

A Big Year for New HIV Prevention Choices

Craig W. Hendrix, MD

Wellcome Professor and Director, Division of Clinical
Pharmacology

Departments of Medicine and Pharmacology
Johns Hopkins University, Baltimore, MD



This activity is jointly provided by Physicians' Research Network and the Medical Society of the State of New York.

Disclosures

- **Research grants:** Gates, ViiV/GSK, Merck, & Gilead managed by JHU
- **Advisory Board:** Population Council, RTI, PREVENT Program, Gilead, Merck, ViiV/GSK, Orion Biopharma
- **Founding Partner** Priönde Biopharma, LLC
- **US Patent** 10,092,509 microbicide formulations

HIV Prevention Milestones in One Year!

- ▶ **FDA approves oral F/TAF for MSM/TGW**
 - ▶ Gilead commits to F/TAF PrEP RCT for cisgender women
- ▶ **Cabotegravir long-acting injectable formulation**
 - ▶ HPTN 083 DSMB stopped early for non-inferiority
 - ▶ Full analysis CAB-LA demonstrates superiority over oral daily F/TDF
- ▶ **Dapivirine vaginal ring**
 - ▶ EMA “positive scientific opinion” public health
 - ▶ Opens the door for rapid regulatory approval in LMIC
- ▶ **HIV Vaccine (RV144 Clade C modification)**
 - ▶ HVTN 702 DSMB stopped early for futility

Objectives

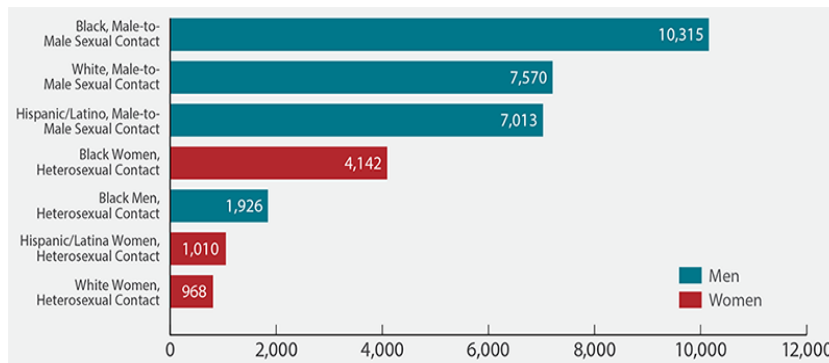
- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ Discuss ongoing development of long-acting PrEP
- ▶ Discuss ongoing development of on demand PrEP

Objectives

- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ Discuss ongoing development of long-acting PrEP
- ▶ Discuss ongoing development of on demand PrEP

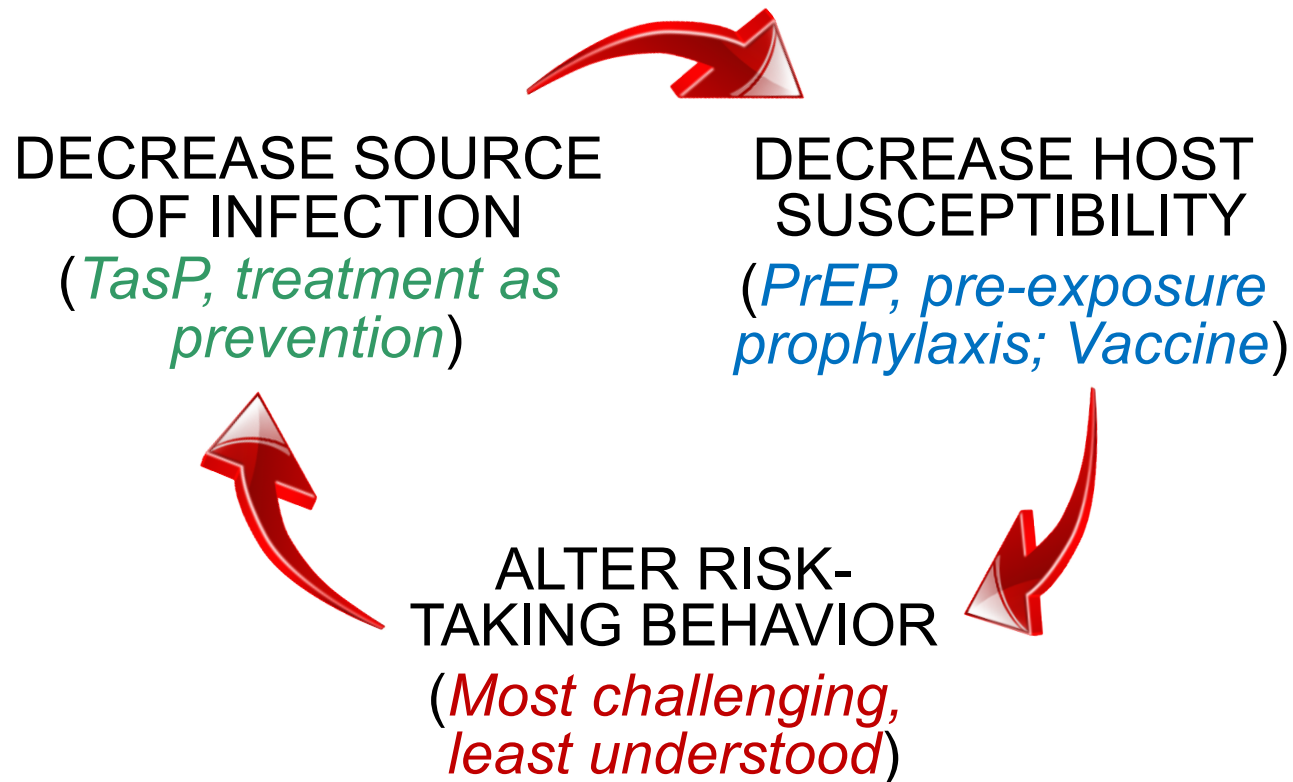
HIV Prevention Need

- ▶ New HIV infections continue each year (~40K US)
 - ▶ Globally 2.7 million - US ~40 thousand



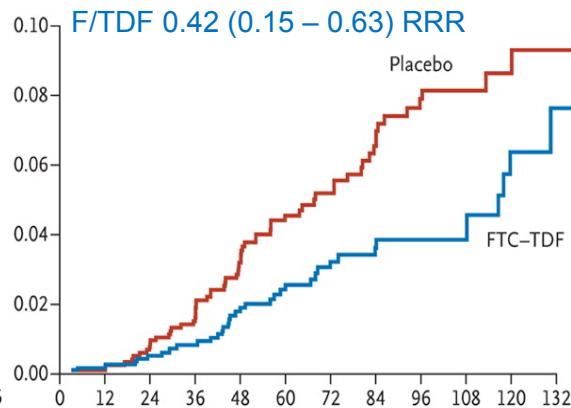
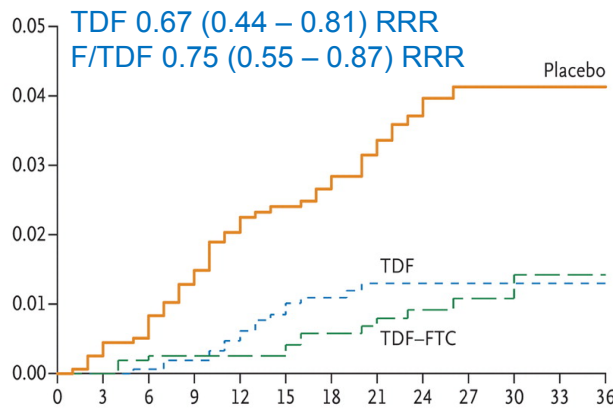
- ▶ Receptive partner lacks prevention control
- ▶ Treatment expensive, not curative
- ▶ Vaccine prevention distant
- ▶ Condoms
 - ▶ Effective, but not often used
 - ▶ Receptive partners lack control
 - ▶ Require behavioral change

HIV Prevention Strategies



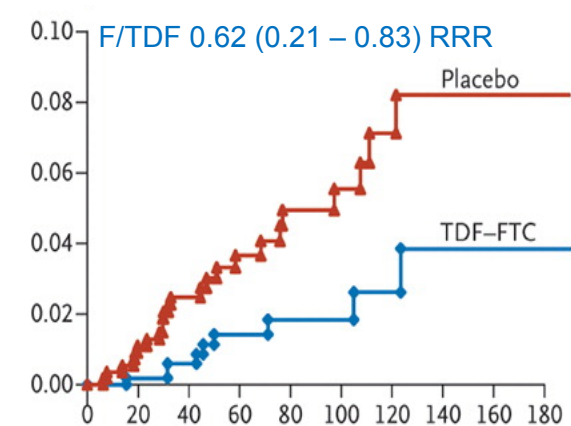
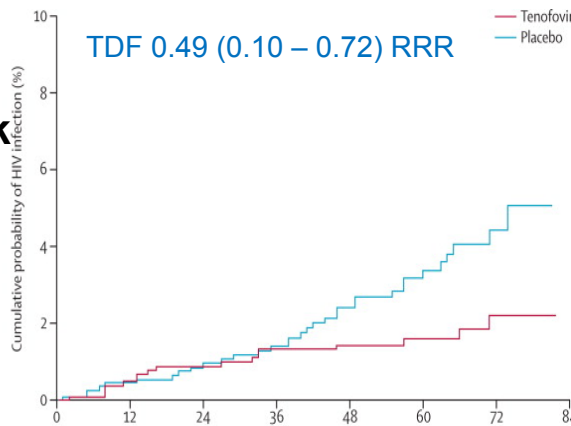
TDF ± FTC* is Effective for HIV PrEP

**Partners
Discordant
Heterosexual
Couples
N= 4,758**



**iPrEx
MSM & TGW
N=2,499**

**CDC Bangkok
PWID
N=2,413**



**CDC TDF2
Heterosexual
Cis Men & Women
N=1,219**

*TDF tenofovir disoproxil fumarate, F Emtricitabine, RRR relative risk reduction, PWID persons who inject drugs
Clockwise from upper left: Baeten NEJM 2012; Grant NEJM 2010; Thigpen NEJM 2012; Choopanya Lancet 2013

“Substantial” or “High Risk” of HIV infection

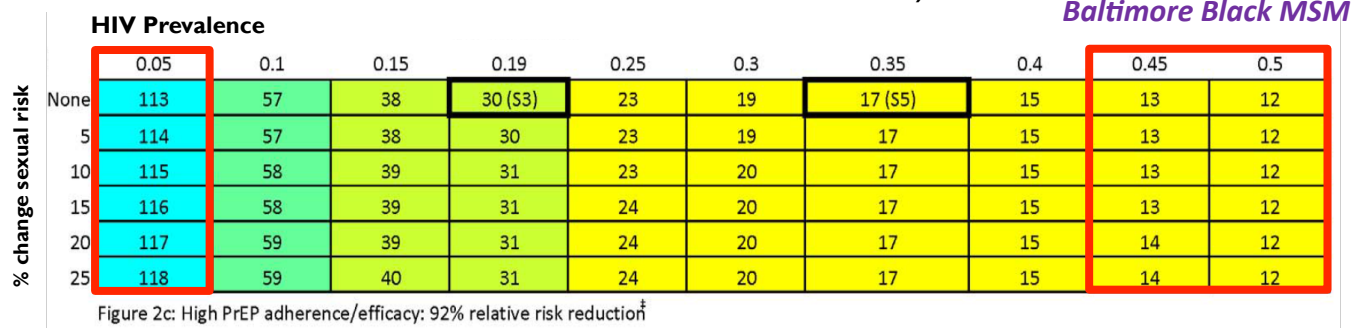
- ❖ FDA - combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in adults at **high risk** (*Truvada™ Package insert 2012*)
- ❖ CDC - one prevention option for sexually-active adults & IDU at **substantial risk** of HIV acquisition (**IA**, *USPHS Clinical Practice Guidelines – 2014*)

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)

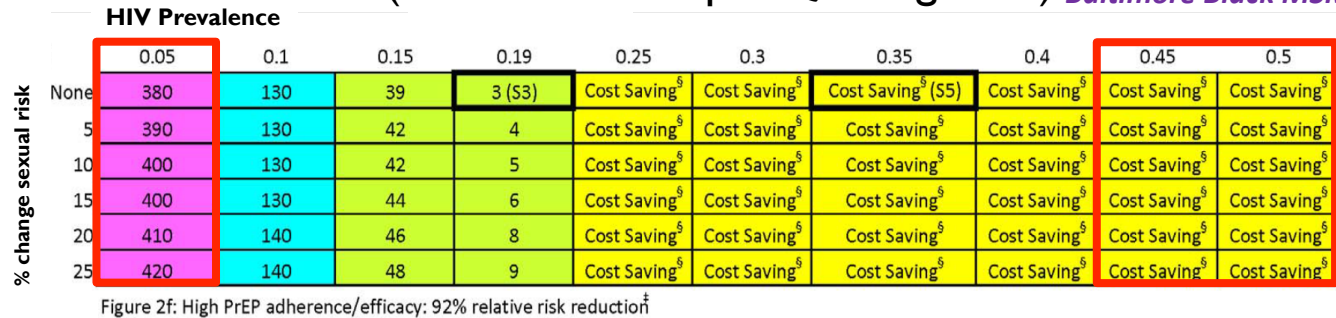
- ❖ WHO - additional prevention choice for people at **substantial risk (>3/100 py)** of HIV infection as part of combination HIV prevention approaches

MSM PrEP Effectiveness Models

Clinical Effectiveness (number needed to treat)



Cost-Effectiveness (thousands \$US per QALY gained) *Baltimore Black MSM*



NNT Comparisons

NNT	Drug	Condition/Duration	Outcome prevented
8	Rhogam	Rh incompatibility	Prevent future pregnancy alloimmunization
8	Antibiotics	COPD exacerbation	Death
39	Statin	Known heart disease/5 yr	Stroke
67	HTN meds	HTN/5 yr	MI
77	Clopidogrel	MI or stroke history/1 yr	MI
83	Statin	Known heart disease/5 yr	Death
100	HTN meds	HTN/5 yr	Stroke
104	Statin	Unknown heart disease/5 yr	Stroke
125	Statin	Known heart disease/5 yr	MI
125	HTN meds	HTN/5 yr	Death
157	Statin	Unknown heart disease/5 yr	MI
200	Clopidogrel	MI or stroke history/1 yr	Stroke
333	Clopidogrel	MI or stroke history/1 yr	Death
2000	Aspirin	No MI/Stroke history/1 yr	MI
3000	Aspirin	No MI/Stroke history/1 yr	Stroke
NB	Statin	Unknown heart disease/5 yr	Death
NB	Aspirin	No MI/Stroke history/1 yr	Death

48% HIV prevalence
(Baltimore BMSM)

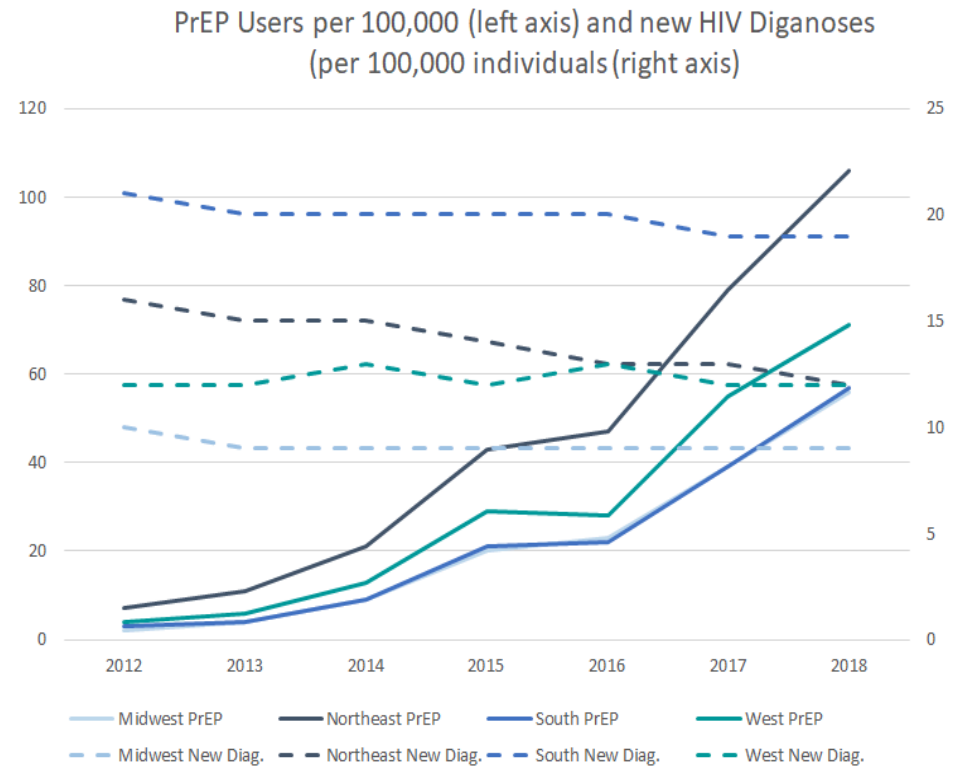
5% HIV prevalence

NB, none benefitted. Source: <http://www.thennt.com>

▶ HIV prevalence NNT with high adherence from Dowdy, et al. PLOS One 2014

POPULATION-LEVEL IMPACT

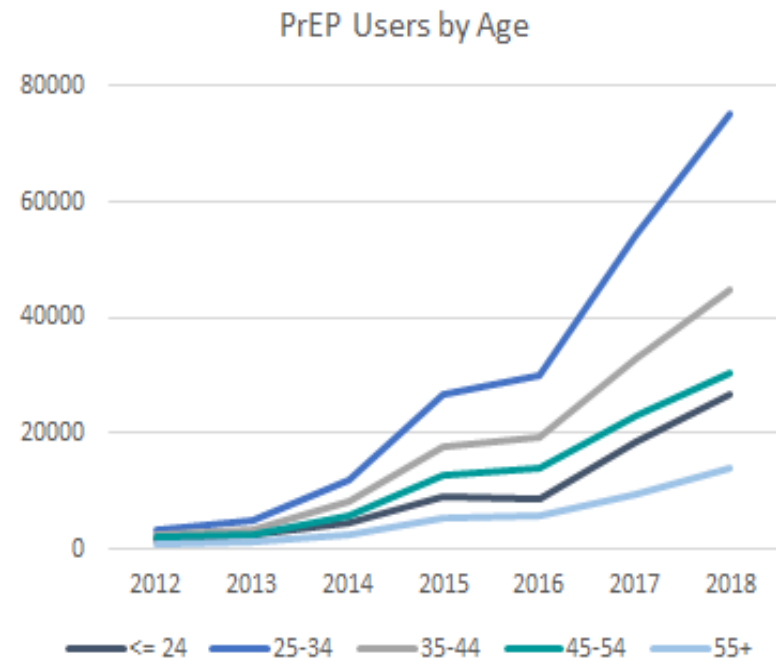
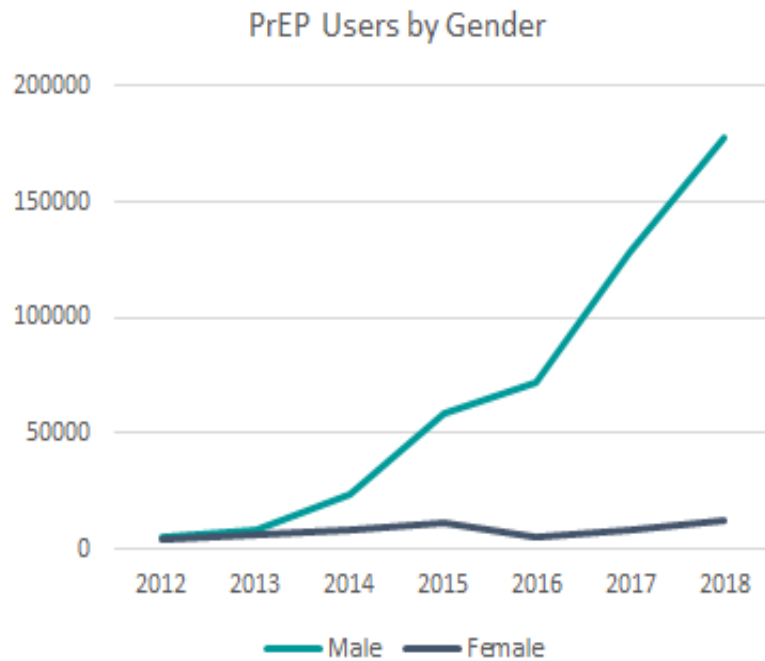
- ▶ New South Wales, Australia (*FIGURE*): PrEP associated with a 25% decrease in new HIV diagnoses among MSM
- ▶ United States: Diagnosis rate decreased by 1.3% for increase in PrEP coverage of 1 per 100 persons
- ▶ King County, WA: Reduced HIV incidence by 84% among MSM & transgender persons with STIs



▶ Grulich et al. 2018; Smith et al. 2020; Pagkas-Bather et al. 2020

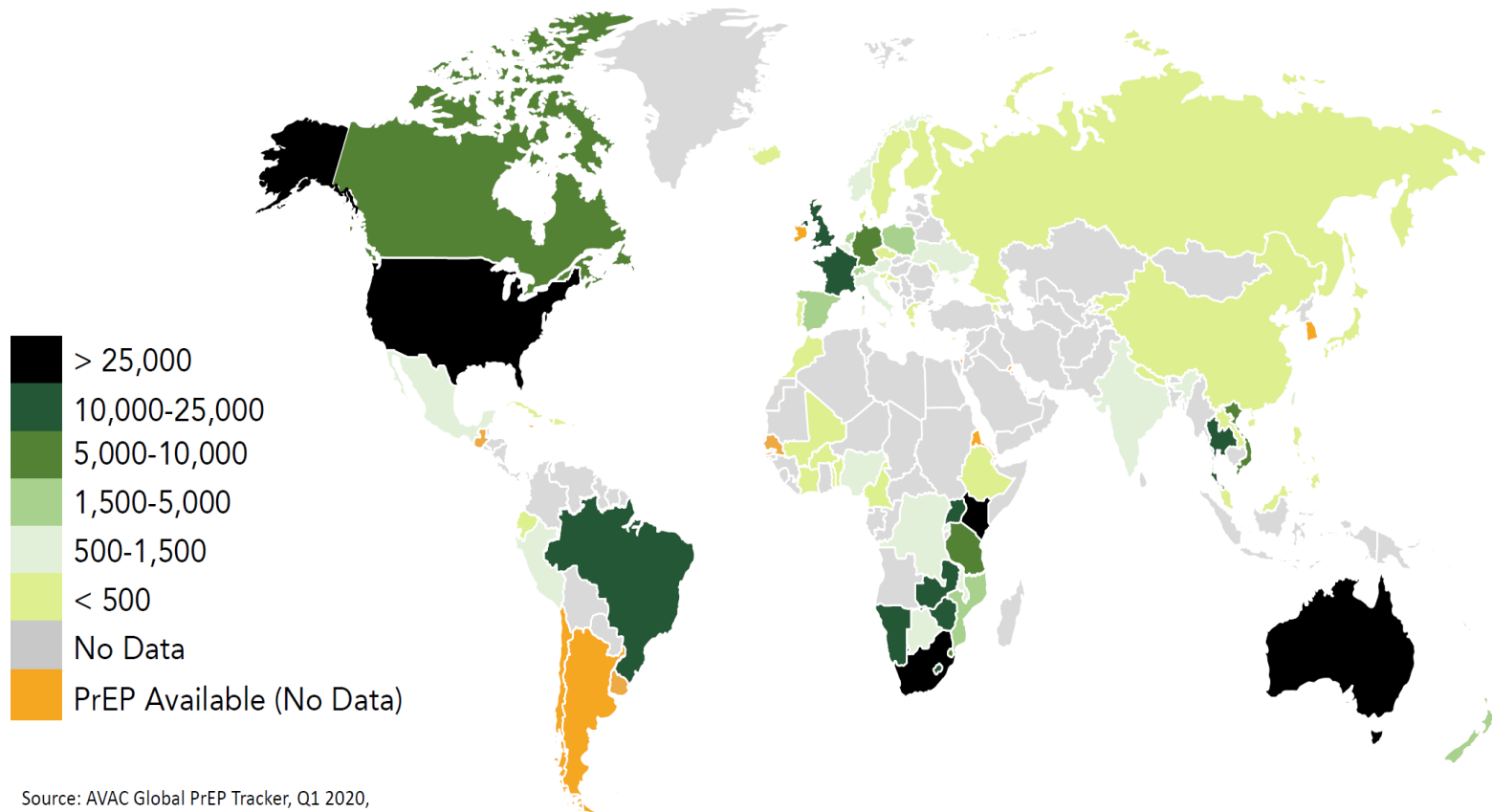
Source: AIDSvu. (2020).

PrEP UPTAKE IN THE US



▶ Source: AIDSvu. (2020).

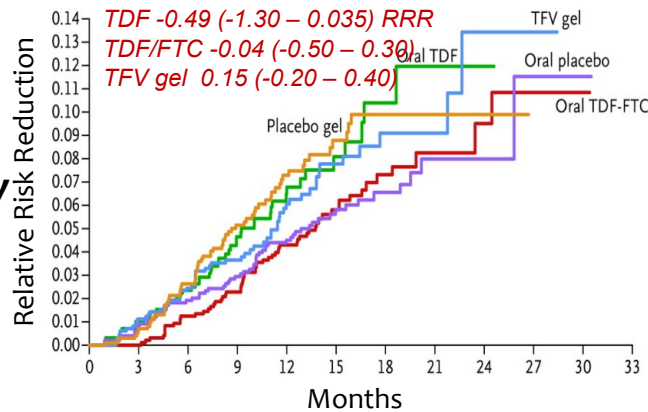
Global PrEP Uptake 2020



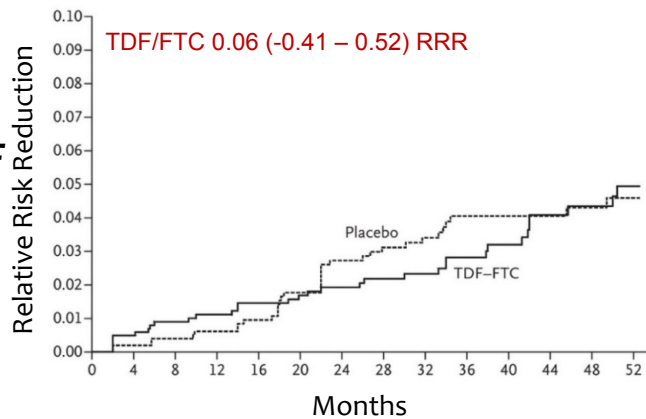
▶ AVAC Global PrEP Initiation Tracker; avac.org. accessed September 2020

PrEP in Women

VOICE
Oral F/TDF
Oral TDF
Vaginal TFV
 Women
 N=5,029



FEM-PrEP
Oral F/TDF
 Women
 N=2,120



Sources of PrEP Failure

- ❑ Poor Adherence
 - ❑ Young, especially women
 - ❑ Repeatedly seen in demonstration projects
 - ❑ Complex risk perception, stigma, power, etc. ...
 - ❑ Fear of systemic drug
 - ❑ Desire for multiple PrEP options
- ❑ Vaginal TFV (CAPRISA 004, VOICE, FACTS 001)
 - ❑ Dysbiotic flora degrades TFV
 - ❑ Vaginal ring & gel don't protect anal sex

Marrazzo NEJM 2015; van Damme NEJM 2012; Klatt Science 2017; Justman JAIDS 2018;

Oral F/TDF PrEP in Women

Pregnant Women

- ▶ HIV risk increased 2-4 times
- ▶ PrEP discontinued in RCTs during pregnancy (so, understudied)
- ▶ Partners Demo. Project (N=37) found 2x TFV conc'n reduction

Population	% Below Protective Threshold	
	Standard Dose TDF/FTC	Double Dose TDF/FTC
Non-pregnant	3.7%	--
1 st Trimester	31.5%	4.4%
2 nd Trimester	47.2%	7.9%
3 rd Trimester	62.6%	14.4%

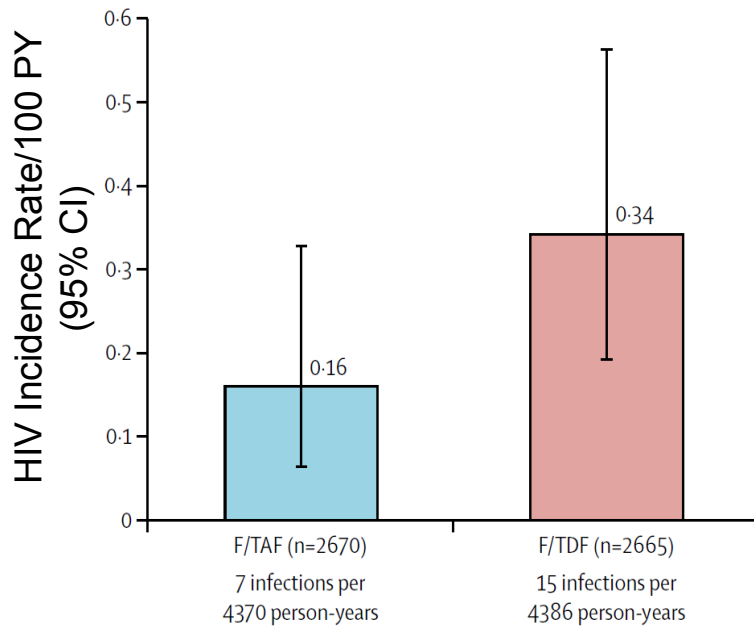
Transgender Women (TGW)

- ▶ Two prospective DDI studies
 - ▶ F/TDF \pm gender affirming hormones (GAHT)
 - ▶ GAHT includes estrogen & anti-androgen
- ▶ Results
 - ▶ No effect of F/TDF on GAHT
 - ▶ 17-32% plasma TFV reduction by GAHT
 - ▶ 17-24% plasma FTC reduction by GAHT
- ▶ Impact
 - ▶ Concern for short “on demand” 2+1+1 regimen (proven effective in MSM)

DISCOVER: F/TAF vs. F/TDF

▶ Efficacy

- ▶ F/TAF **non-inferior** to F/TDF
- ▶ All failures w/ DBS **<2/wk adherence**
- ▶ Few TGW (N=74, 1%, no failures)



▶ Toxicity (Wk48 minor differences)

Variable	TDF-FTC	TAF-FTC
Mean estimated glomerular filtration rate, mL/min/1.73 m ²	-2.0	+2.0
Mean hip bone mineral density, %	-1.0	+0.2
Median fasting low-density lipoprotein cholesterol level, mmol/L	-0.17	+0.03
mg/dL	-6.5	+1.0
Mean body weight, kg	0	+1.1
Cost		
Average wholesale price per month, \$	2110	2110
Year in which generic version will be available	2020	2022 to 2025

Wholesale acquisition cost 30-day supply: Teva \$1,455, Gilead \$1,600-\$1,800

▶ Mayer Lancet 2020; Krakower AIM 2020; FDA Briefing Document (AVAC F/TAF) August 19, 201

Oral F/TDF PrEP in Cisgender Women

▶ 8/2019 FDA Advisory Committee

- ▶ FDA Brief: ...important to compare TFV-DP concentrations in the same mucosal tissues if bridging of efficacy between F/TDF and F/TAF is being proposed. Bridging of efficacy results from men to cisgender women based on mucosal tissue concentrations, however, is not possible because the effective drug concentrations could be different for rectal and vaginal HIV exposures.
- ▶ Recommends F/TAF approval for MSM/TGW, not GCW

▶ 10/2019 FDA

- ▶ Post-marketing commitment in F/TAF PrEP approval

▶ 12/2019 Gilead

- ▶ Commitment to Phase 3 F/TAF PrEP RCT in women
- ▶ Not listed yet in clinicaltrials.gov

Barriers to PrEP Uptake/Persistence/Impact

- ▶ Awareness of PrEP
- ▶ HIV Risk Perception
- ▶ Stigma
- ▶ Provider bias
- ▶ Healthcare System Distrust
- ▶ Access to Medical Care
- ▶ Lack of Access to Financial Assistance
- ▶ Side Effects
- ▶ Daily tablet dissatisfaction

Objectives



- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ Discuss ongoing development of long-acting PrEP
- ▶ Discuss ongoing development of on demand PrEP

METHOD EXPLORER /

★ most effective	Y party ready	🛡️ STI prevention	🚫 hormone free	🔍 easy to hide	❤️ do me now
---------------------	------------------	----------------------	-------------------	-------------------	-----------------

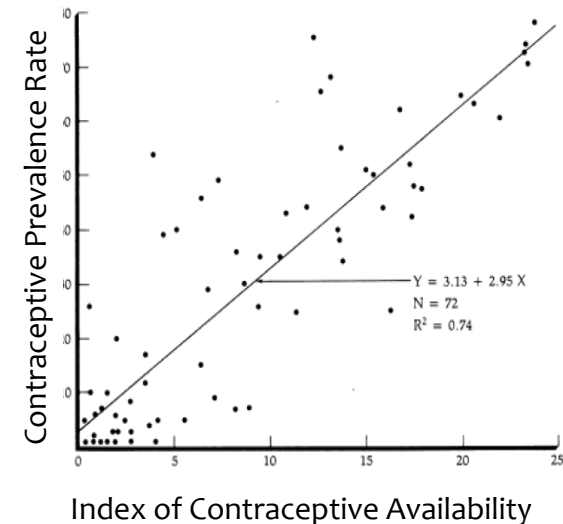


<https://www.bedsider.org/methods>

share this /  

CHOICE: Proven Benefit in Contraception

- ▶ WHO Systematic Review (231 articles)
- ▶ CHOICE associated with better:
 - ▶ Contraceptive **Uptake**
 - ▶ Contraceptive **Persistence**
 - ▶ Health outcomes (↓ pregnancies, ↓ STIs)
- ▶ CHOICE, as with needs, vary over a lifetime
- ▶ *Why should PrEP be different?*



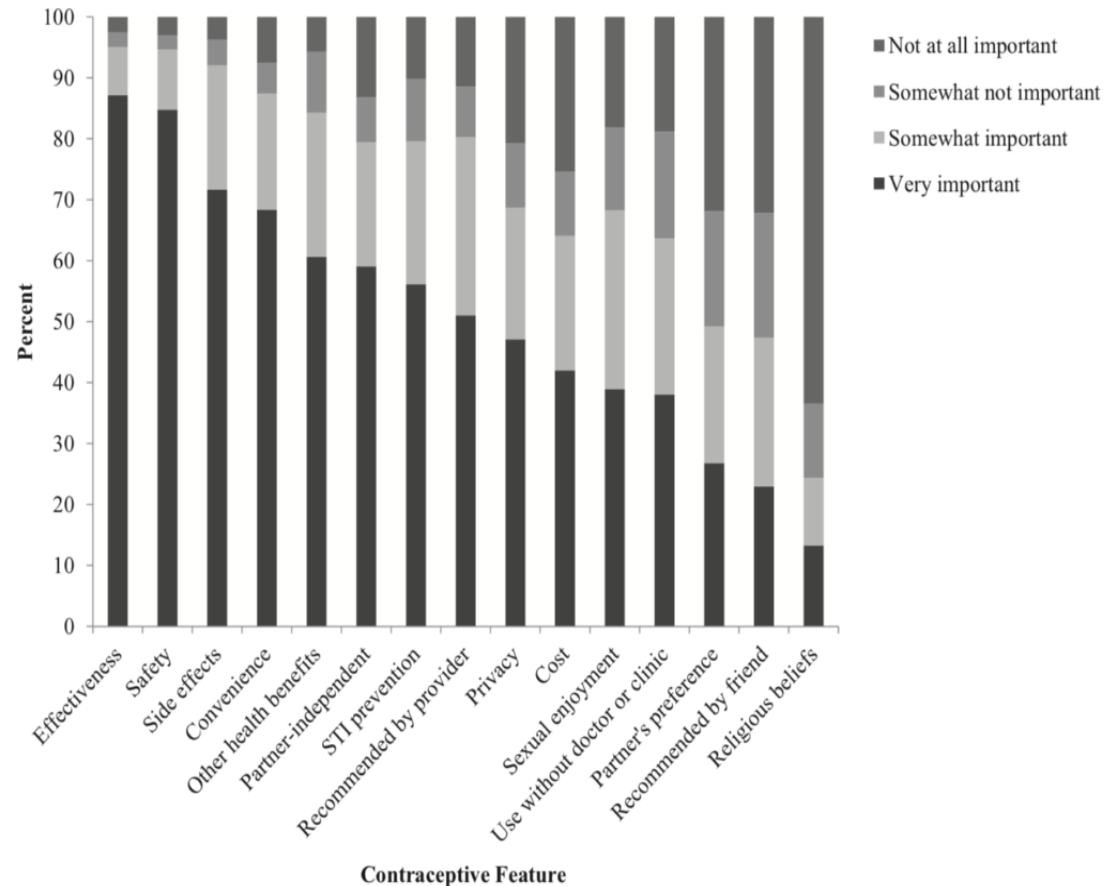
- EACH add'l product option yields 12% increase in contraceptive use
- **How much will it be for PrEP?**

▶ Gray AL, et al. WHO RHRU 2006

Jain AK, et al. *Stud Fam Plan* 1989

Many Factors Influence Choice

- **Effectiveness** does not drive all decision-making
- **Safety** similarly important
- **Convenience, other health benefits, control, privacy, etc.,** important, too



Womens' PrEP Desires



Injectables



Implants



Vaginal Ring



Oral Tablets



Vaginal Film



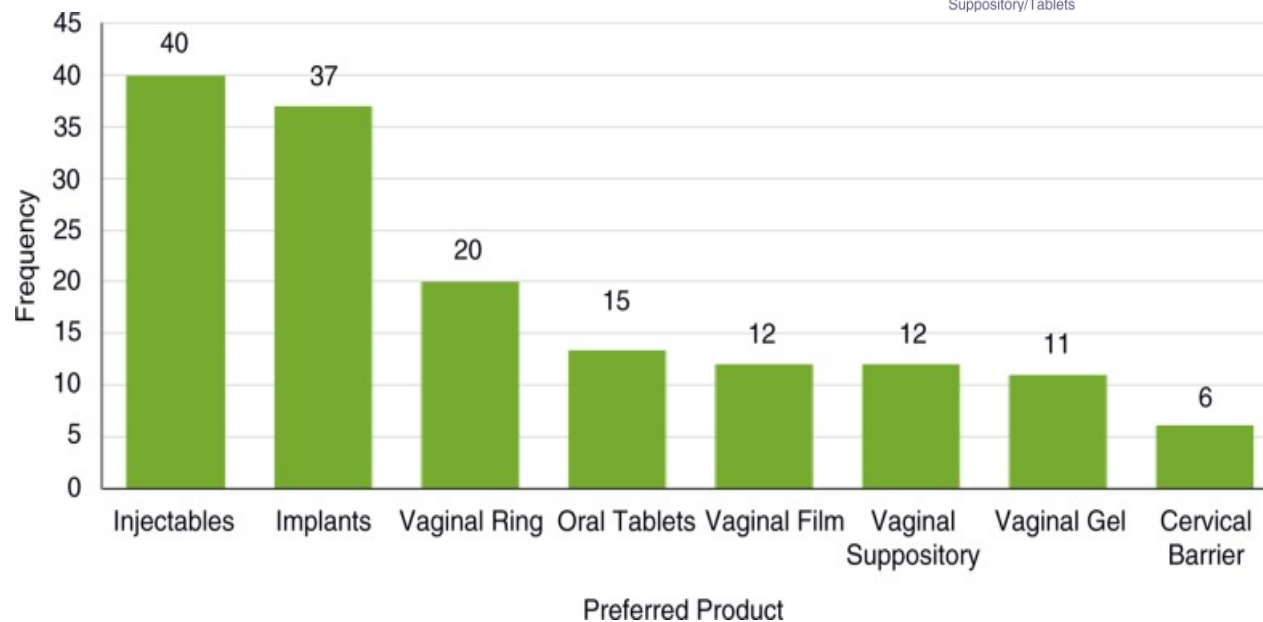
Vaginal Suppository/Tablets



Vaginal Gel



Barrier Methods

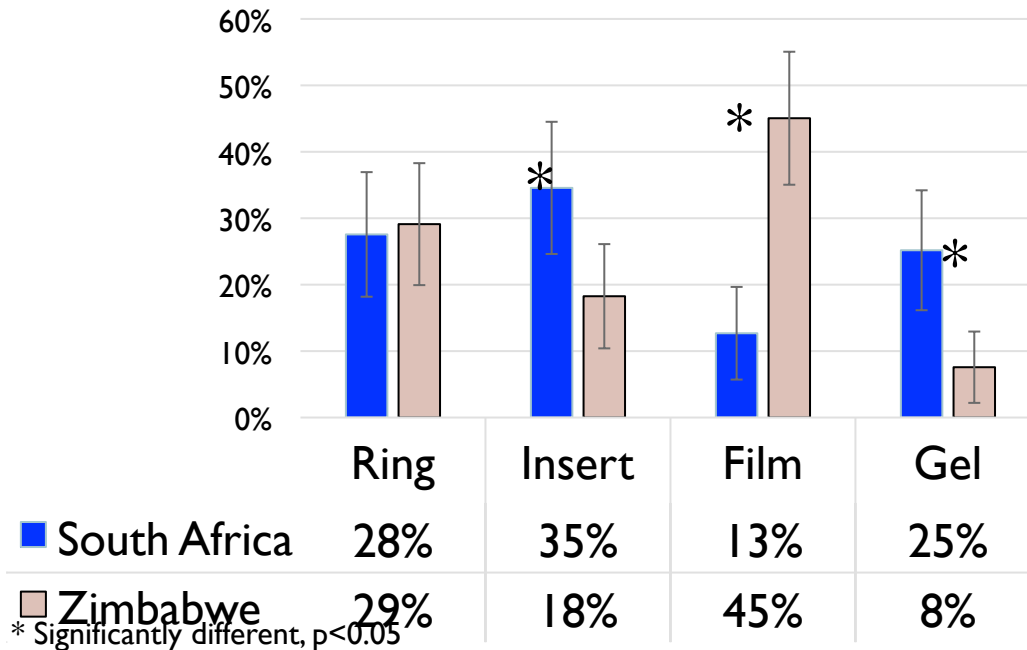


▶ VOICE-D (MTN-003-D): Luecke, JIAS 2016

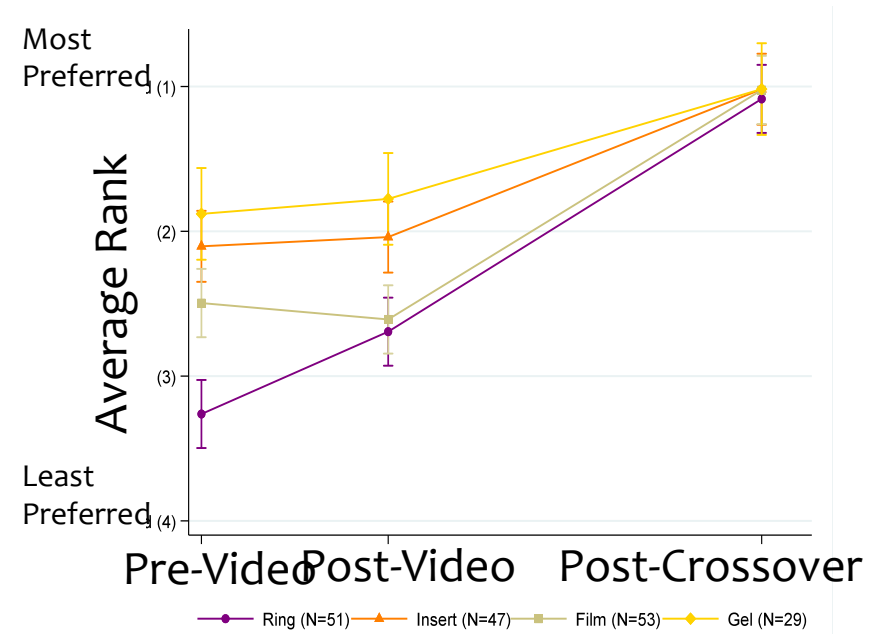
Women's Choice Matters

- Discrete Choice Study of Vaginal PrEP Products

Preference varies *Geographically*



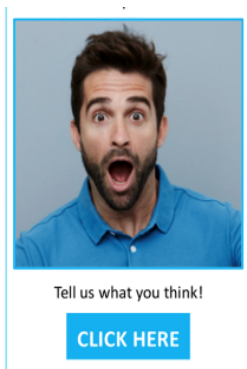
Preference varies with *Experience*



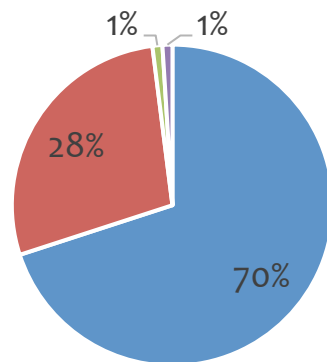
Grindr Survey

Especially with sex product, Essential to build around user experience

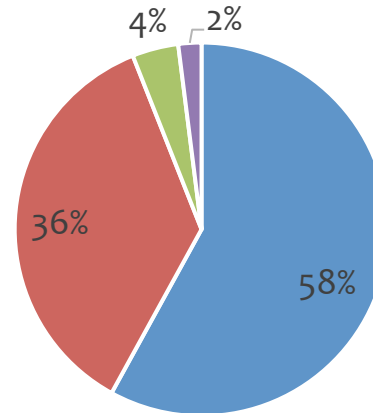
- 4,751 Took Grindr Survey
 - 78% RAI last 3 months
 - 80% douche before RAI
 - 27% douche after RAI



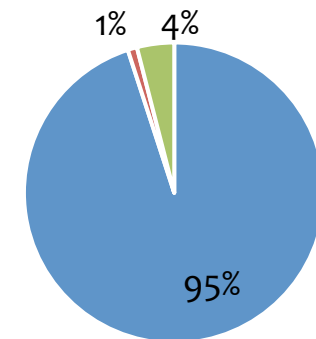
Likely use microbicide douche (currently douche) 98%



Likely use microbicide douche (currently do not douche) 94%



Insertive partner supportive of RM douching partner 96%



■ Definitely Yes

■ Probably Yes

■ Supportive

■ Opposed

Generally much higher than similar survey research for vaginal products

Likely use stats replicated in Latin America & Africa

Alex Carballo-Diequez, et al. AIDS Behav 2019 Jun;23(6):1484-1493; Giguere CROI 2020

More Formulation CHOICE, Better Adherence

**Uptake/Persistence Challenges Motivate
Alternative Formulation Development**

**Long-Acting
Formulations**

- Parenteral
- Oral
- Topical

On Demand

± Behaviorally Congruent

- Oral
- Topical

Infrequent dosing to minimize need for adherence Infrequent dosing to minimize need for adherence
*Trade-off increased exposure for improved adherence Reduced systemic exposure & **minor behavior change***

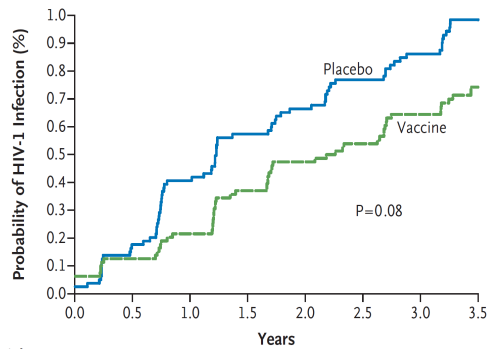
Objectives

- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ **Discuss ongoing development of long-acting PrEP**
- ▶ Describe ongoing development of on demand PrEP

HIV Vaccine Setbacks

RV144: 31% RRR Low

Intention-to-Treat Analysis

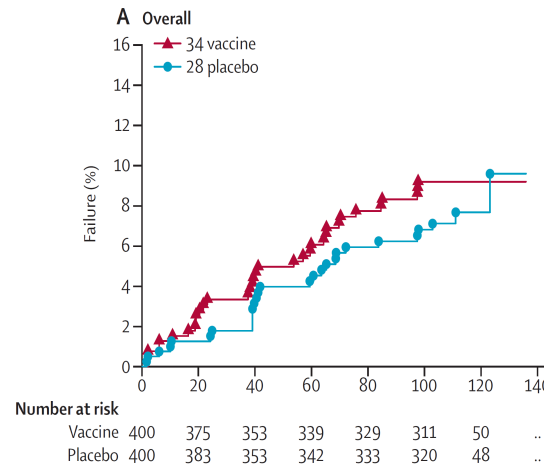


No. at Risk		Years				
Placebo	8200	7775	7643	7441	7325	
Vaccine	8202	7797	7665	7471	7347	
Cumulative No. of Infections		Years				
Placebo		32	52	67	76	
Vaccine		17	37	50	56	

Prime-Boost Vector + Protein

4 priming recombinant canarypox vector (ALVAC-HIV)
2 boosters of recombinant gp120 subunit vaccine (AIDSVAX B/E)

HVTN 502: Enhancement



Vector + Protein

MRKAd5 HIV-1 gag/pol/nef
0, 1, 6 month schedule

Antibody dependent enhancement

HVTN 702: Futility

- Enrolled > 5400 across 14 sites
- 6 injections over 18 months
- Trial stopped FEB 2020 futility
- No safety concerns

Prime-Boost Vector + Protein

Recombinant canarypox vector ALVAC-HIV & 2-component gp120 protein subunit vaccine (for **Clade C**) with adjuvant (adjuvant & proteins modified from RV144)

► [Rerks-Ngarm, et al. N Engl J Med 2009](#); [Buchbinder Lancet 2008 \(HVTN 502\)](#); [NIAID News](#)

Long-Acting Dapivirine Vaginal Ring

- ▶ Vaginal Ring Design
 - ▶ Silicone matrix ring, 25 mg of dapivirine (NNRTI)
 - ▶ Monthly replacement, trivial systemic exposure
- ▶ Two phase III placebo-controlled trials
 - ▶ Well tolerated
 - ▶ Reduced HIV incidence ~30%
 - ▶ Greater protection (up to 85%) with high adherence
- ▶ OLEs High uptake, better adherence
- ▶ 90-day Ring in Development
- ▶ EMA favorable scientific review

ASPIRE

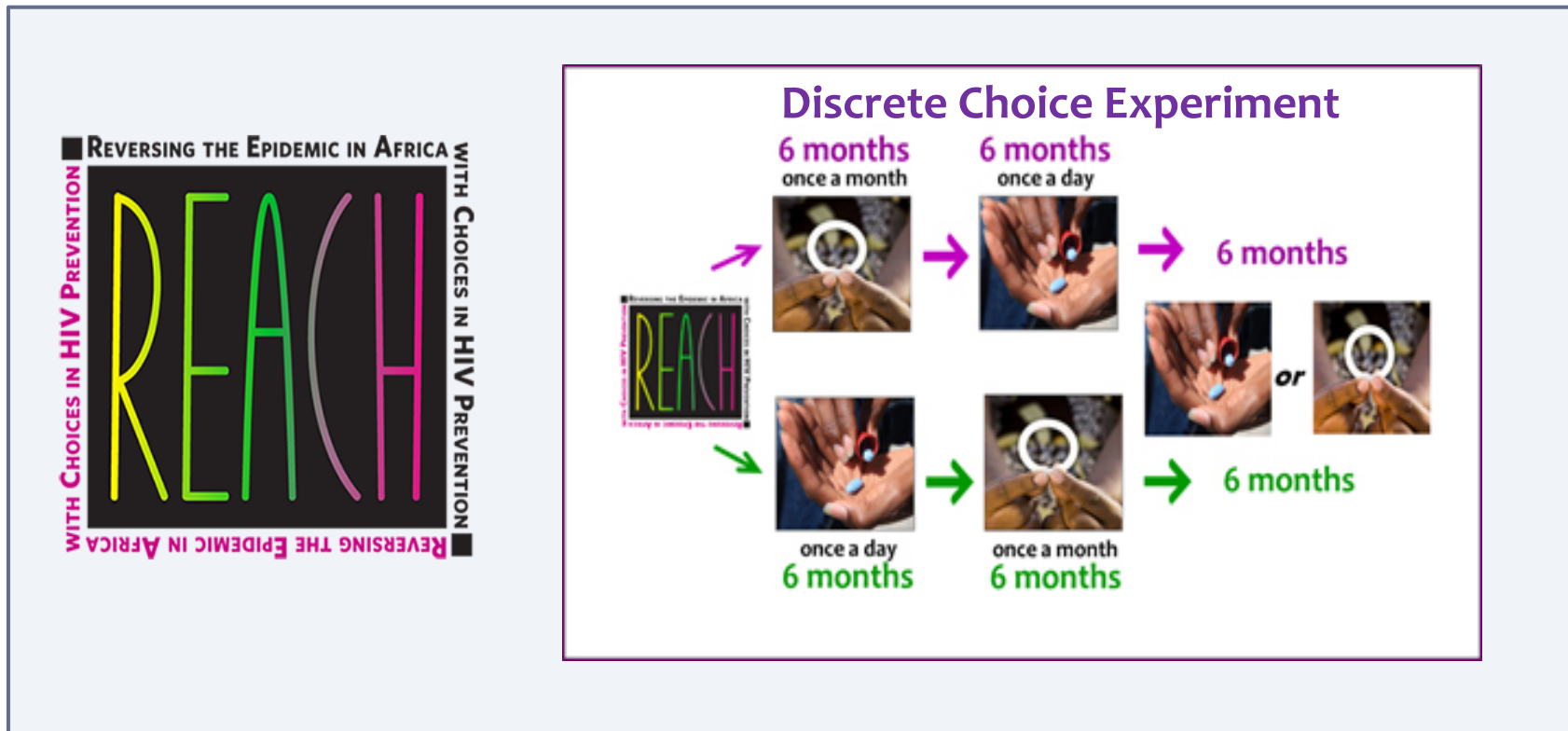


HOPE
HIV Open-label Prevention Extension
Out of ASPIRE, there is HOPE



▶ Baeten, et al., ASPIRE & Nel, et al., The Ring Study (IPM) NEJM 2016; International Partnership for Microbicides (IPM)

Impact: Persistence - Adherence - Protection



^{1,2}Based on 12 month data; adherence \geq mod-high; ³protection associated with mod adherence
Grant Lancet HIV 2014, Brown AIDS 2016, Baeten CROI 2019, Celum IAS 2019

Impact of Choice

Commentary

HIV Prevention: The Need for Methods Women Can Use

ZENA A. STEIN, MA, MB, BCH

“...a less efficacious [method], frequently used, might serve the public health as well or better than a more efficacious, but less frequently used [method], and ...**play an important role in preventing transmission at the population level.**”

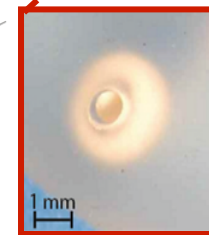
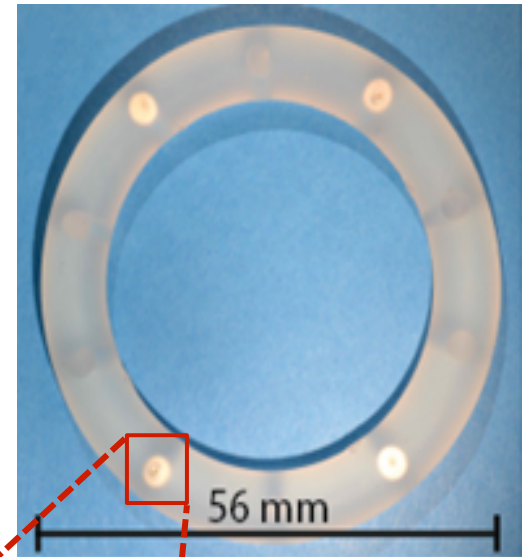
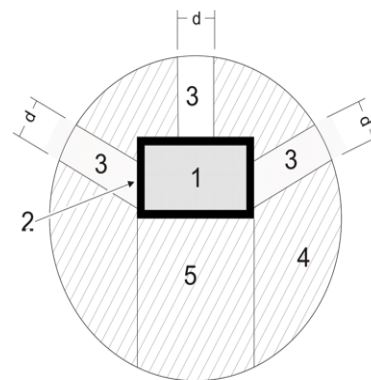
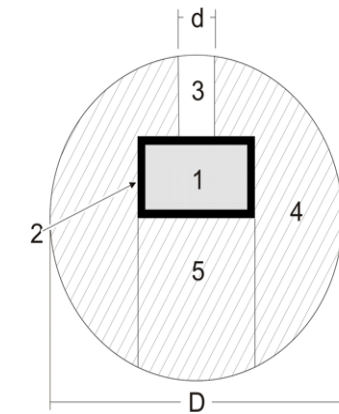
(Am J Pub Health, 1990)

Dapvirine Ring Regulatory Status

- ▶ IPM & MTN:
 - ▶ Release The Ring Study & ASPIRE positive results (FEB 2016)
- ▶ IPM: initiates Article 58 procedure (JUN 2017)
 - ▶ EMA (with WHO) provides scientific opinion on safety, efficacy & quality of medicines marketed exclusively in LMIC for diseases of major public health interest
- ▶ EMA:
 - ▶ Announced a “positive benefit-risk opinion” (JUL 2020)
- ▶ WHO:
 - ▶ Guideline development & prequalification review
- ▶ African Countries:
 - ▶ parallel regulatory review
 - ▶ EMA’s Article 58 opinion recognized by many countries in Africa
 - ▶ IPM submitting to those countries through WHO-coordinated process
 - ▶ First submissions where ring studies took place
- ▶ FDA NDA submission (late 2020)

Pod-IVR : Flexible MPT Capability

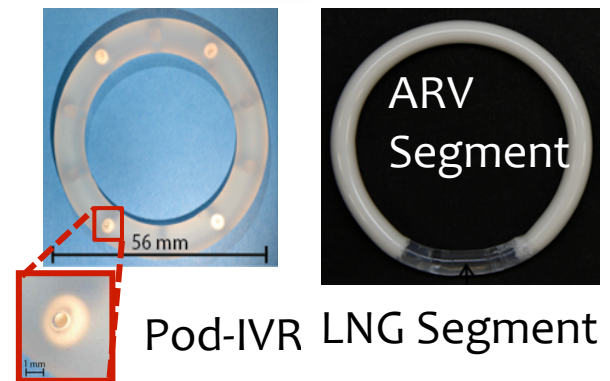
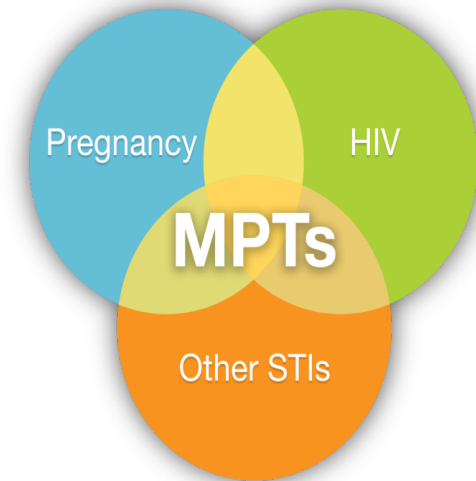
- ▶ **≤10 Polymer-coated drug “pods”**
- ▶ An un-medicated, torus-shaped elastomeric support holds the pods
- ▶ Release rate controlled through delivery channels size
- ▶ **Flexible drug combinations** unlike matrix of single reservoir rings
- ▶ MPT (contraception/ARV) pre-clinical
- ▶ Clinical studies **one month** IVRs



▶ Marc Baum & John Moss, Oakcrest Institute of Science

Multipurpose Prevention Technologies (MPT)

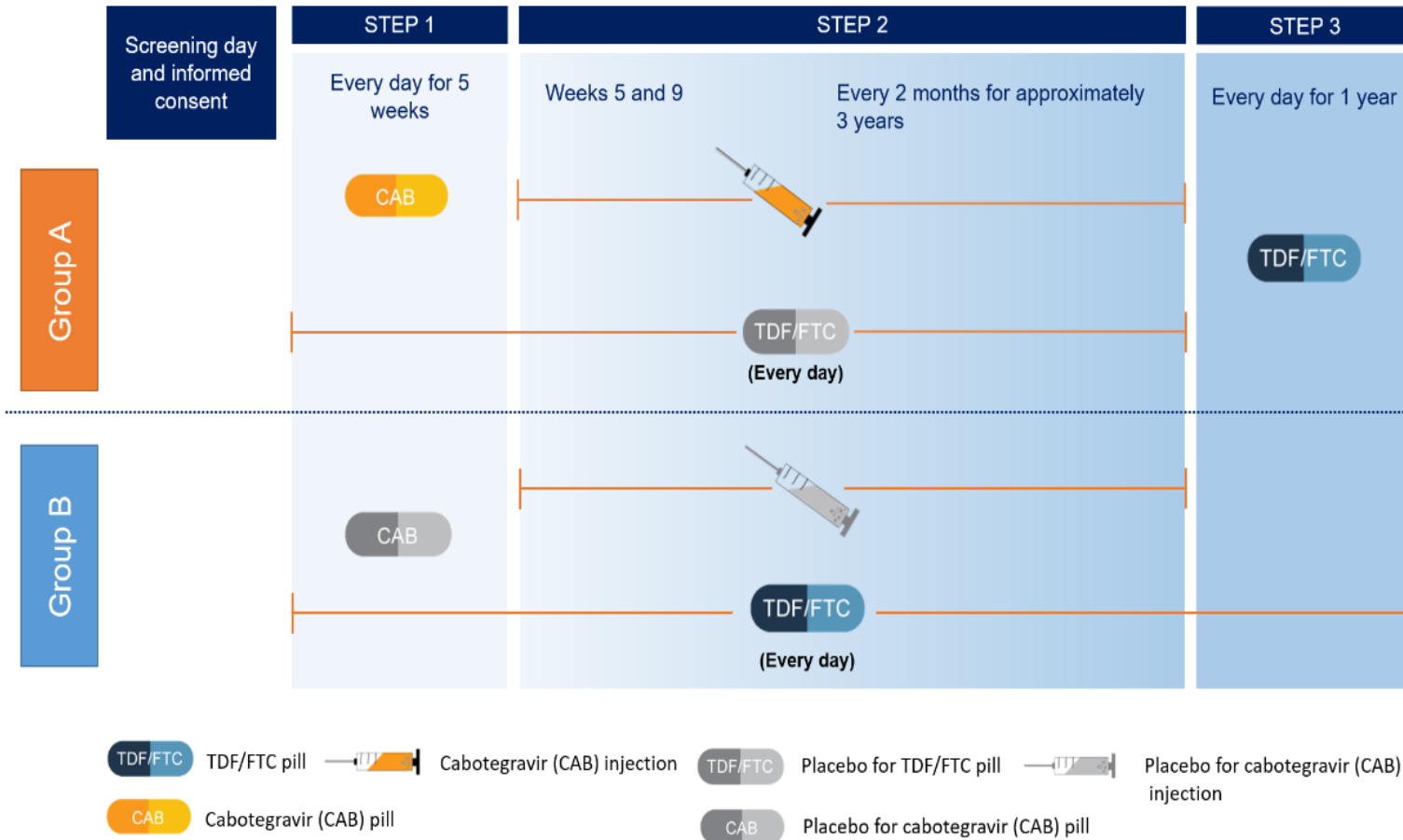
- Concept:
 - Many women at risk of HIV also want family planning
 - Why not combine HIV prevention with contraception?
 - Improve adherence with single product
- MPT IVRs – phase I / early phase II
 - Tenofovir / levonorgestrol ring (CONRAD)
 - Dapivirine / levonorgestrol ring (IPM, MTN044/IPM-053/CCN019)
 - Pod-IVRs ARVs / contraceptive / α -STI (Oak Crest Institute of Science)
- Development trade-offs:
 - Combination requires compromise, e.g., duration



Cabotegravir-LA Nanosuspension PrEP

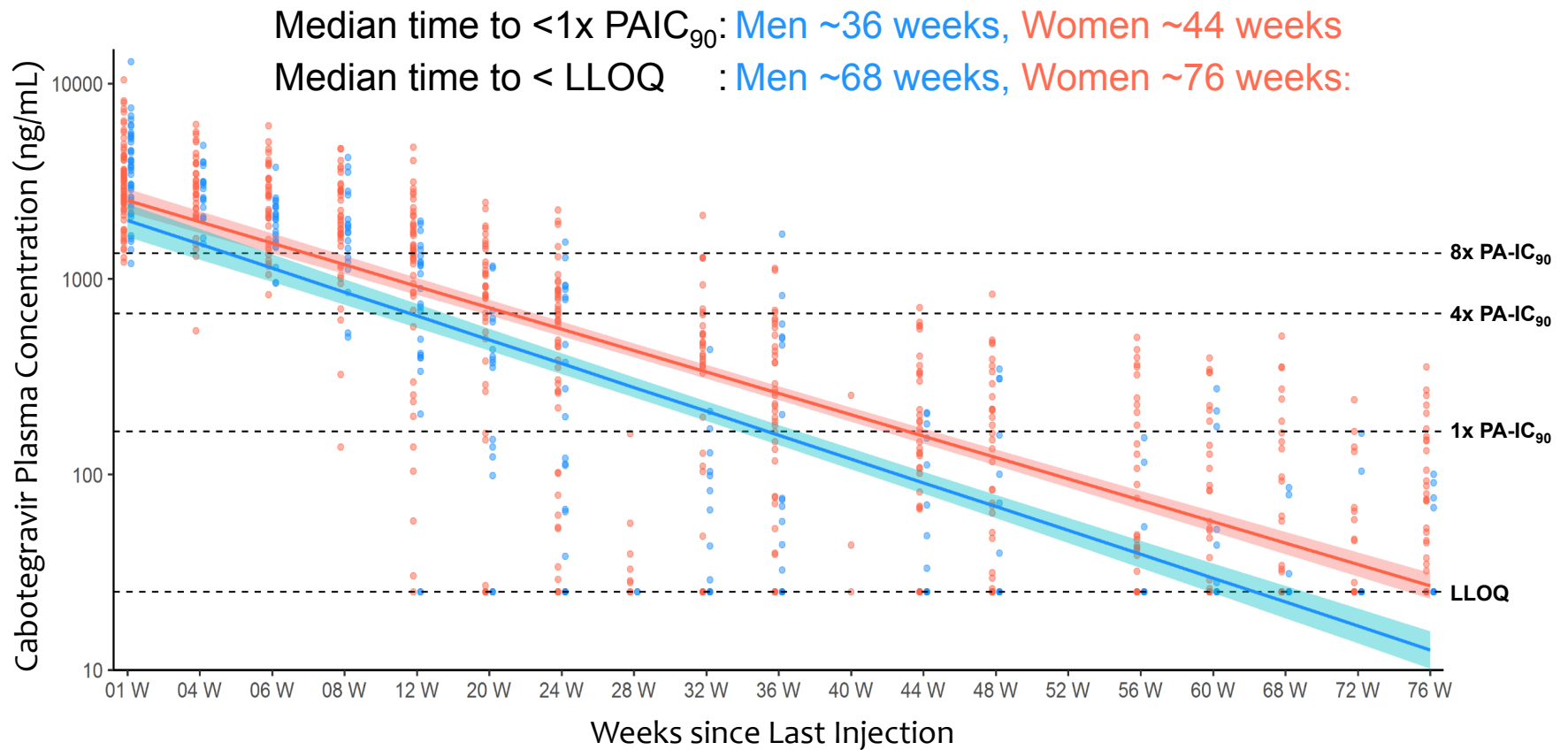
- Goal: Provide *alternative to oral daily PrEP*
- HIV InSTI
 - Similar to Dolutegravir (proven effective HIV treatment)
 - Proven effective for treatment
- Bi-monthly intramuscular injection
- Non-removable, non-dialyzable following injection
 - *Oral cabotegravir one month* lead-in to rule out toxicity
- Long period of inadequate drug concentrations (“PK Tail”)
 - Below protection for months to more than a year (more in women)
 - *Oral PrEP for one year* to protect from resistance if HIV infection

HPTN 083 Study Design



Landovitz RJ et al. AIDS 2020, #OAXLB0101

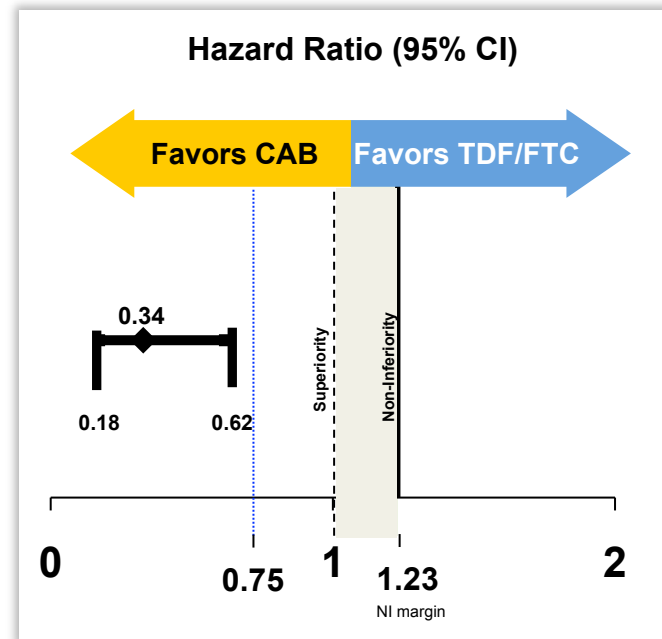
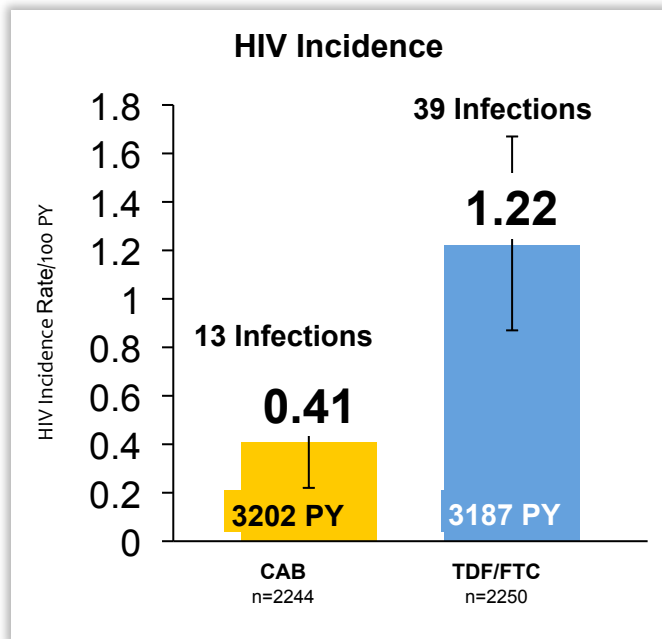
Long PK Tail CAB-LA (HPTN 077)



► Landovitz, et al. Lancet HIV 2020 Jul;7(7):e472-e481.

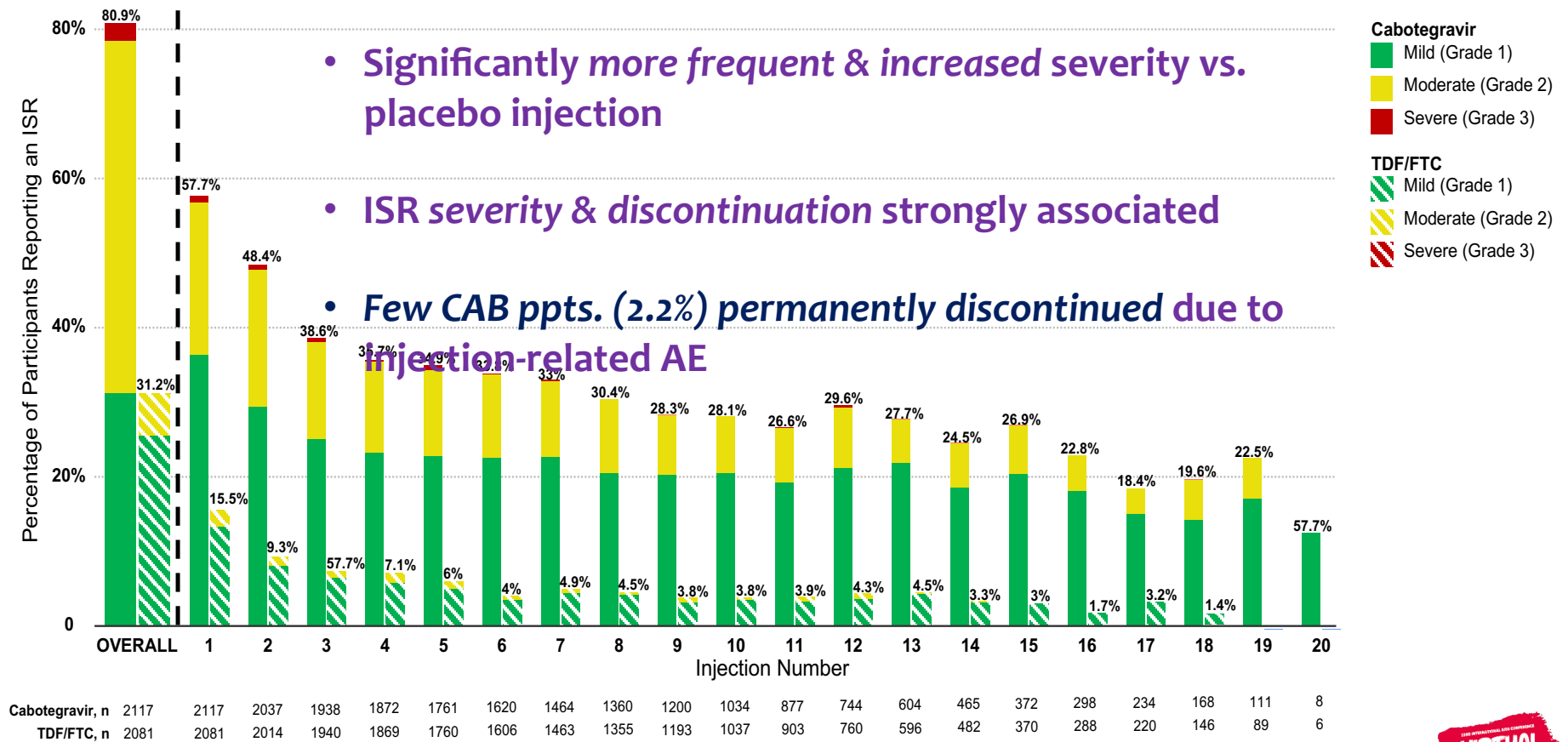
HIV Incidence

52 HIV infections in 6389 PY of follow-up
1.4 (IQR 0.8-1.9) years median per-participant follow-up
Pooled incidence 0.81 (95%CI 0.61-1.07) per 100 PY



CI, confidence interval

Injection Site Reactions



Landovitz RJ et al. AIDS 2020, #OAXLB0101



Grade 2+ Adverse Events ($\geq 5\%$)

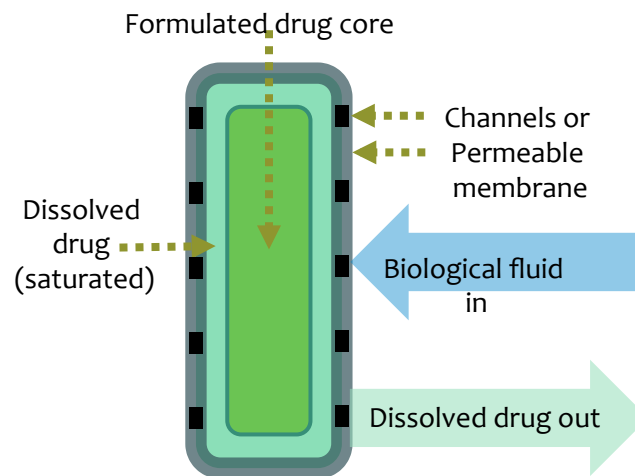


	TOTAL (n=4566)	TDF-FTC (n=2284)	CAB (n=2282)	p-value
Participants with grade 2+ AEs, n (%)	4202 (92.1%)	2106 (92.3%)	2096 (91.9%)	
Creatinine clearance decreased	3204 (70.2%)	1642 (72.0%)	1562 (68.5%)	0.01
CPK increased	937 (20.5%)	460 (20.2%)	477 (20.9%)	0.52
Nasopharyngitis	828 (18.1%)	388 (17.0%)	440 (19.3%)	0.04
Creatinine increased	775 (17.0%)	412 (18.1%)	363 (15.9%)	0.06
Upper Respiratory Infection	510 (11.2%)	255 (11.2%)	255 (11.2%)	0.99
Musculoskeletal discomfort	507 (11.1%)	253 (11.1%)	254 (11.1%)	0.95
Lipase increased	495 (10.9%)	252 (11.0%)	243 (10.7%)	0.68
Headache	448 (9.8%)	216 (9.5%)	232 (10.2%)	0.42
AST/SGOT increased	382 (8.4%)	197 (8.6%)	185 (8.1%)	0.53
ALT/SGPT increased	347 (7.6%)	191 (8.4%)	156 (6.8%)	0.05
Blood glucose increased	323 (7.1%)	117 (5.1%)	206 (9.0%)	<0.001
Amylase increased	316 (6.9%)	166 (7.3%)	150 (6.6%)	0.36
Diarrhea	306 (6.7%)	158 (6.9%)	148 (6.5%)	0.56
Rash	253 (5.5%)	139 (6.1%)	114 (5.0%)	0.11
Hypoglycemia	241 (5.3%)	123 (5.4%)	118 (5.2%)	0.75
Pyrexia*	181 (4.0%)	60 (2.6%)	121 (5.4%)	<0.001

*70% of pyrexia events in CAB were within 7 days of an injection (event probability 0.65%)
 16% of pyrexia events in TDF/FTC were within 7 days of an injection (event probability 0.05%)

Implantable ARV-Eluting Devices

- Sustained release of PrEP drugs with constant release over time
- User-independent, subcutaneous implant
- ±Biodegradable
- Compatible with existing contraceptive implant trocar applicators

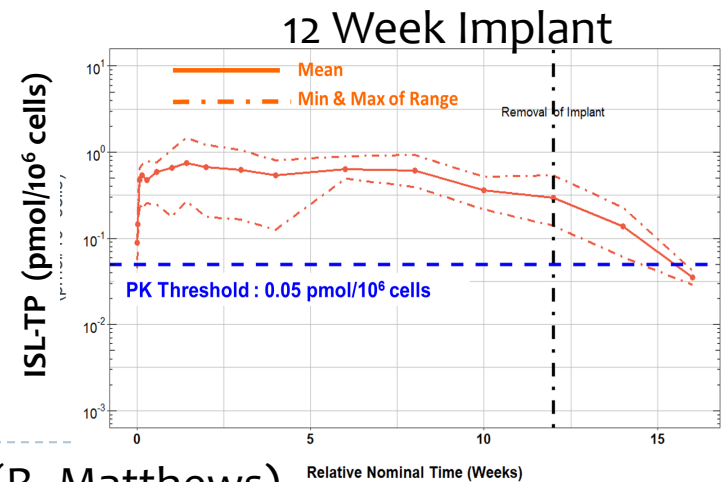
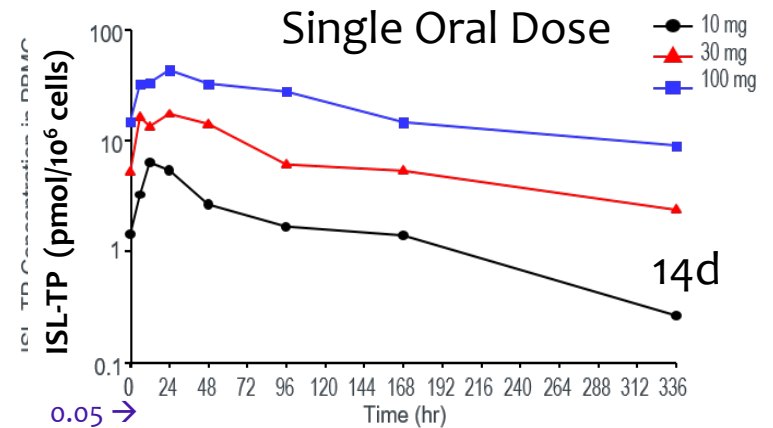


Compatibility with Existing Trocars



Islatravir Oral & Implantable Formulations

- ▶ Multiple mechanisms of action
- ▶ Good safety profile oral & implantable
- ▶ Pharmacokinetics
 - ▶ PBMC ISL-TP $t_{1/2}$ 120-177 hr
 - ▶ ISL-TP rectal & vaginal tissue similar to PBMC
- ▶ Pharmacodynamics
 - ▶ Monotherapy antiviral effect NHP & clinical
 - ▶ Target 0.05 pmol/10⁶ cells (NHP & clinical Rx)
 - ▶ In vitro WT IC₅₀ ~0.01 pmol/10⁶ cells
 - ▶ 0.05 pmol/10⁶ cells > in vitro IC₅₀ M184I/V
- ▶ *Likely monthly oral (& yearly implantable)*



▶ Matthews R, et al. IAS 2019; data courtesy Merck (R. Matthews)

Objectives

- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ Discuss ongoing development of long-acting PrEP
- ▶ Discuss ongoing development of on demand PrEP

On Demand Oral

▶ Ipergay – *Effective*

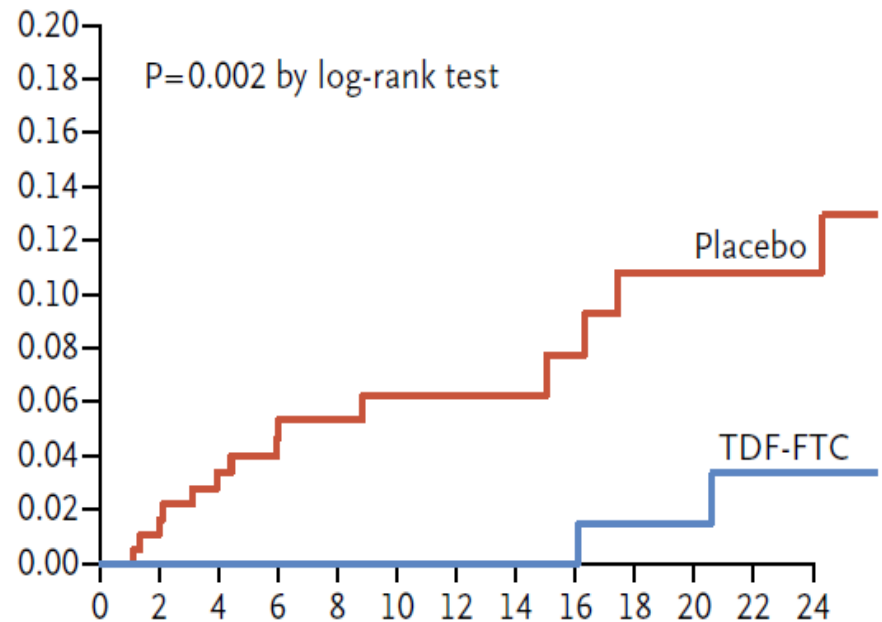
▶ RCT On demand 2+1+1

- ▶ 2 TDF-FTC 2 - 24 hours before sex
- ▶ 3rd 24 hours after the first dose
- ▶ 4th 24 hours after the 3rd

▶ 40% < weekly dosing

▶ Prevenir – *Popular*

- ▶ Open label
- ▶ Ppts select on demand (54%) or daily (45%)
- ▶ Acquisition Risk 0 (95%CI 0.0, 0.7) & 0 (0.0, 0.8), no infections in 506 & 443 PY, respectively

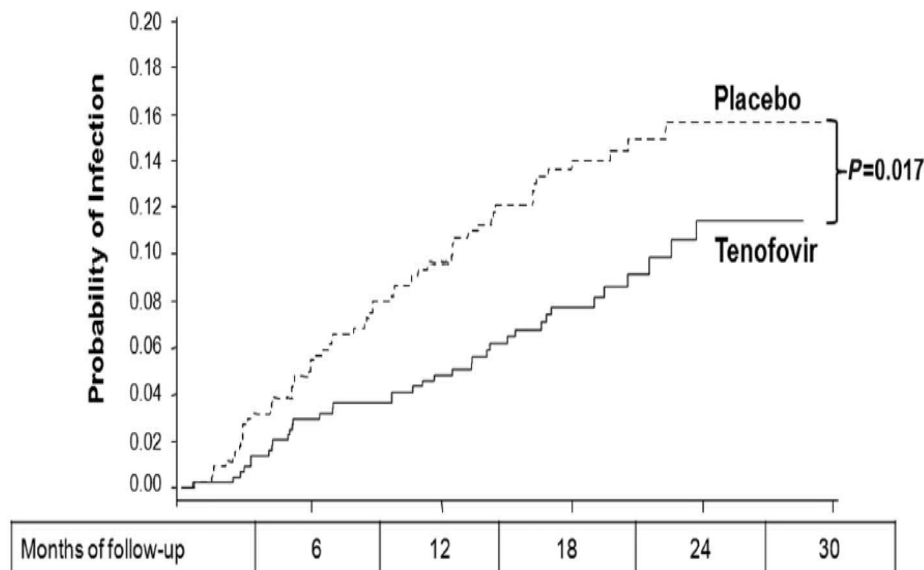


▶ Molina NEJM 2015; Molina IAS 2018

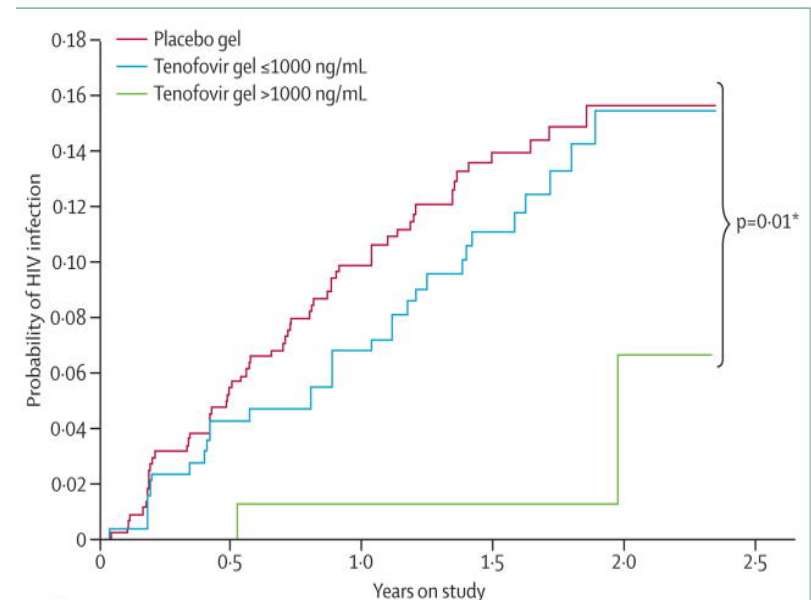
On Demand Topical

- ▶ CAPRISA 004 TFV Vaginal Gel – Highly effective when used

mITT Analysis



PK-Adjusted Log Reg – 73% RRR



- ▶ Karim *Lancet* 2010; Karim *Lancet* 2011

On Demand & Behaviorally-Congruent PrEP

- ▶ *Behaviorally-congruent* medicated product already in common use
- ▶ Common health fortification of existing products
 - ▶ Fluoridated water & toothpaste; vitamin fortified bread & milk
- ▶ PrEP-medicated Sexual Lubricants
 - ▶ Very high levels (>85%) of sexual lubricant use among MSM
 - ▶ Modest levels among women, but higher among FSW (>60%)
- ▶ PrEP-medicated Douches
 - ▶ High levels of anal douching among MSM (>80%)
 - ▶ Not well studied among women, but modest to high among FSW (22-56%)
- ▶ On Demand Advantages
 - ▶ Do not require learning an entirely new PrEP taking behavior
 - ▶ Very high local tissue & very low systemic levels of ARVs

Anal Lube or Douche as Microbicide

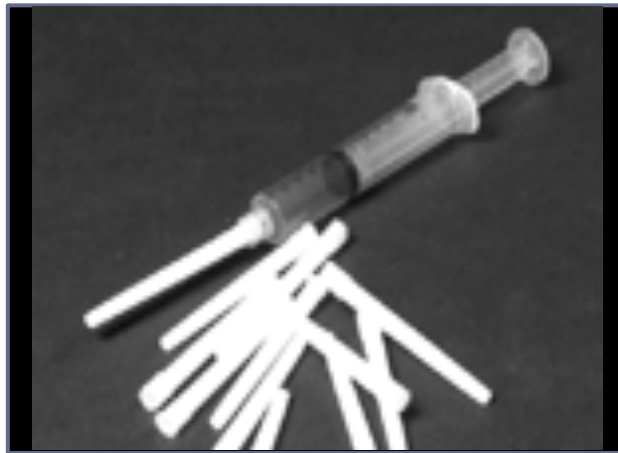
Douche

Saline-like 125 mL



Gel - Applicator

HEC 10 mL



Lube

Wet™ 10 mL

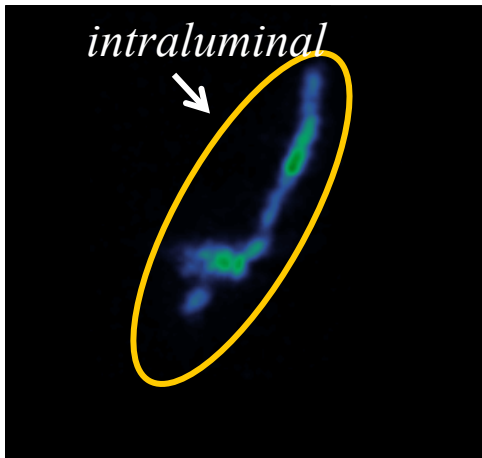


- How much product is delivered?
- Where is the gel distributed?

Anal Lube or Douche as Microbicide

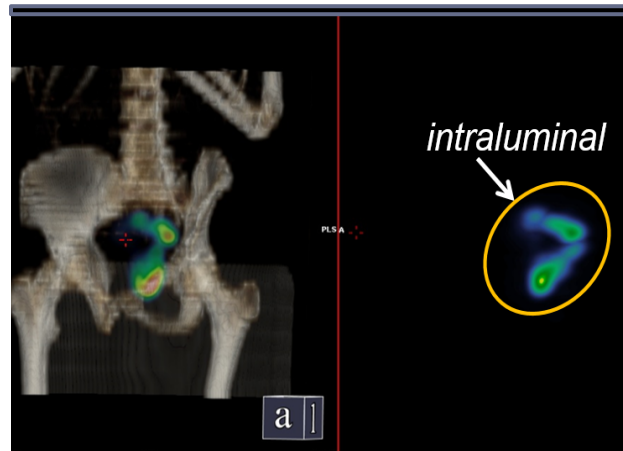
Douche

Saline-like 125 mL



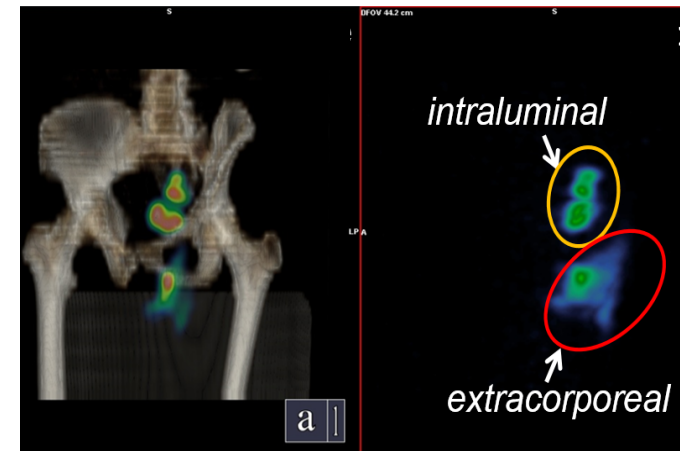
Gel - Applicator

HEC 10 mL



Lube

Wet™ 10 mL



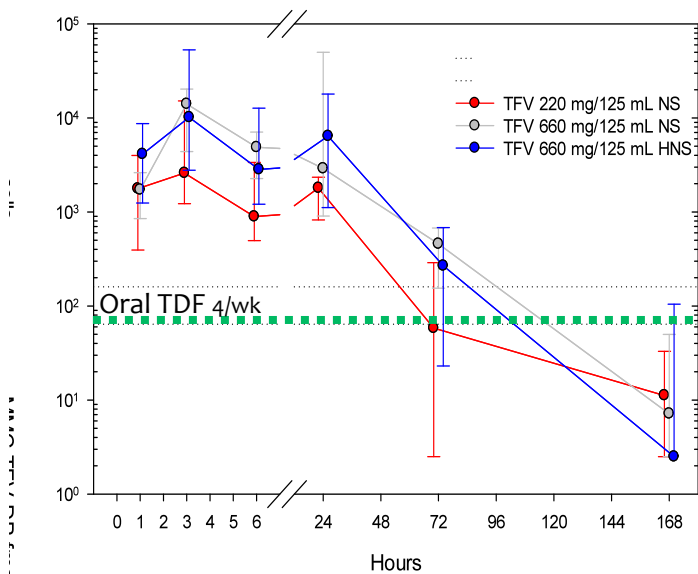
- Retention: 60%
- Distribution: 60 cm

95%
5.9–7.4 cm

10% (3.5 mL gel)
4.4–15.3 cm
(requires 10x [API] increase)

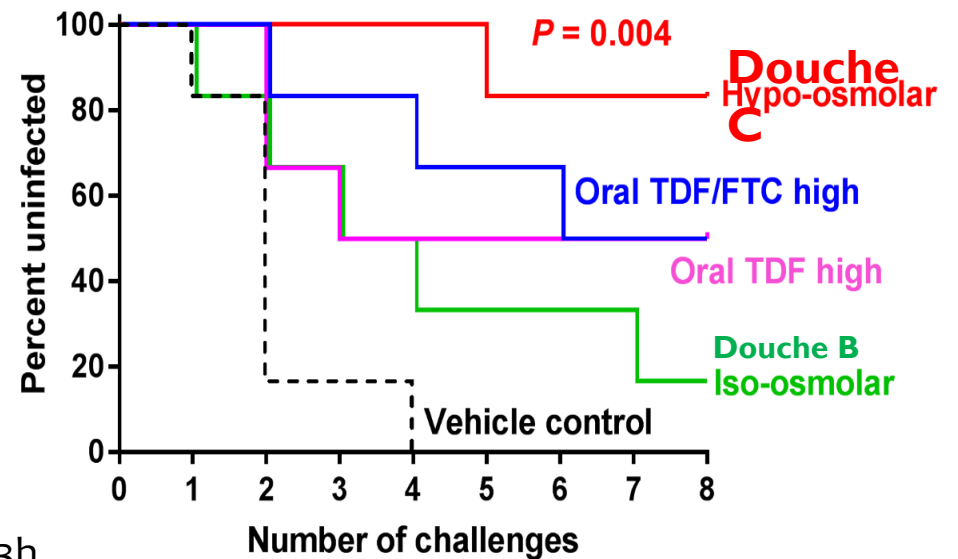
Rectal Douche as Microbicide

Human: Colon Cell TFV-DP



Macaque: Rectal SHIV Challenge

Daily Oral F/TDF vs. Single Douche 1 hr before SHIV



- High dose exceeds **Target** >30x @ 1h, >100x @ 3h
- High dose exceeds target x 4 days (~Ipergay 2+1+1)
- Plasma C_{max} 5x < daily oral C_{tau}
- High dose douche superior to daily oral F/TDF

Objectives

- ▶ Describe the limitations to PrEP impact
- ▶ Describe the benefits of choice to PrEP products
- ▶ Discuss ongoing development of long-acting PrEP
- ▶ Discuss ongoing development of on demand PrEP

Questions?



Thank You for Your
Attendance!

Please visit us at:
www.prn.org