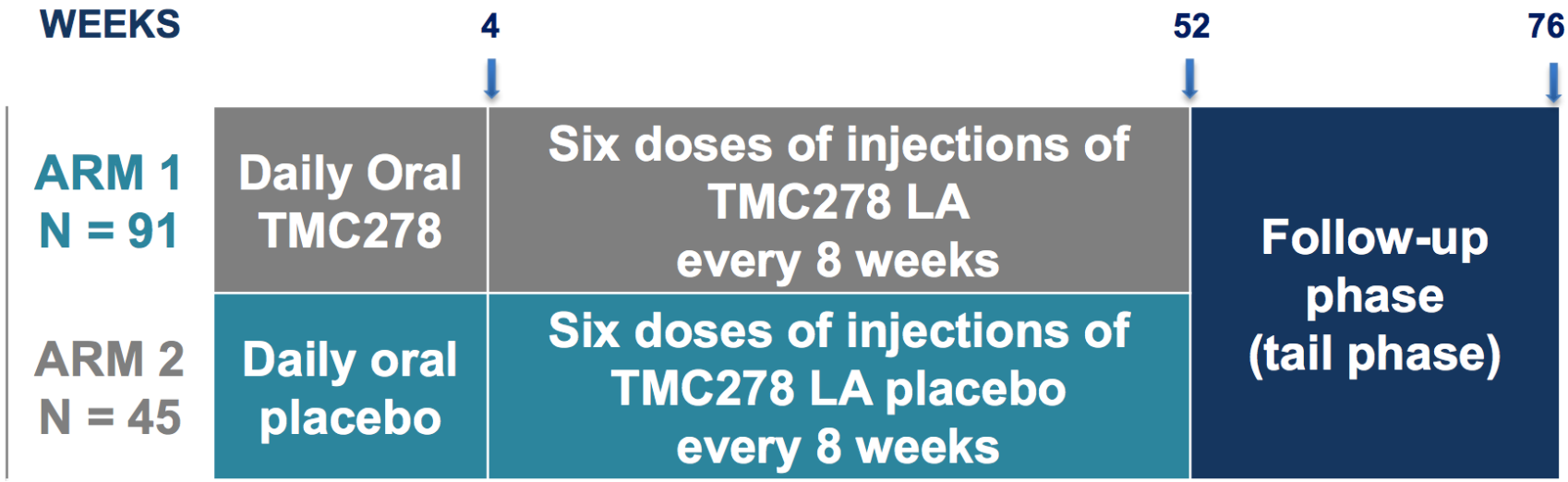
Cons

- Cannot be removed once given → prolonged side effects
- Long pharmacologic tail after last injection (up to 48 weeks)
  - safety
  - resistance if infected

HPTN 076: Study design



136 **HIV-uninfected, ages 18-45**



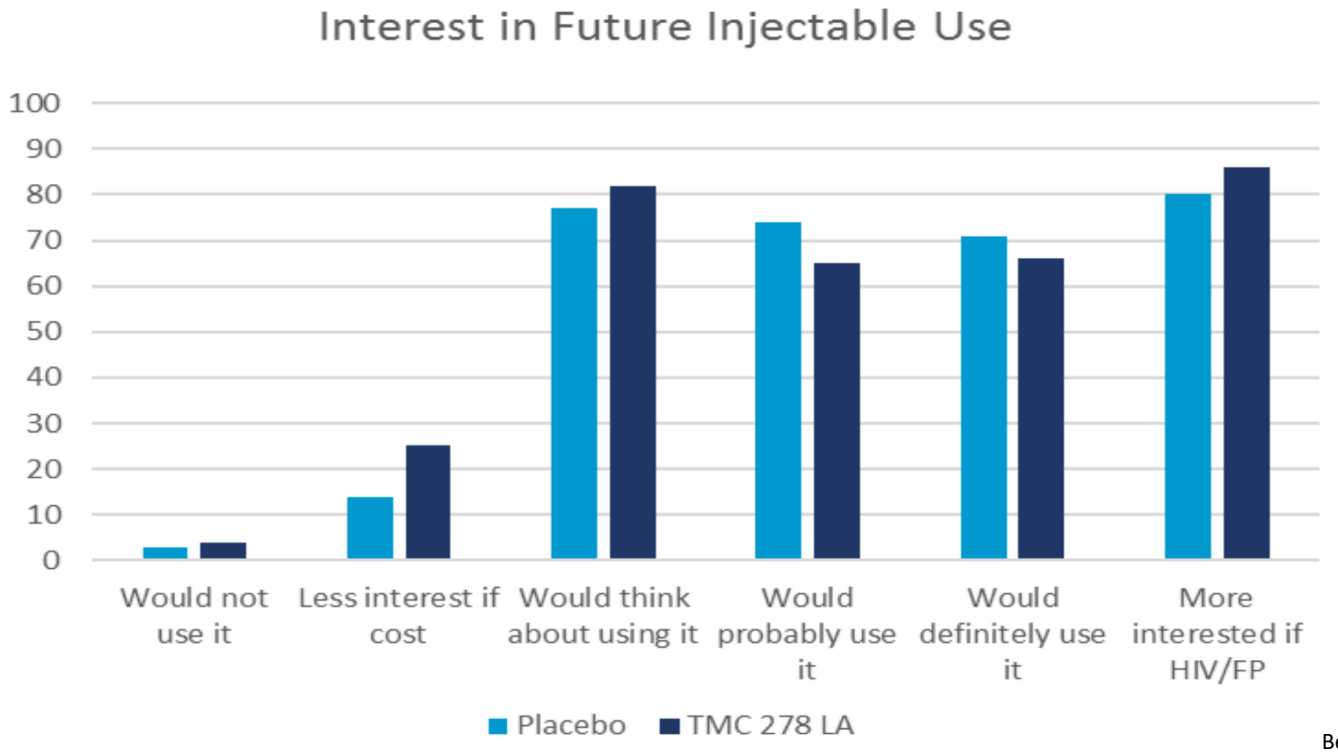
Primary objective: Evaluate the safety of TMC278 LA, through 48 weeks after initial injection in women in sub-Saharan Africa and the U.S.

Bekker L-G, et al. CROI 2017.

HPTN 076: Results

- Transient Grade >2 liver abnormalities occurred in 9 (11%) LA participants compared with 4 (10%) in the P arm.
- 3 LA participants (4%) developed Grade >3 injection site reactions compared with 0 (0%) in the P arm.

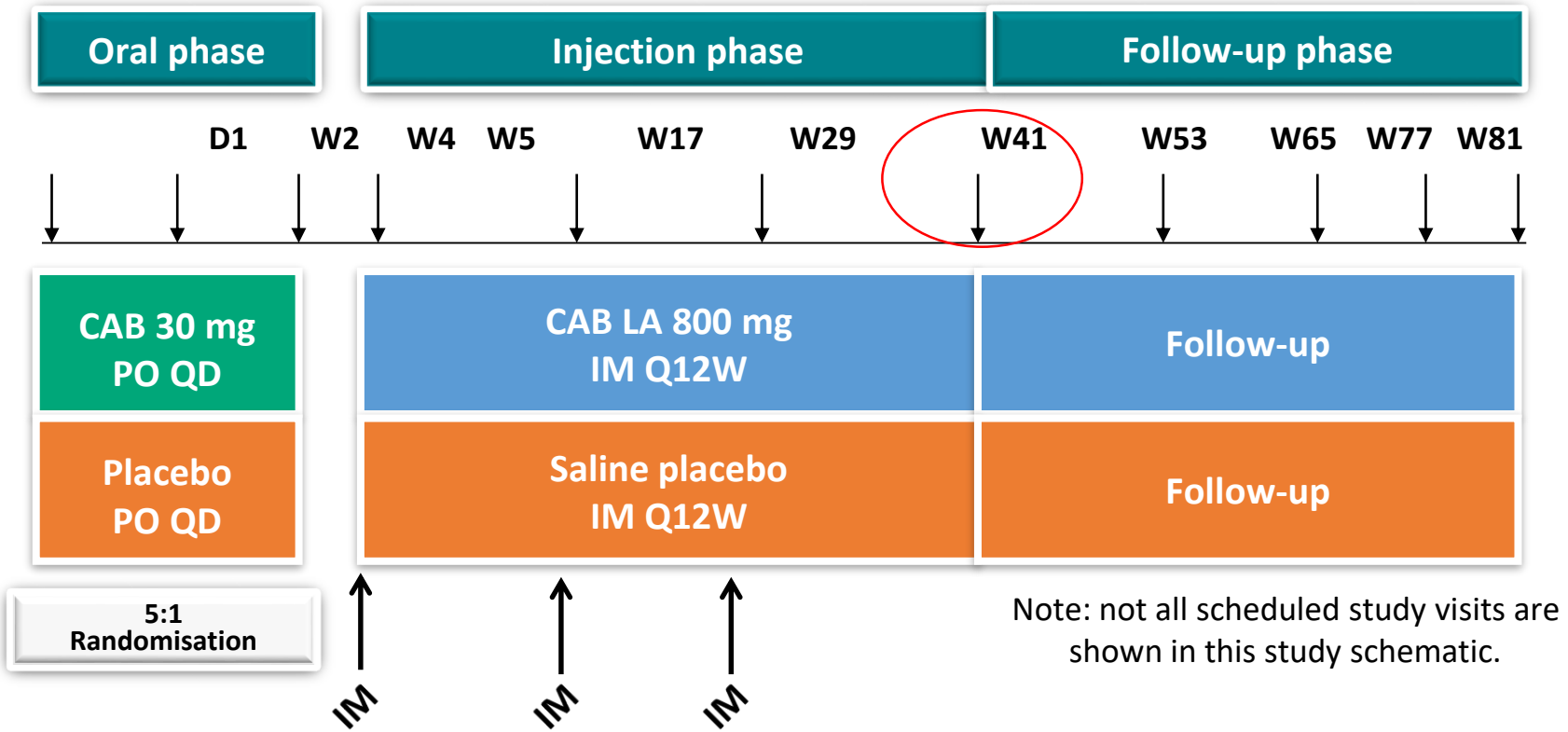
No significant difference was observed between the two arms and study product was well tolerated.



Bekker L-G, et al. CROI 2017.

ÉCLAIR: Study design

Phase 2a, randomised, multisite, 2-arm,
double-blinded study in men at low risk of acquiring HIV

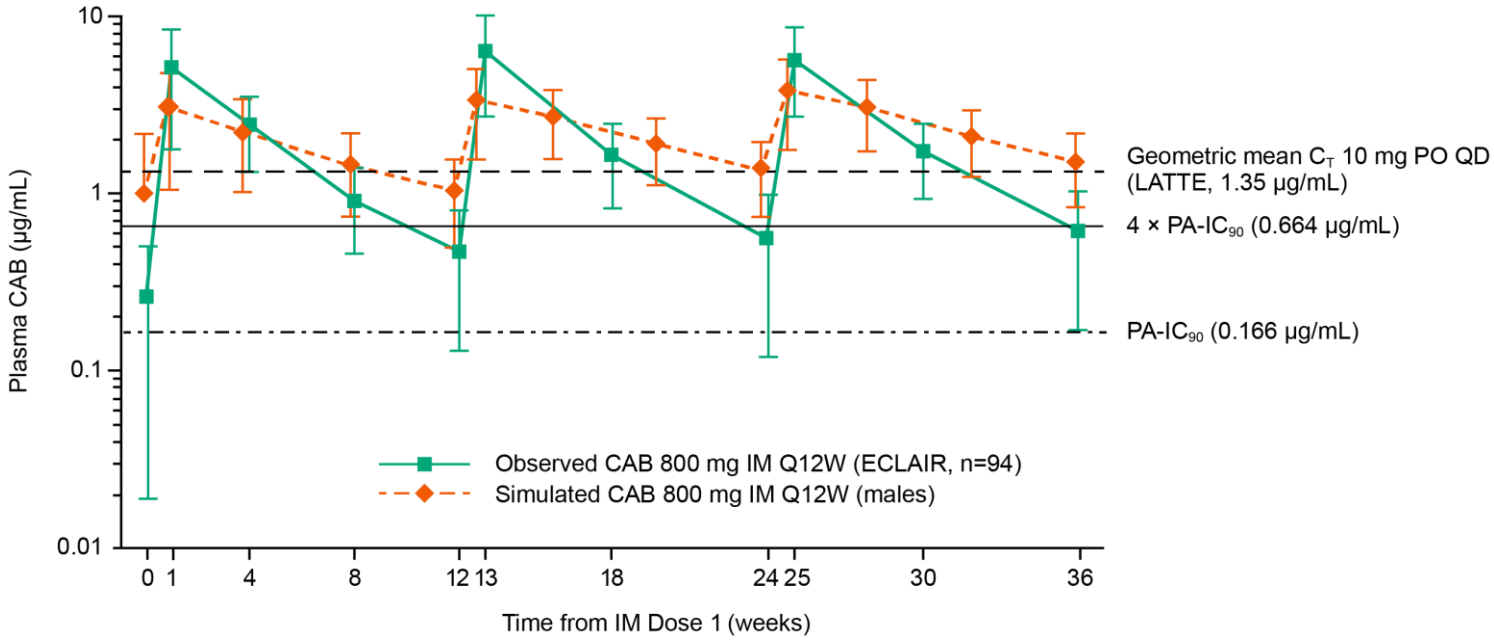


Note: not all scheduled study visits are shown in this study schematic.

- PO, orally; Q12W, every 12 weeks; QD, once daily.

Markowitz et al. CROI 2016; Boston, MA. Abstract 106.

ÉCLAIR: Results

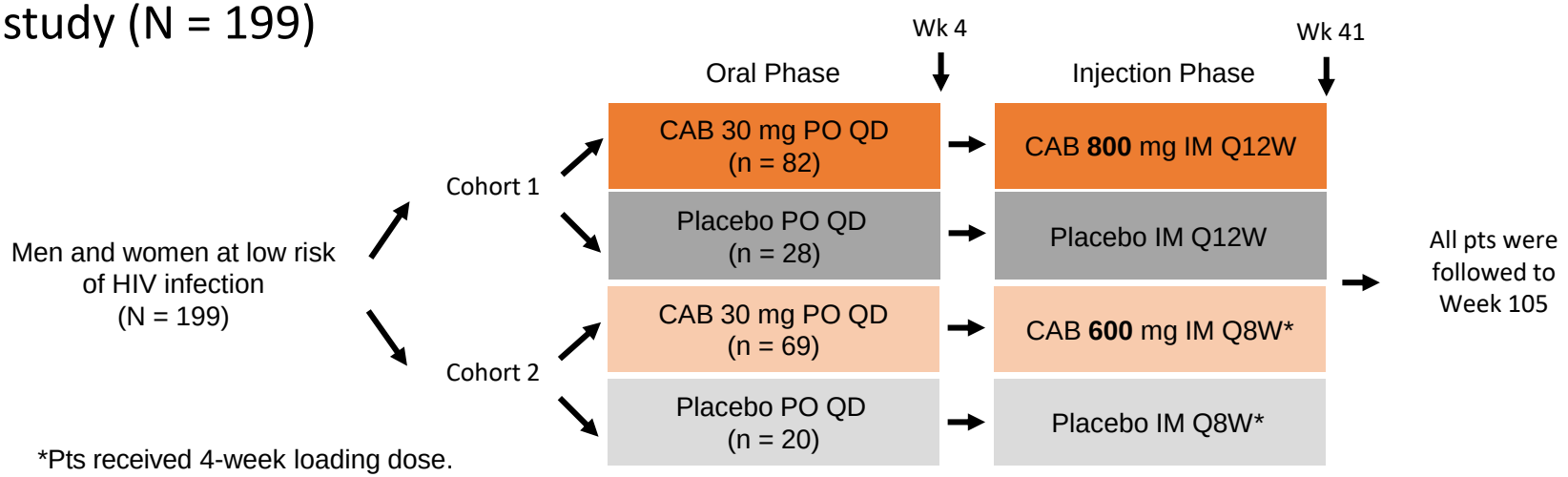


- Both CAB oral and LA were **well tolerated**
- The absorption rate after CAB LA injection faster than predicted by PK population models, leading to higher peak and **lower trough** exposures
- **High participant satisfaction** with IM CAB LA injections, including a preference for injections Q12W compared with oral CAB once-daily tablets

Markowitz et al. CROI 2016; Boston, MA. Abstract 106.

HPTN 077: Cabotegravir for PrEP in low-risk persons

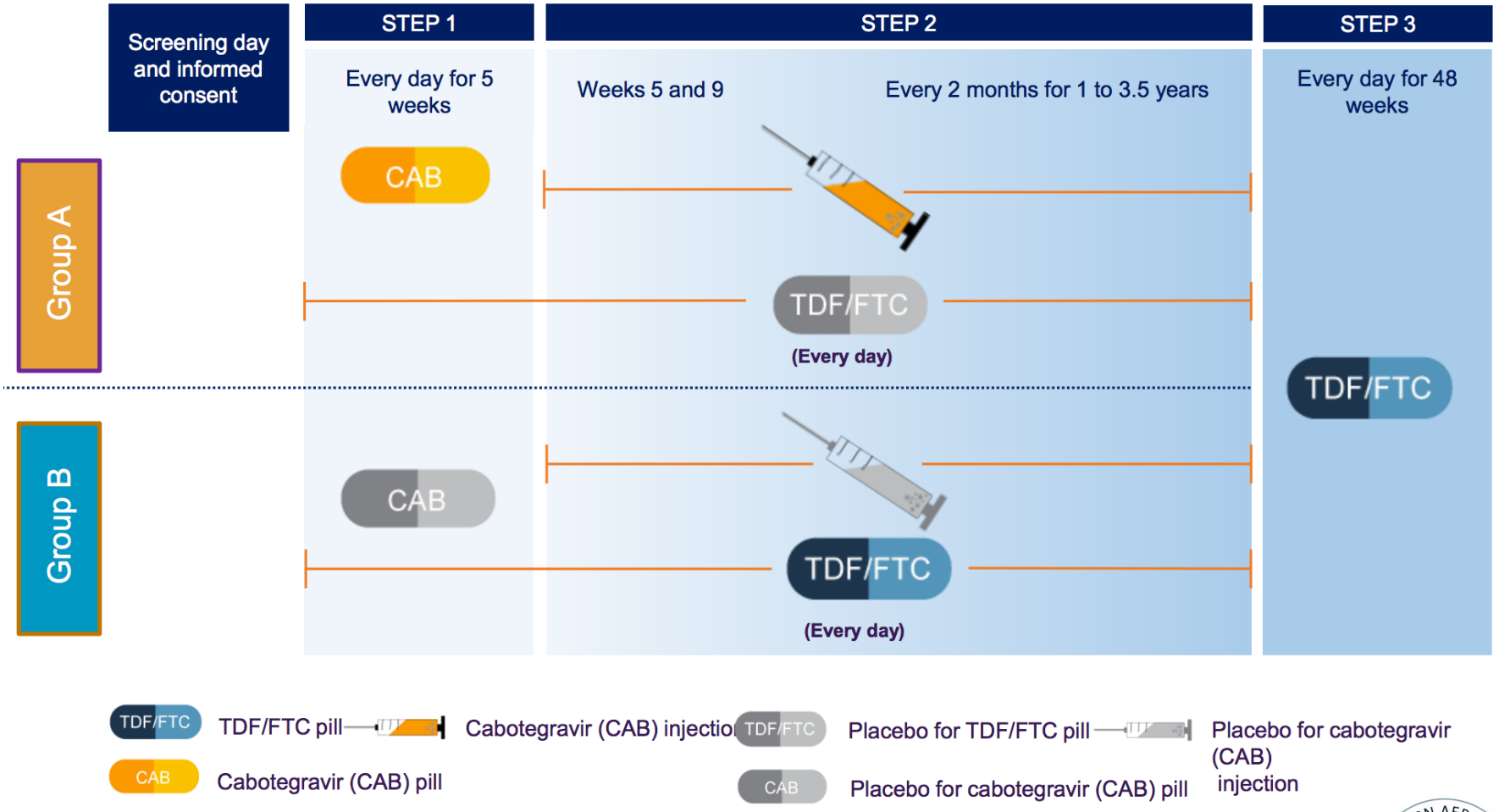
International, randomised, double-blind, placebo-controlled phase 2a study (N = 199)



- Grade ≥ 2 AEs significantly different between CAB and PBO during injection phase: injection-site pain (34% vs 2%; P < 0.0001), headache (15% vs 2%; P = 0.03)
  - Most injection-site reactions mild/moderate; 1 discontinuation due to injection-related AE
- 1 seroconversion (CAB cohort 1): detected 48 weeks after final injection; CAB levels undetectable
- Participants in cohort 2 (600 mg IM Q8W) consistently met prespecified PK targets; this dose will be assessed in phase 3 studies

Landovitz R, et al. IAS 2017. Abstract TUAC0106LB. ClinicalTrials.gov. NCT02178800.

HPTN 083/084: Study design

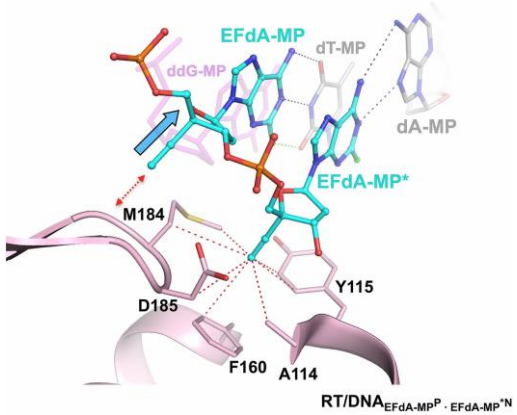


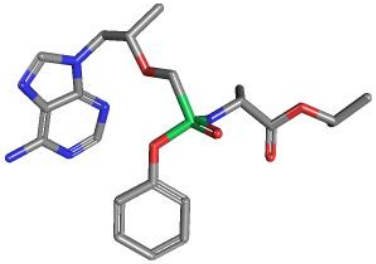
Phase 3 double blind, double dummy trials of CAB LA vs. TDF/FTC

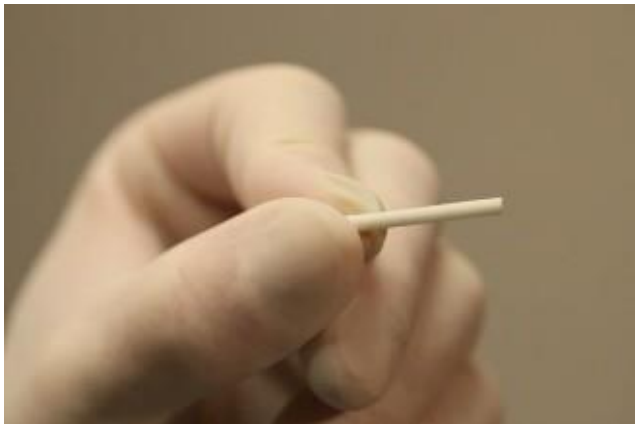
Then there are implantables…

Subcutaneous PrEP implants modelled after Implanon contraception

- Simple insertion AND removal
- Long-acting (months to years)
- PrEP PLUS contraception?
- Current development
  - TAF
  - EFdA (MK-8591)







ARV-based prevention pipeline

AVAC

GUIDELINES

Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection

GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

GUIDANCE ON PRE-EXPOSURE ORAL PROPHYLAXIS (PrEP) FOR SERODISCORDANT COUPLES, MEN AND TRANSGENDER WOMEN WHO HAVE SEX WITH MEN AT HIGH RISK OF HIV:

Recommendations for use in the context of demonstration projects

July 2012

World Health Organization

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

Southern African guidelines on the safe use of pre-exposure prophylaxis in persons at risk of acquiring HIV-1 infection

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

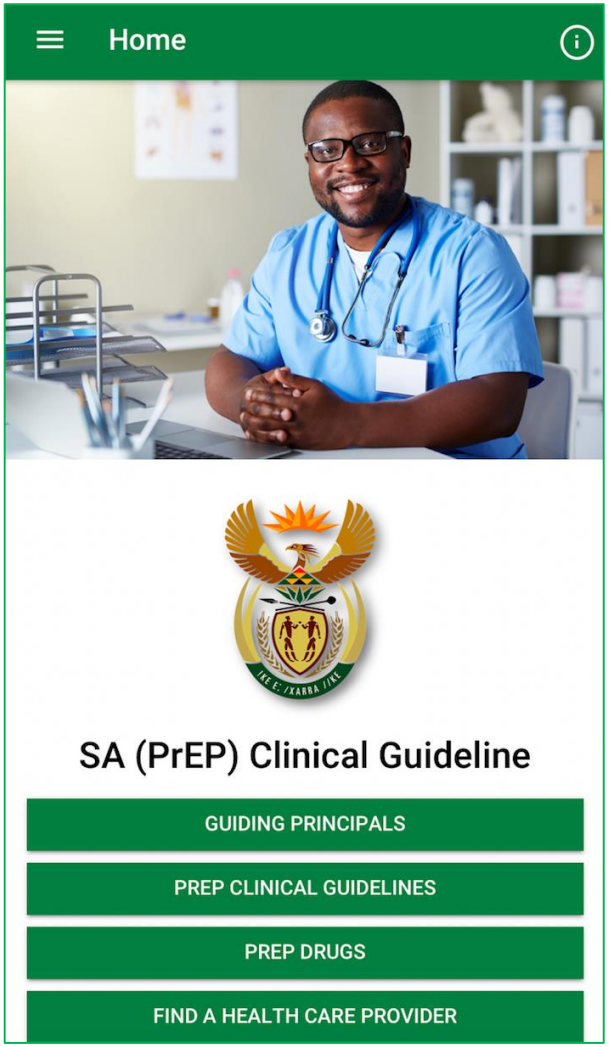
GUIDELINES

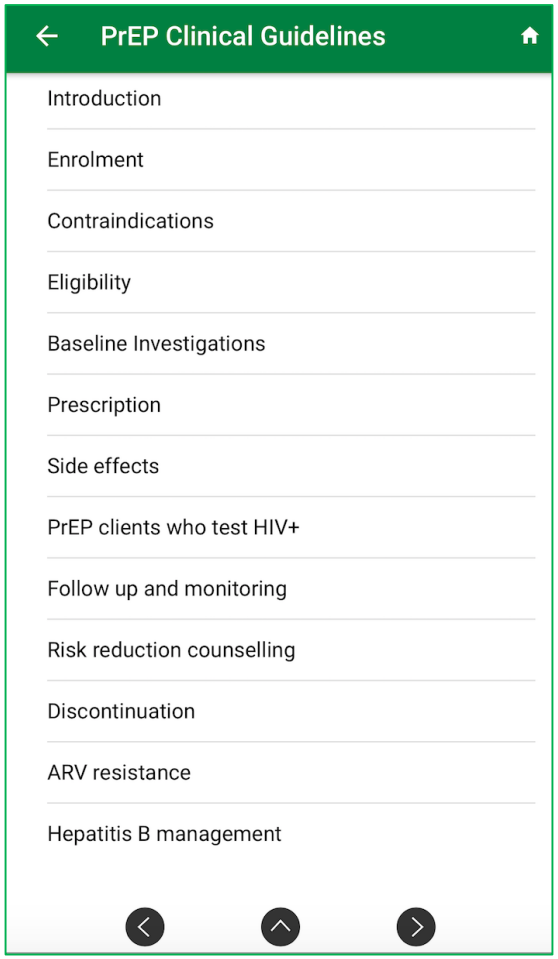
Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection

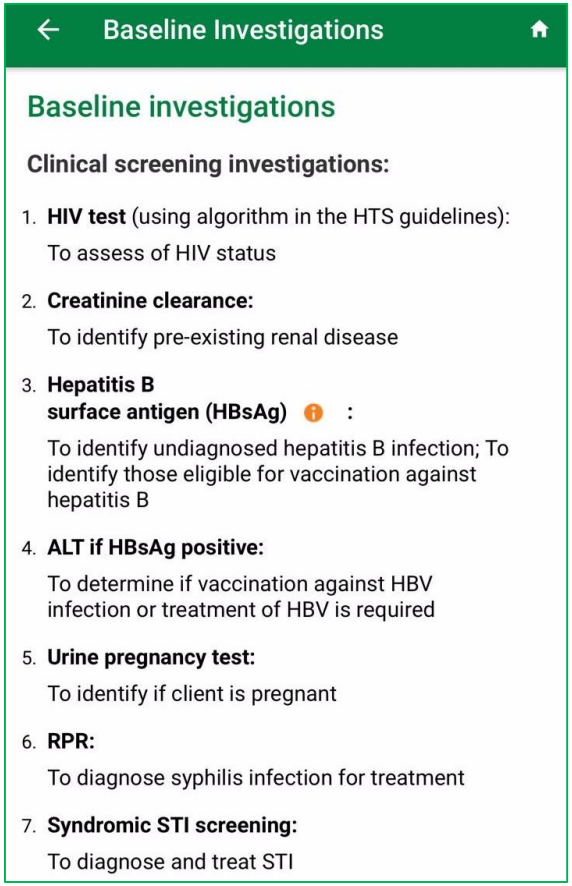
African guidelines on the safe use of pre-exposure prophylaxis in persons at risk of acquiring HIV-1 infection

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

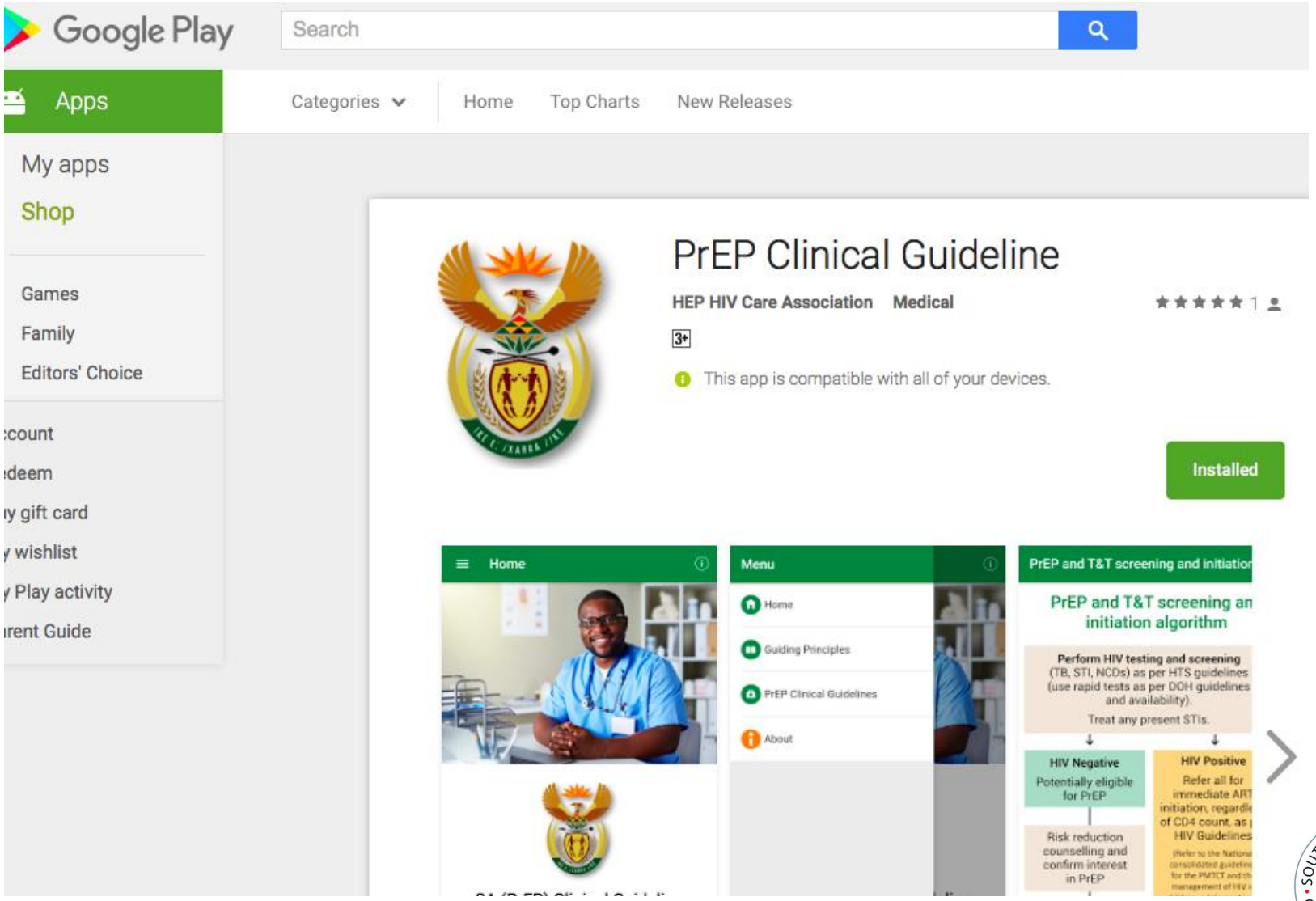
Other resources







How to find it…



Indications for PrEP

PrEP should be considered for people who are HIV-negative and at significant risk of acquiring HIV infection

1. Any sexually active HIV-negative *MSM or transgender person* who wants PrEP
2. *Heterosexual* women and men who want PrEP
3. People who inject *drugs*
4. Include *adolescents* and *sex workers*
   - especially vulnerable: young MSM and adolescent girls.

Contra-indications to PrEP

1. HIV-1 infected or evidence of possible acute infection
2. Suspicion of window period following potential exposure
3. Adolescents <35 kg or <15 years who are not ≥Tanner stage 3
4. Poor renal function (creatinine clearance <60 mL/min)
5. Other nephrotoxic drugs (eg aminoglycosides)
6. Unwilling or unable to return for 3-monthly visits
7. Pregnant or breastfeeding women

Eligibility criteria

1. Anyone identified as being at high risk for HIV exposure
2. No contraindications to FTC/TDF FDC
3. HIV-negative / not thought to be in the window period
4. Absence of symptoms of acute HIV infection
5. Willing and able to attend 3-monthly visits
6. Understands that the protection provided by PrEP is not complete
7. [Recurrent] use of PEP

The “how to” of PrEP

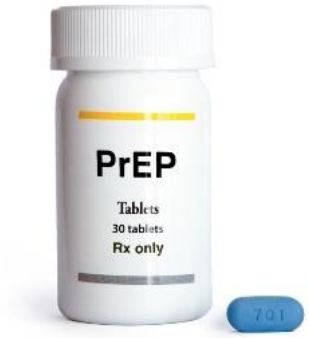
Screening

PrEP initiation visit

One month follow up

Three monthly maintenance visits

The new ABC of prevention



- Awareness
- Behaviour
- Combination
- Drugs
- Effective use

A
B
C

Acknowledgements

Save the Date

XXVI INTERNATIONAL WORKSHOP ON HIV DRUG RESISTANCE AND TREATMENT STRATEGIES

6 - 8 November 2017 Johannesburg, South Africa

6 – 8 November 2017

26th International Workshop on HIV Drug Resistance and Treatment Strategies

Johannesburg, South Africa

www.HIVresistance2017.co.za

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