



June 29, 2023

# PrEP That Booty

**The latest on rectal microbicide research for the back door**

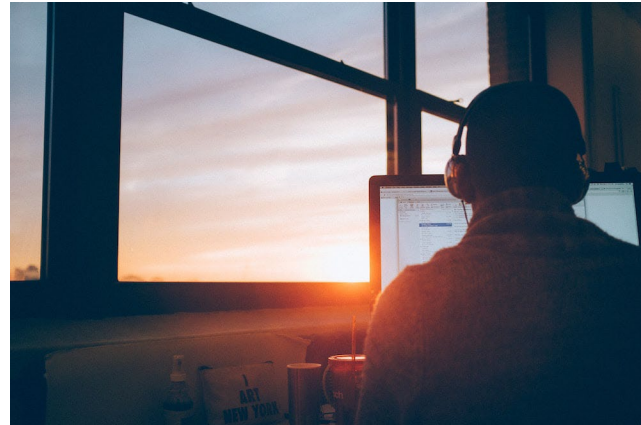
**Thank you for joining this webinar from The Choice Agenda**



HIV prevention research - a new forum  
for advocacy on the latest

[avac.org/choice-agenda](http://avac.org/choice-agenda)

Please  
join us in  
July and  
August



# **THE CHOICE AGENDA**

HIV prevention research - a new forum  
for advocacy on the latest

July 18, 2023

**ClusterF\*#k:  
Molecular HIV Surveillance, Criminalization,  
and The Real Risks to PLHIV**

Register & more info  
<https://tinyurl.com/clustermhs>



August 3, 2023

## Tales from Two Cities: HIV and STI research highlights from Brisbane and Chicago

Register & more info  
[tinyurl.com/talesfromtwocities](https://tinyurl.com/talesfromtwocities)



# What is a rectal microbicide?

## Answer

Microbicides are products that can be applied to the vaginal or rectal mucosa to prevent, or significantly reduce, the risk of acquiring HIV and/or other STIs.

They could provide protection that is short-acting, non-systemic, and user-controlled.

Rectal microbicides remain in the research and development phase – there are currently no rectal microbicides available for use as of 2023.

# Answer

An act of receptive anal intercourse that is not protected (condoms, oral or injectable PrEP, U=U) is the most efficient way of sexually transmitting HIV.

An act of unprotected receptive anal intercourse is significantly more likely to result in HIV infection compared to unprotected insertive anal intercourse and unprotected penile-vaginal intercourse (receptive and insertive.)

## Who needs a rectal microbicide? Part 1

# Answer

Anal intercourse is a common human behavior practiced by people of all gender and sexual identities across the entire world.

Not all people have access to currently available HIV prevention options. And not all people desire these options. It is therefore critically important to provide a wide array of choices – a prevention basket – for all kinds of people to select from throughout the course of their sexual lives.

Oral and long-acting injectable PrEP may not be accessible, available and/or desired among various people.

**Who needs a  
rectal microbicide?  
Part 2**



# Behavioral congruence

Behavioral congruence refers to a product whose characteristics, mode of use, and adaptability to users' needs is as close as possible to the real-world experiences and ongoing practices of potential users.

Because rectal douching is a common behavior among many people who have anal intercourse, efforts are underway to develop a safe, effective, *behaviorally congruent* rectal microbicide douche that could provide the desired hygiene plus robust HIV protection.



# The Pleasure Principle:

AN EVOLUTION IN RECTAL MICROBICIDE RESEARCH



*Love me, hey yeah, love me yeah.  
It's the pleasure principle.*  
-From the Janet Jackson song,  
[The Pleasure Principle](#)

Pop star Janet Jackson cooed about it in the 1980s. Sigmund Freud wrote about it much earlier as a driving force within our personalities. Pleasure, undeniably, has long played an essential role in our lives.

Yet, in the field of HIV prevention, there has been a reluctance to talk openly about pleasure and sex. For most of the past 40 years, our efforts focused on the prevention of HIV (a virus that is predominantly transmitted sexually) have largely dismissed the role of pleasure, or the act of sex itself. Especially in the context of anal sex.

Little to no consideration has been given to what people who engage in anal sex want or even desire in an HIV prevention product. It's been generally assumed that if a product is safe and protects against HIV, then surely people will use it.

## Read the story of rectal microbicide research.



**The Choice Agenda presents...**

# PrEP That Booty



The latest on rectal microbicide research for the back door

June 29, 2023

Co-moderator:

Juan Michael Porter II, The Body

Jonathan Baker, IG @rectalrockstar

Dr. Sharon Riddler, U. of Pittsburgh

Performance: Eddie "Kelly" Wiley

Dr. Craig Hendrix, Johns Hopkins



# PrEP That Booty! Anal Sex & Pleasure

Jonathan Baker, PA-C, MPAS, DFAAPA (*He/Him*)

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# Financial Disclosures

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**Jonathan Baker** has no relevant relationships with ineligible companies to disclose within the past 24 months

Jonathan's employer receives salary support, but Jonathan receives no direct remuneration from Frantz Therapeutics, Antiva Biosciences, Inovio Pharmaceuticals, and Merck & Co.

“ Sexual Health is  
a state of physical, emotional,  
mental, and social well-being  
in relation to sexuality;  
it is **not** merely the absence of  
disease, dysfunction or infirmity. ”

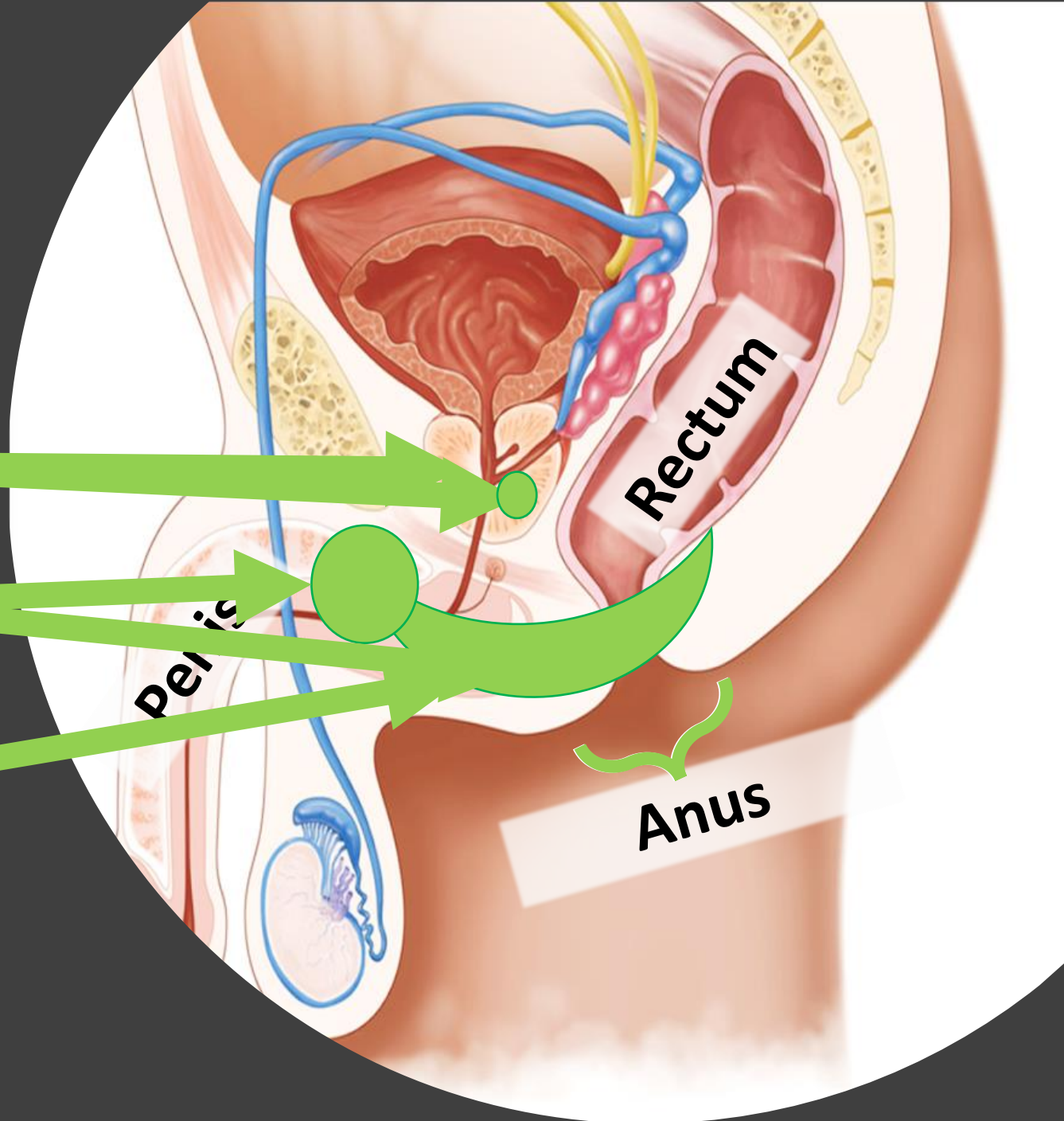
-World Health Organization

# Anal Sex & Pleasure

**Skene's Gland**

**Penile Bulb**

**Clitoral Crux  
"Legs"**





# Butt, Let's Not Forget About

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Intimacy & Connection

Pleasing Partner(s)

Visual Stimulation

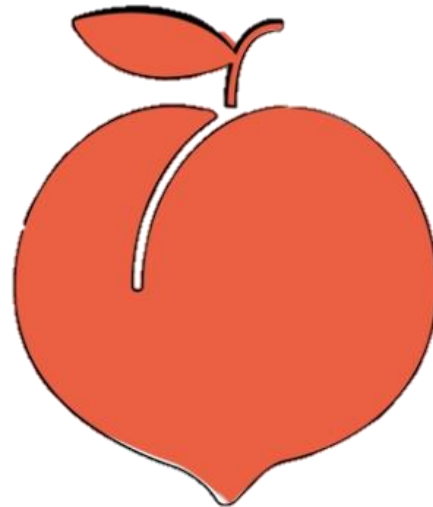
Excitement, Risk, & Taboo



# Queer Health Podcast

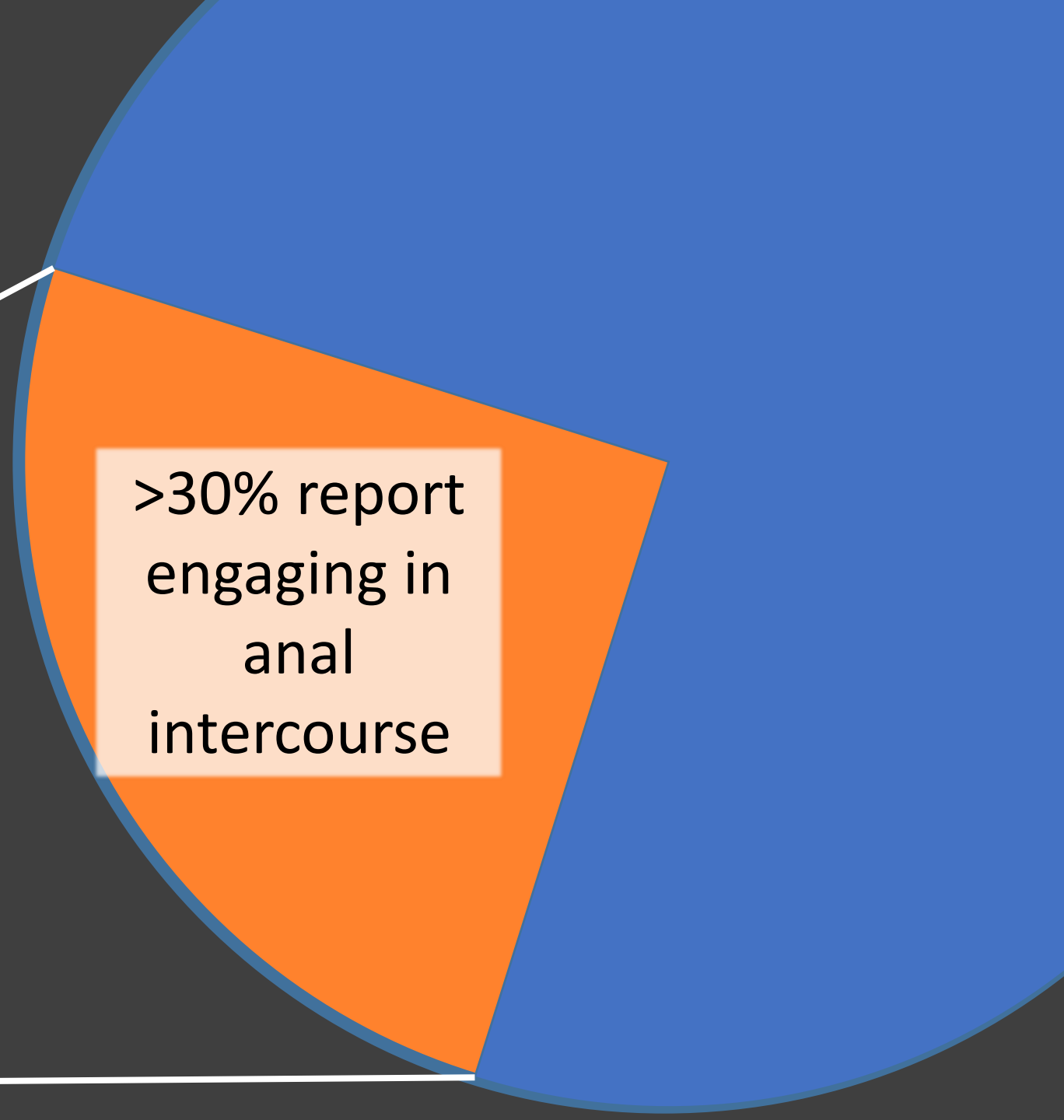
December 1, 2020 · 2 Comments

## #1: Douching



Episode #1: Douching (A Sudden Urge To Learn The Facts About It)  
Queer Health Pod

# Anal Sex: United States

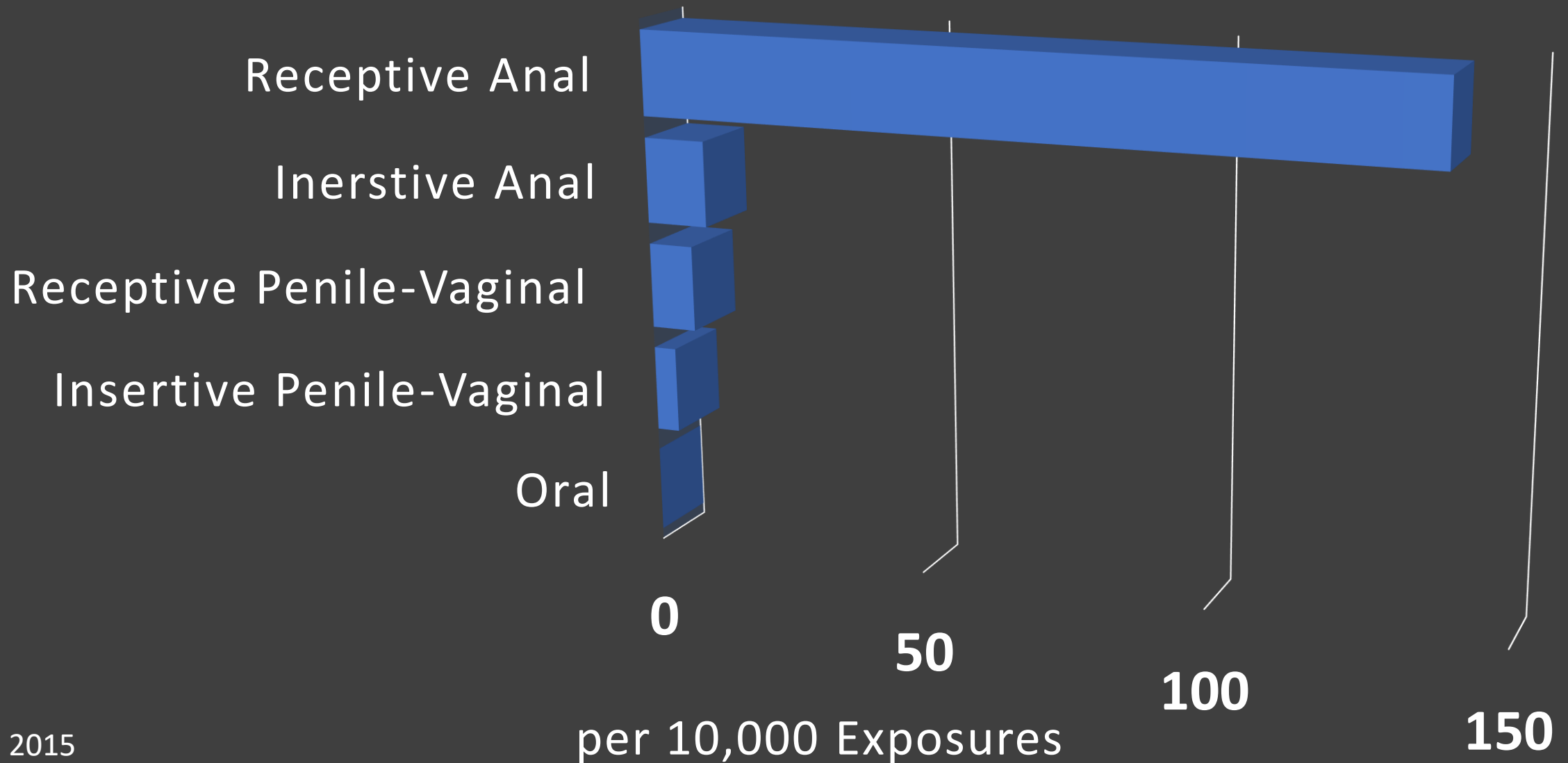


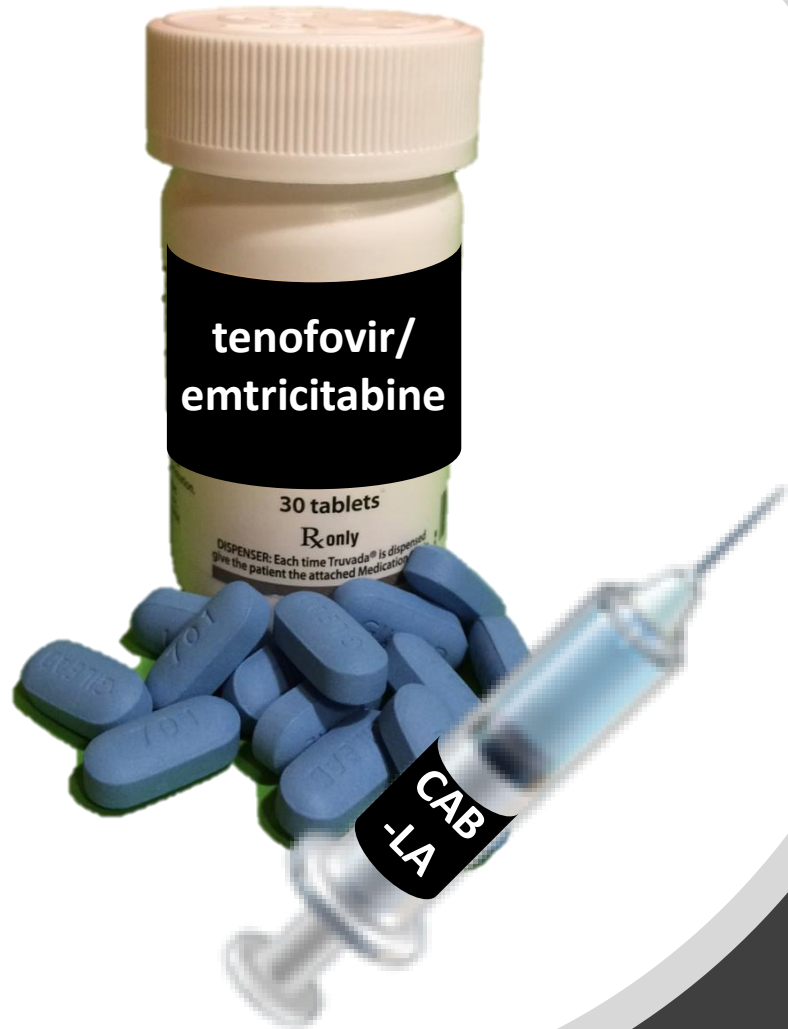
>30% report  
engaging in  
anal  
intercourse

# Anal Sex: Worldwide (\*Reported)



# Estimated Risk of Acquiring HIV from a Person Living with HIV During a Sexual Act





# HIV Preexposure Prophylaxis (PrEP)

**Tenofovir/emtricitabine PO QD** or  
**Cabotegravir-LA IM Q2 months**

- >99% effective at reducing risk of HIV
- Limited side effects: “safer than aspirin”

## Recommendation Summary

Population	Recommendation	Grade (/uspstf/grade-definitions)
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition.	<b>A</b>

“ *All sexually active  
adult & adolescent patients should receive  
information about PrEP.* ”

-US Centers for Disease Control (CDC)

# CDC Recommendations for PrEP

Anal or vaginal sex in past 6 months AND any of the following:

- Sexual partner LWH
- Bacterial STI\*\* in past 6 months
- History of inconsistent/no condom use

>600,000 heterosexual individuals &  
~500,000 MSM in the US meet this criteria

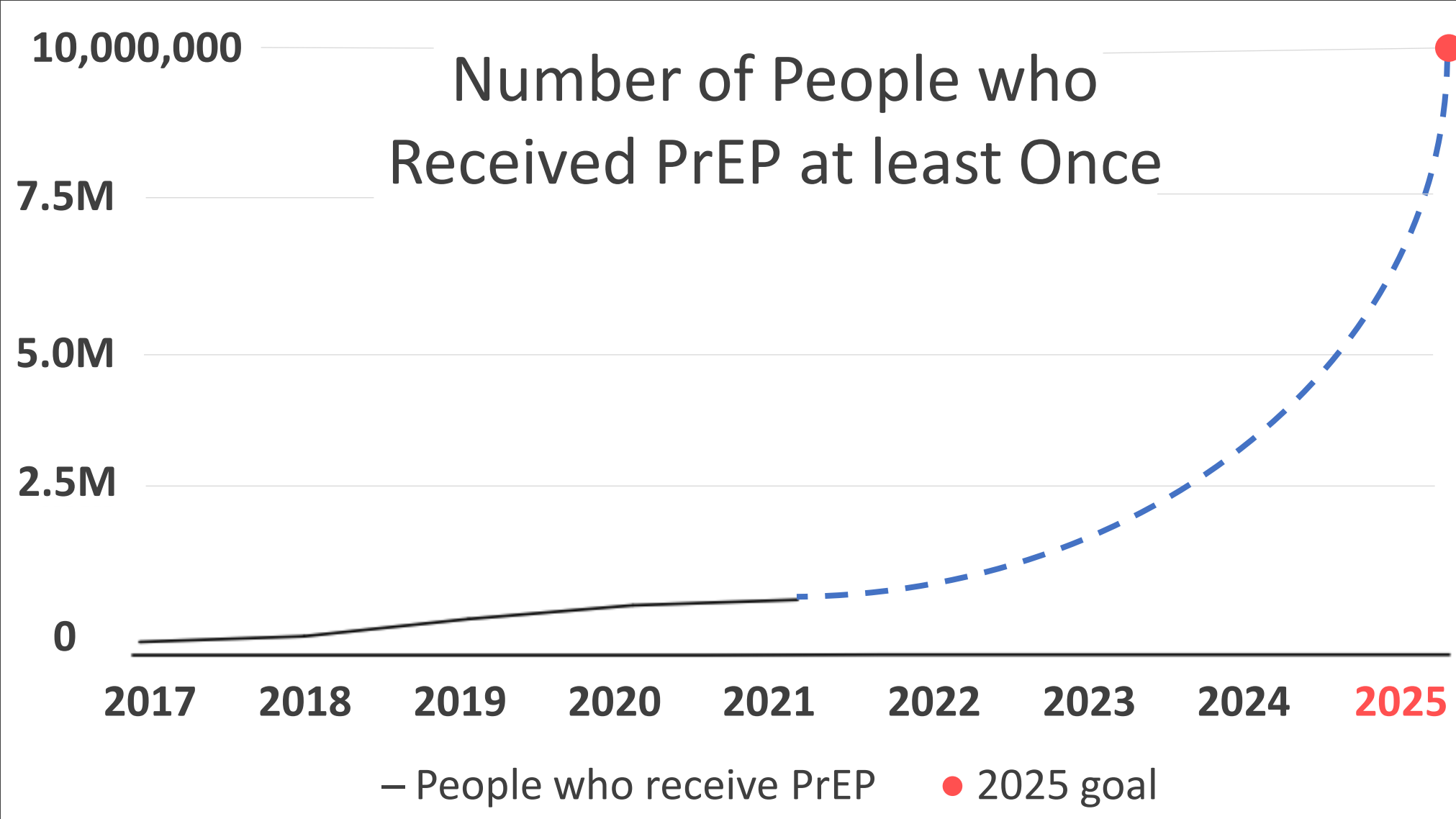
115,000 PWID with an injecting partner LWH  
or who share injection equipment

\*Adolescents weighing at least 35 kilograms/77 pounds

\*\*Syphilis or gonorrhea; or chlamydia among MSM, transgender women who have sex with men



Number of People Receiving PrEP at least once



Adapted from: IN DANGER: UNAIDS Global AIDS Update 2022.  
Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.

Number of People Receiving PrEP at least once



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Geneva: Joint United Nations Programme on HIV/ AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.

# Just Some Barriers to PrEP

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Lack of public awareness/knowledge

- 🍊 Healthcare provider lack of awareness/knowledge/comfort
- 🍊 Barriers to healthcare access including cost
- 🍊 Institutional, healthcare, personal, and other stigma
- 🍊 Criminalization of sex work, homosexuality, sodomy, HIV, etc
- 🍊 Individuals user's personal barriers to PrEP formulations



**@RectalRockstar**

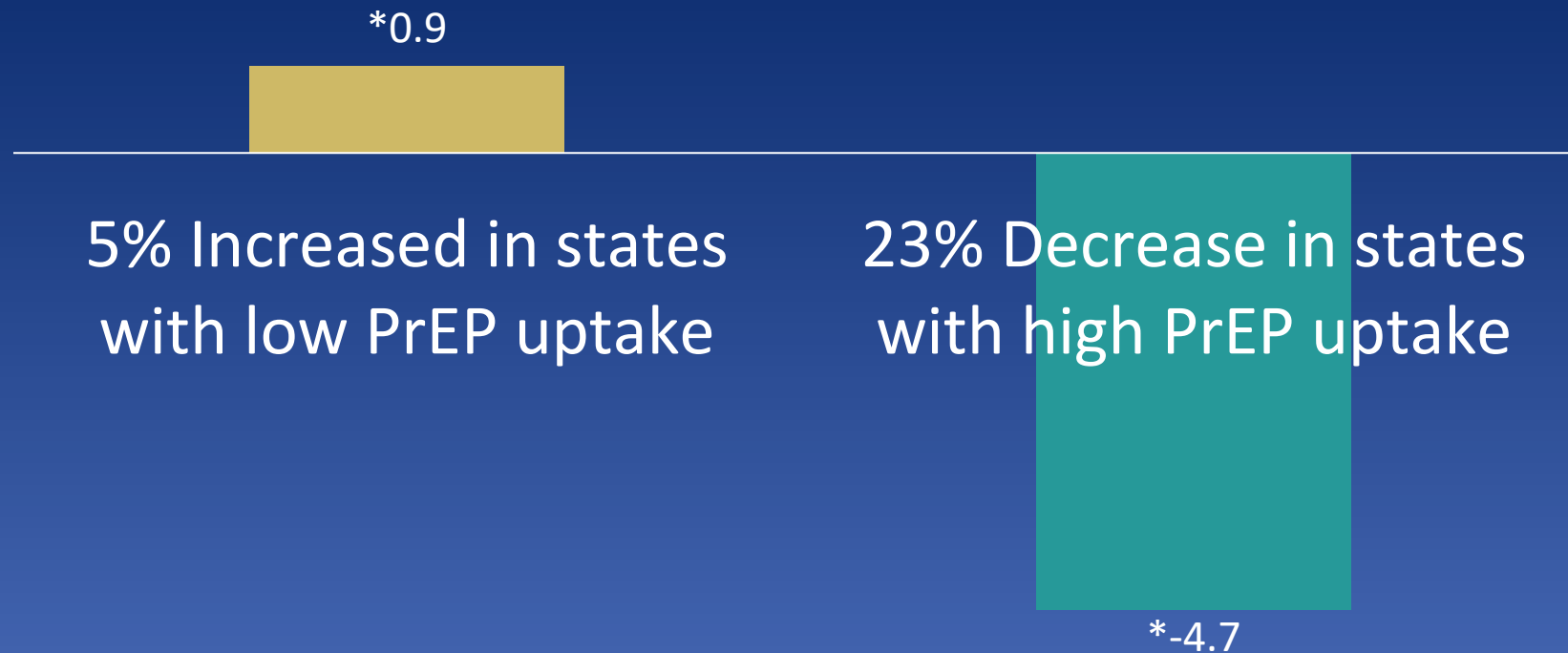
**JonathanBaker.PA@gmail.com**





- This slides are in case a question comes up better answered with a slide

# Reduction in HIV Diagnosis



\*EAPC of states in the top quintile and lowest quintile of PrEP uptake  
2012-2016

## F/TDF



Approved 2012  
Brand or **generic**



May ↓GFR (↑Cr)  
Recovers in 4wks

~1%

May ↓BMD (No DEXA)  
Recovers in 6mos

2

Reported cases  
of Fanconi syndrome

2-5%

Weight loss in some  
patients

## F/TAF



Approved 2016 (HIV)  
Approved 2019 (PrEP)



No effect on BMD/Cr  
Approved CrCL >30



Possible ↑ in lipids,  
triglycerides, & weight  
(check annually)



**Not approved for  
vaginal exposure**

## <Daily



**Not FDA approved**  
Limited evidence

**2-1-1**

2 doses before &  
after each encounter

**S&T**

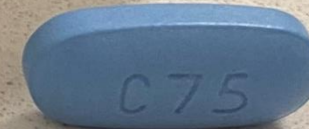
Sat, Sun, Tues, Thurs



Less drug =  
less cost, less S/E







Still monitor every 3  
months (esp HIV)





# PrEP: Injectable Cabotegravir

<b>CAB- LA</b>	
	Approved 12/2021 Brand only
<b>2 mo</b>	IM injection in office Q2 months
	Injection site reaction common (<3% d/c)
	Initiate w/ 1 mo oral or 2 doses, 1 month apart
	Similar efficacy to daily PrEP



# STI Risk in PrEP Users

**275 MSM at risk of HIV exposure in DC:**

**41%** who were using PrEP were:

**3X** more likely to self report an STI in the past year

**=** Just as likely to have a current STI

**1922 MSM in 5 cities\***

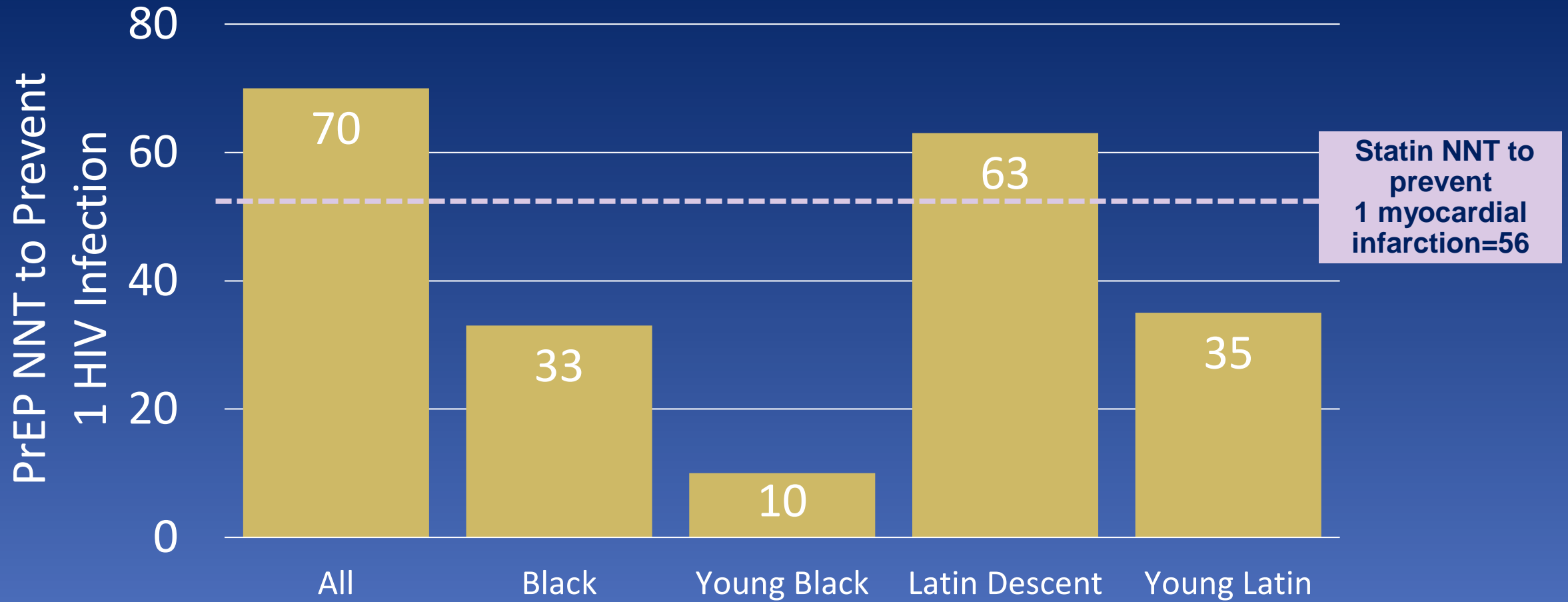
**29%** who were using PrEP were:

**2X** as likely to be tested in the past year

**↑/=** Slightly more likely to have gc/Ct detected at any site (15% vs 12%)

**↑/=** ↑ risk of rectal Ct otherwise similar

# PrEP NNT MSM to Prevent 1 HIV Infection



# Sexual Diversity in the US

- 3.5% of adults in the US identify as LGB
  - 1.8% bisexual; 1.7% gay/lesbian
- 8.2% of US adults report engaging in same-sex sexual behavior
  - 11% report same sex attraction
- The majority (61%) of LGBTQ people are partnered

# Consensual Nonmonogamy (CNM)

- 20% of people report engaging in CNM in their lifetime
- 5% of relationships are CNM
- 1/3 of people describe their ideal relation as “something other than monogamous”
- SGM 2-3x more likely to engage in CNM



# Gender Diversity in the US

- 0.6% of US adults identify as transgender in the US
  - Over 1.6 million adults (ages 18 and older)
  - 38.5% TG women
  - 35.9% TG men
  - 25.6% NB
- Youth (13-17yo) are significantly more likely to identify as transgender (1.4%) than 65+ yo adults (0.3%)

# The Gender Unicorn

Graphic by:  
**TSER**  
Trans Student Educational Resources



To learn more, go to:  
[www.transstudent.org/gender](http://www.transstudent.org/gender)

Design by Landyn Pan and Anna Moore

# Language: Gender Diversity

**ASAB** Assigned Sex At Birth

AMAB Assigned Male At Birth

AFAB Assigned Female At Birth

Transgender ASAB does not match gender identity

Intersex Genetics/anatomy/hormones do align with norms

Nonbinary Do not identify as a binary gender (male/female)

Queer Diversity beyond heteronormative culture

*\*Categories used to identify genders*



# Gender Nonbinary

*"I've always been very free in terms of thinking about sexuality, so I've just tried to change that into my thoughts on gender as well.*

***Non-binary/genderqueer is that you do not identify in a gender. You are a mixture of all different things. You are your own special creation.***

*I've sometimes sat and questioned, do I want a sex change? It's something I still think about: 'Do I want to?' I don't think it is,*

*When I saw the word non-binary, genderqueer, and I read into it, and I heard these people speaking, I was like [...] that is me."*



@SAMSMITH

# “They”

According to Merriam Webster, “**they**,” can be

- Used to refer to a single person whose gender is intentionally not revealed
- Used to refer to a single person whose gender identity is nonbinary

Practice by

- Referring to pets as “they”
- Gender neutral charting



# Language: Sexual Diversity

Heterosexual Sexual attraction to opposite gender presenting partners

Gay Same gender sexual attraction; **an identity**

Bisexual Sexual attraction to more than 1 gender

Pansexual Sexual attraction regardless of gender of partners

**MSM Men who have Sex with Men**

WSW Women who have Sex with Women

Queer Diversity beyond heteronormative culture

*\*Identities may be temporary, before sexual debut, or after sexual sunset*

# Language: What to **NOT** Say

Homo **Instead** → Gay, Lesbian, Bisexual, or it's unnecessary

Transvestite **This means** → Sexual fetish

MSM, WSW, ASAB **Instead** → Use patients' language

Non-conforming **Instead** → Non-binary, or their language

Preferred pronouns/name/gender **Instead** → Pronouns/name/gender

Transgendered **Instead** → Transgender

Queer **Instead** → Anything above ↑

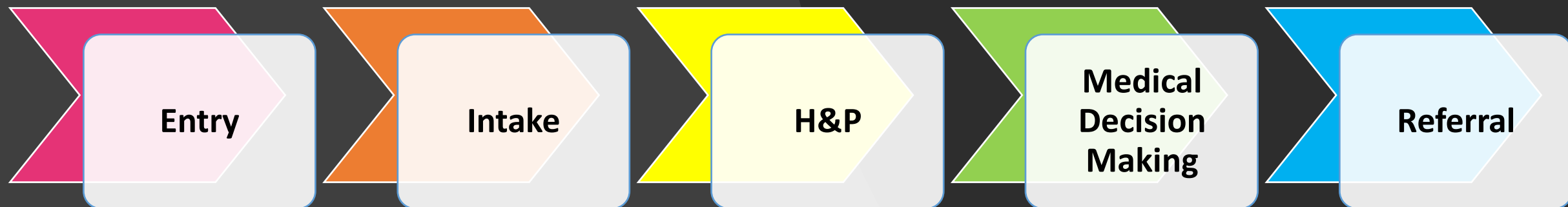
# Sexual and Gender Minority (SGM) Health

## **Come Out to your Healthcare Provider**

- Cancers: Gynecologic, HPV-related, Prostate, Testicular, & Colon
- Vaccinations: Hepatitis & HPV
- Mental Health
- Tobacco
- Substance Use/Alcohol
- Fitness
- Cardiovascular Health
- Intimate Partner Violence
- Sexual Health, STIs, & Protection

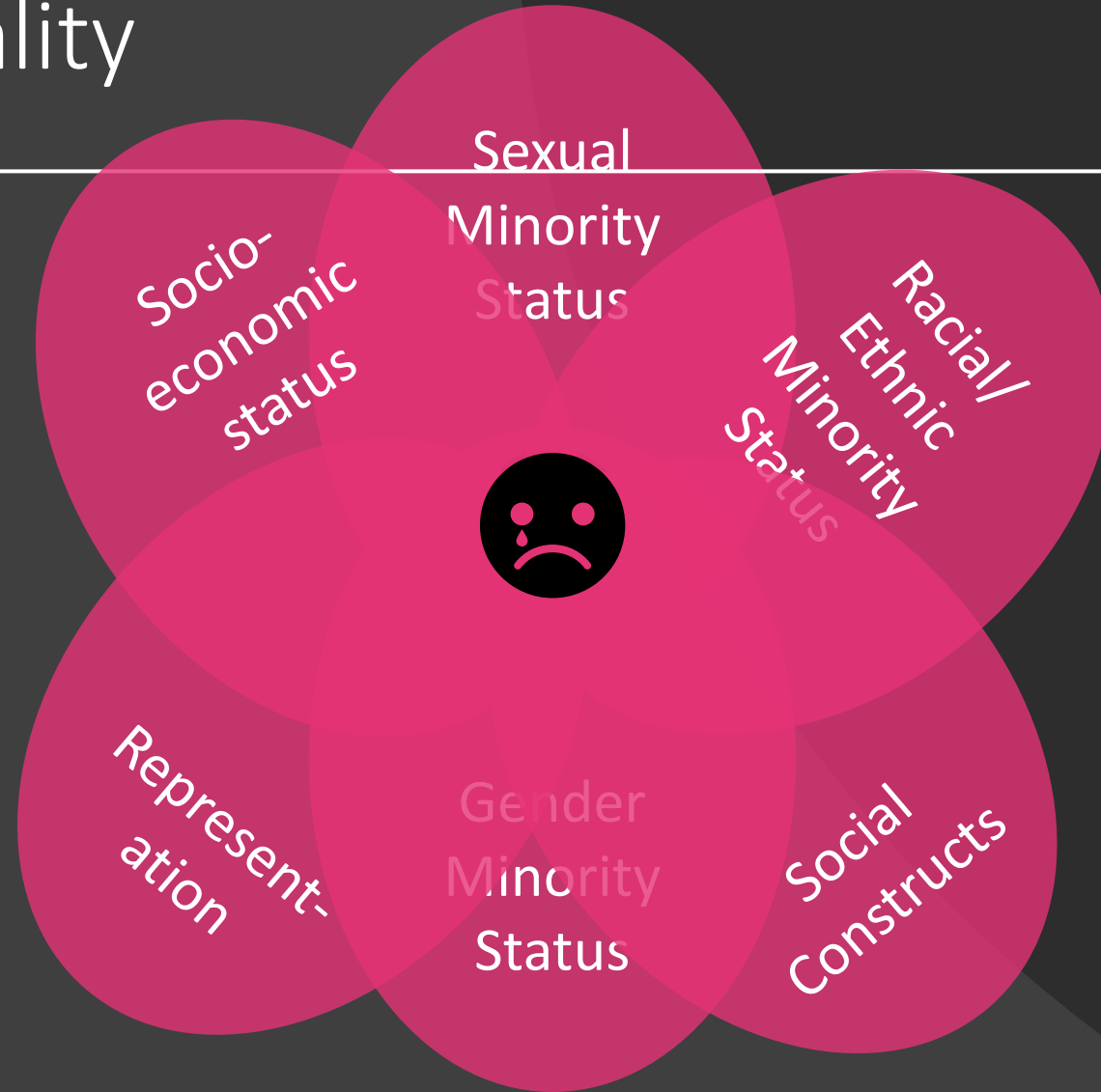
# Opportunities

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# Intersectionality

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# Intersectionality & HIV

4,298 HIV-negative MSM observed over 48 months

- Depression
- Polydrug use
- Stimulant use
- Heavy alcohol use
- Childhood sexual abuse



Overall 6% HIV seroconversion



# DoxyPEP: Bacterial STI Prophylaxis

A trial of 554 MSM and TGW found doxycycline a safe, acceptable, and effective means to reduce risk of bacterial STIs (gonorrhea, chlamydia, and syphilis)

**200 mg taken within 72 hours of exposure**

<b>Risk Reduction Among:</b>	<b>HIV PrEP Users</b>	<b>People LWH</b>
<b>Overall</b>	<b>66%</b>	<b>62%</b>
Chlamydia	88%	74%
Gonorrhea	55%	57%
Syphilis	87%	77%*

*\*All values statistically significant except 77% was trending*

**Doxycycline for STI prophylaxis is OFF-LABEL**

# Anal Dyspareunia

- Not everyone will enjoy RAI
- RAI should not be painful (uncomfortable OK)
- Minor painless bleeding can be normal
  - If it is painful or persistent, it's time for a workup



# Approach to Anal Dyspareunia

Pathological	Fissure, hemorrhoids, dermatitis *R/O STIs (even if monogamous)
Sphincter Tone	Graduated dildo protocol
Positioning	“Bottom on top” Bulbocavernosus reflex
Sexual Habits	Enemas; condom/lube sensitivity
Bowel Habits	Fiber intake, wiping
Psychological	Expectation vs reality (porn) History of trauma & abuse
*Refer	Colorectal, PT, psych

# Preparing for Anal Sex

## FIBER FIBER FIBER!

- Enema's can cause:
  - Associated w infection (LGV, HPV)
  - Discharge & tissue destruction (hyperosmolar)
  - Removal of natural lubricant
- “I don't recommend enema use but...”
  - 1-3 injections of tap water with syringe or Fleet



# Lubricant Safety

- Lubricants tested for dermatologic safety
- Water-based lubricant
  - Hyperosmolar may cause tissue destruction
- Silicone-based lubricant
  - Last longer, maybe too long? (don't over-wipe)
- Oil-based lubricant
  - Not safe with condoms
- Potentially sensitivity to lube components

# Resources

- **PA State Org Diversity Committee**
- **Health Care Equity & CME: LBGT PA Caucus, GLMA**
- **Medical Care of SGM: Fenway Guide, GLMA Guide**
- **Transgender Care Guidelines: WPATH, UCSF, Fenway**
- **Infectious Diseases: CDC, NYC/NYS DOH**
- **Anal HPV & Paps: IANS, UCSF (HRA directory)**
- **HRC: LGBTQ healthcare index & training modules for staff**
- **CDC: Collecting Sexual Orientation and Gender Identity Information**



Clinicians routinely addressing anal intercourse in a culturally sensitive manner also seems to be rare

As a gay man,  
Andrew's  
concerns are  
compounded

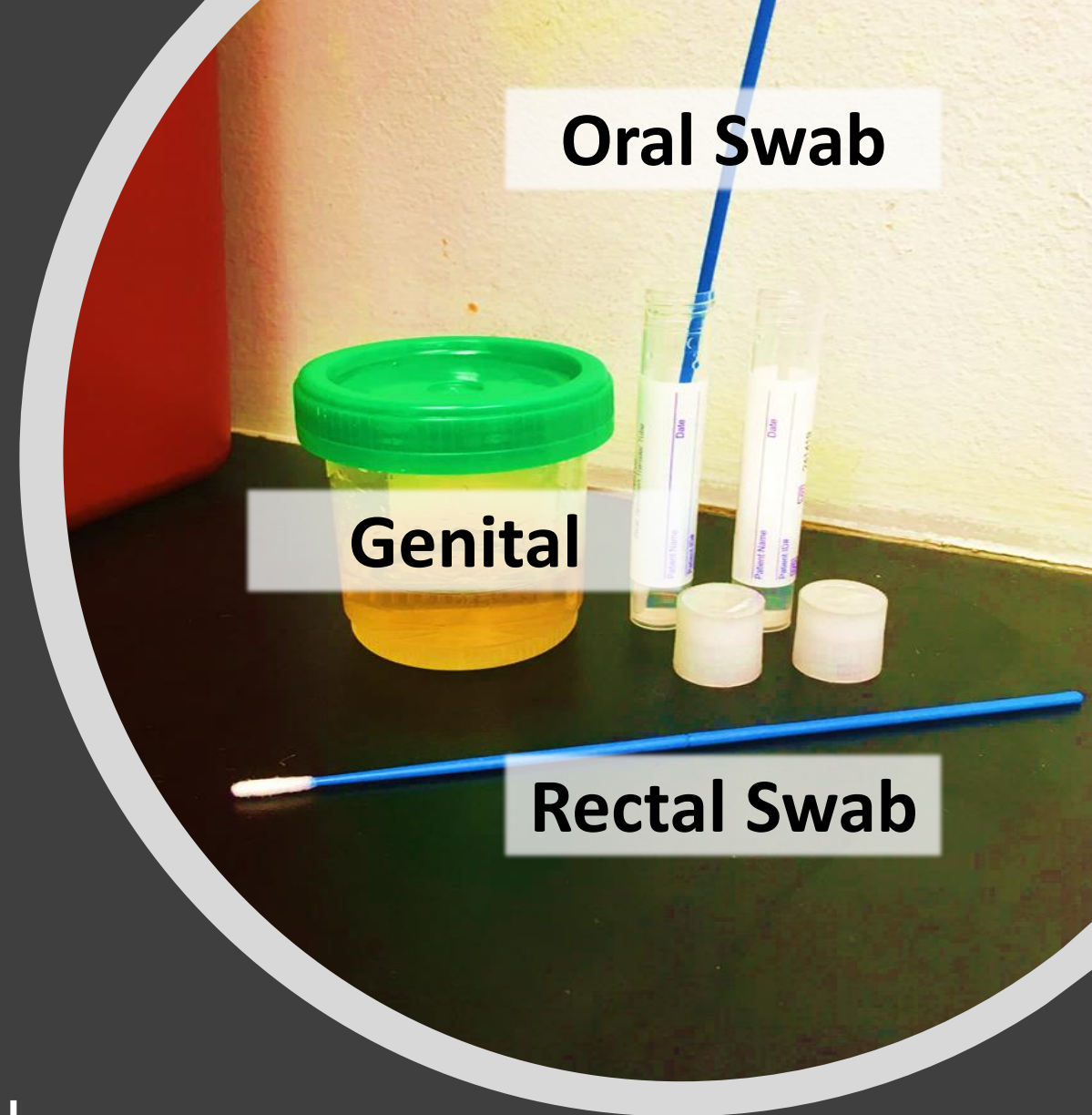
- 56% of LGBTQ report health care discrimination
- ~10% of LGB & ~30% of TG/NB have been refused health care
- After experiencing health care discrimination, patients are 3x more likely to postpone care that year
- LGBTQ people of color are more than 2X as likely to avoid a medical office than white LGBTQ individuals



If I saw Andrew

🗨️ **When you have sex, does it involve your anus?** 🗨️

- Ask about relationship of symptoms to sex
- Screen for STIs at site of exposure
- Consider how symptoms and care will impact his sex life





# **A Phase 1 Open Label Safety and Pharmacokinetic Study of Rectal Administration of a Tenofovir Alafenamide/Elvitegravir Insert at Two Dose Levels**

The Choice Agenda – PrEP Webinar

June 2023

# TAF/EVG Insert



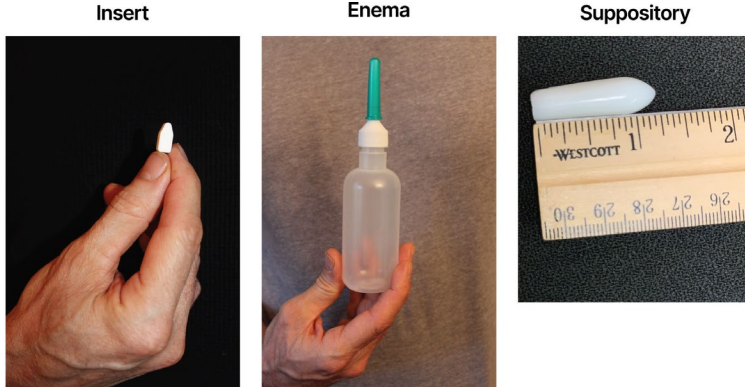
- Small bullet shaped tablet; fast-dissolving
- Each insert contains 2 anti-HIV drugs:
  - tenofovir alafenamide (TAF) 20 mg
  - elvitegravir (EVG) 16 mg
- Both drugs are safe and well tolerated with daily oral dosing

# TAF/EVG Insert



- Developed by CONRAD
- In animal studies, the insert was tested in the vagina and in the rectum, and prevented infections with SHIV
- In an animal study of rectal insert, 2 inserts worked better than 1 insert for preventing infection
- A safety and drug level study with 1 insert for vaginal use has been completed

# MTN-035 Acceptability Study



- Participants were TGM, TGW and cis-MSM ages 18-35
- 217 participants enrolled in 5 countries
- Cross-over design – each participant used all 3 products for 4 weeks
- “High acceptability” reported by 72% for inserts, 66% for suppositories, 73% for enema

# MTN-039 Primary Objectives

- To evaluate the safety of the TAF/EVG Insert, 20/16 mg administered rectally at two dose levels: 1 insert and 2 inserts
- To characterize the systemic and rectal pharmacokinetics of the TAF/EVG Insert, 20/16 mg applied rectally at two dose levels: 1 insert and 2 inserts
  - **Drug levels** in blood, rectal fluid, and rectal tissue

# MTN-039 Study Design

**Phase 1, Single Arm, Open-label Trial**

**Population:**  
**Healthy HIV uninfected**  
**Low-risk; not on PrEP**  
**Age 18+**  
**Target N=20**  
**Randomized to 2 groups for**  
**sampling timepoints (10 per group)**

## Study Visit Schedule



PK Assessments:

	Baseline	Dosing Visit	24 h	48 h	72 h
Blood	X	X	X	X	X
Rectal Fluid	X	X	G2	G1	G2
Rectal Tissue	X	G1	G2	G1	G2
CV Fluid	X	X	G2	G1	G2

**Blood: 1, 2, 4, 6 hours**  
**RF: 2, 4, 6 hours**  
**RT: 2 hours**  
**CVF: 2, 4, 6 hours**

**All participants**  
**Group 1**  
**Group 2**

# Participant Characteristics

- Participants enrolled/randomized: 23
  - 21 completed first dosing visit (1 insert)
  - 19 completed second dosing visit (2 inserts)
- Median Age: 34 years (IQR 24,43)
- Sex (at birth): 17 Male, 6 Female
- Ethnicity: 8 (35%) Black, 13 (57%) White, 2 (9%) Other



# Side Effects

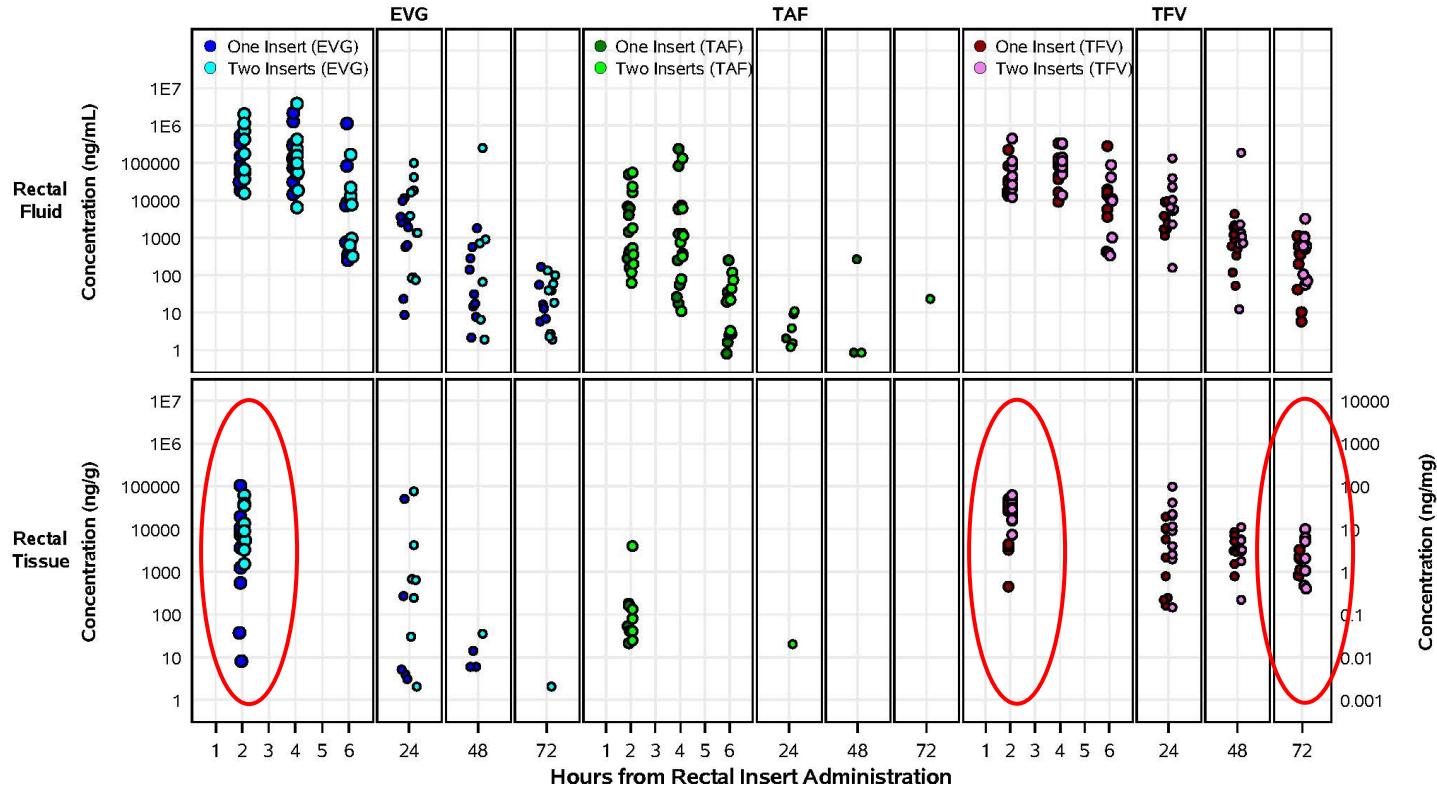
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- TAF/EVG insert was well tolerated
- 17 Adverse Events (AEs) reported for 9 participants
- **Only 1 event related to study product – mild anal erythema**

# Participant Experience

- How easy or difficult was it to use the study product when inserted by clinic staff?
  - 100% Easy or Very Easy
- How did it feel to have the insert inside you?
  - 2 (10%) uncomfortable with 1 insert, 1 (5%) with 2
- Did you experience any leakage after you used the insert?
  - Yes, 1 (5%) participant each for 1 and 2 inserts

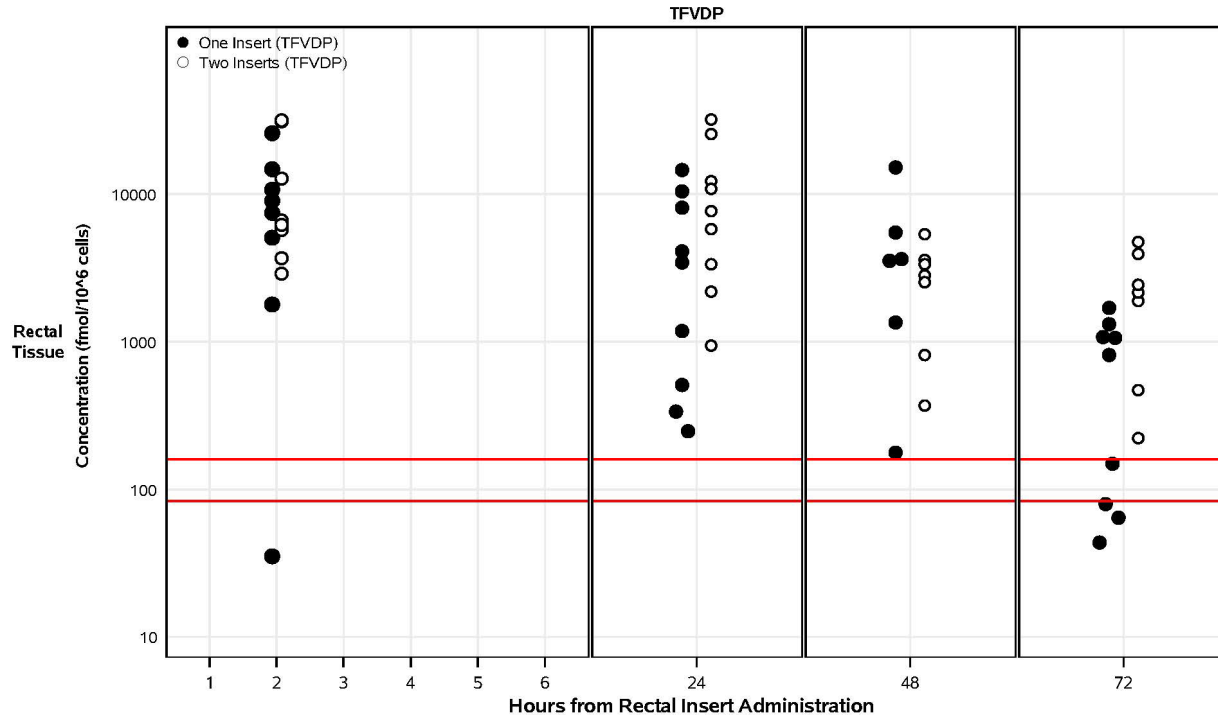
# Rectal Fluid and Rectal Tissue Drug Concentrations



By 2 hours, high levels of EVG and TFV present in rectal tissue.

TFV levels in tissue remained present for up to 3 days.

# Rectal Tissue TFV-DP Concentration

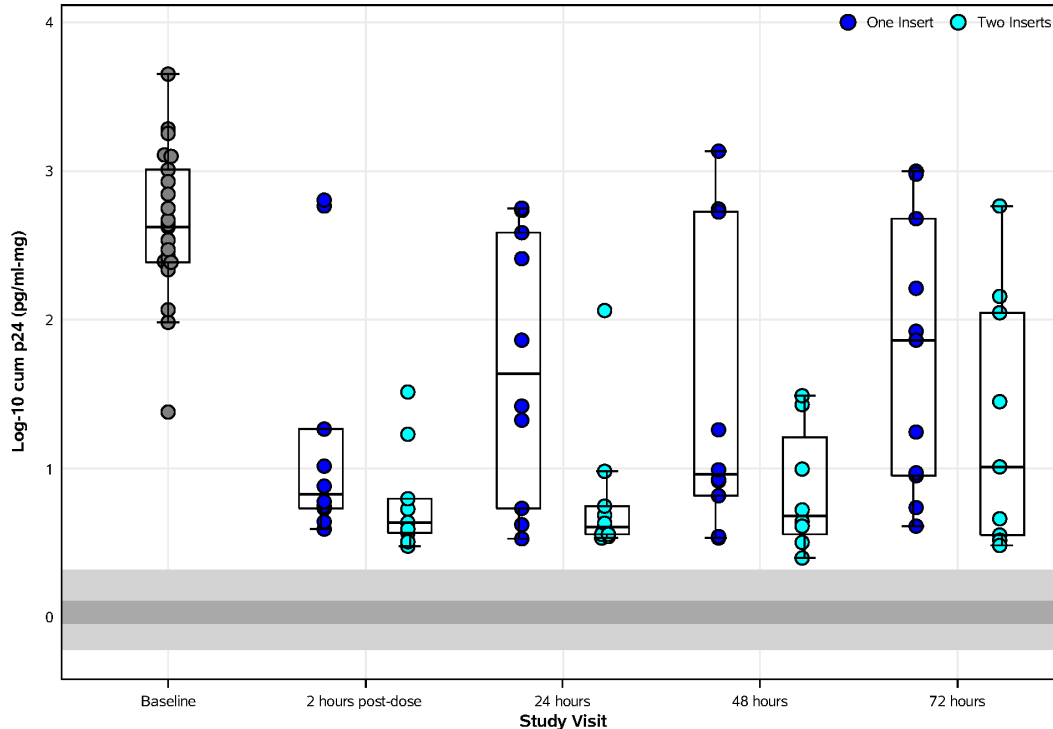


Rectal tissue levels of the tenofovir were higher than rectal levels with oral Truvada (from another study).

From HPTN 066: rectal TFV-DP with oral TDF at steady state:  
4 dose/week: 83 fmol/10<sup>6</sup>  
7 dose/week: 160 fmol/10<sup>6</sup>

*Hendrix, et al. AIDS Res Human Retroviruses. 2016.32-43*

# Explant Challenge in Rectal Biopsy Supernatant



Rectal tissues from the participants were exposed to HIV in the laboratory. Compared to baseline, the tissue biopsies after the insert was given had lower amounts of HIV detected.

The gray horizontal bars represent the inter-quartile range (dark gray) and range (light gray) of the weight-adjusted LLOQ of cumulative p24 concentrations.

# Summary

- Rectal administration of 1 and 2 TAF/EVG inserts was **safe and well tolerated**.
- **High levels of both drugs** were detected in rectal fluid and rectal tissues.
- Compared to baseline, **rectal biopsy tissues taken after dosing were protected from infection by HIV**.
- The results from this study and in vivo protection in the animal studies support continued evaluation of the TAF/EVG insert for rectal use.

# Thanks

## Study Participants

- **UAB Study Staff:** Craig Hoesley/Faye Heard
- **Pitt Study Staff:** Ken Ho/Stacey Edick
- **MTN Network Labs** – Pam Kunjara; Mark Marzinke (PK); Rhonda Brand (p24 tissue)
- **SCHARP** – Yuqing Jiao and Cliff Kelly
- **Behavioral Team** – José Bauermeister
- **FHI 360** – Sherri Johnson, Nicole Macagna
- **CONRAD** – Gustavo Doncel
- **DAIDS** – Jeanna Piper
- **MTN Rectal Microbicide Lead** – Craig Hendrix
- **MTN Leadership** – Sharon Hillier

The study was designed and implemented by the Microbicide Trials Network (MTN), funded by the National Institute of Allergy and Infectious Diseases through individual grants (*UM1AI068633*, *UM1AI068615* and *UM1AI106707*), with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. The TAF/EVG inserts were provided by CONRAD and funded by a cooperative agreement between the US Agency for International Development (USAID) and Eastern Virginia Medical School (AID-OAA-A-14-00010) for development and manufacture. TAF and EVG were provided by Gilead. This presentation content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, USAID or USG.

*TCA PrEP That Booty Webinar*

# ***The Rectal Road ... Behavioral-Congruence***

Craig Hendrix  
Johns Hopkins University





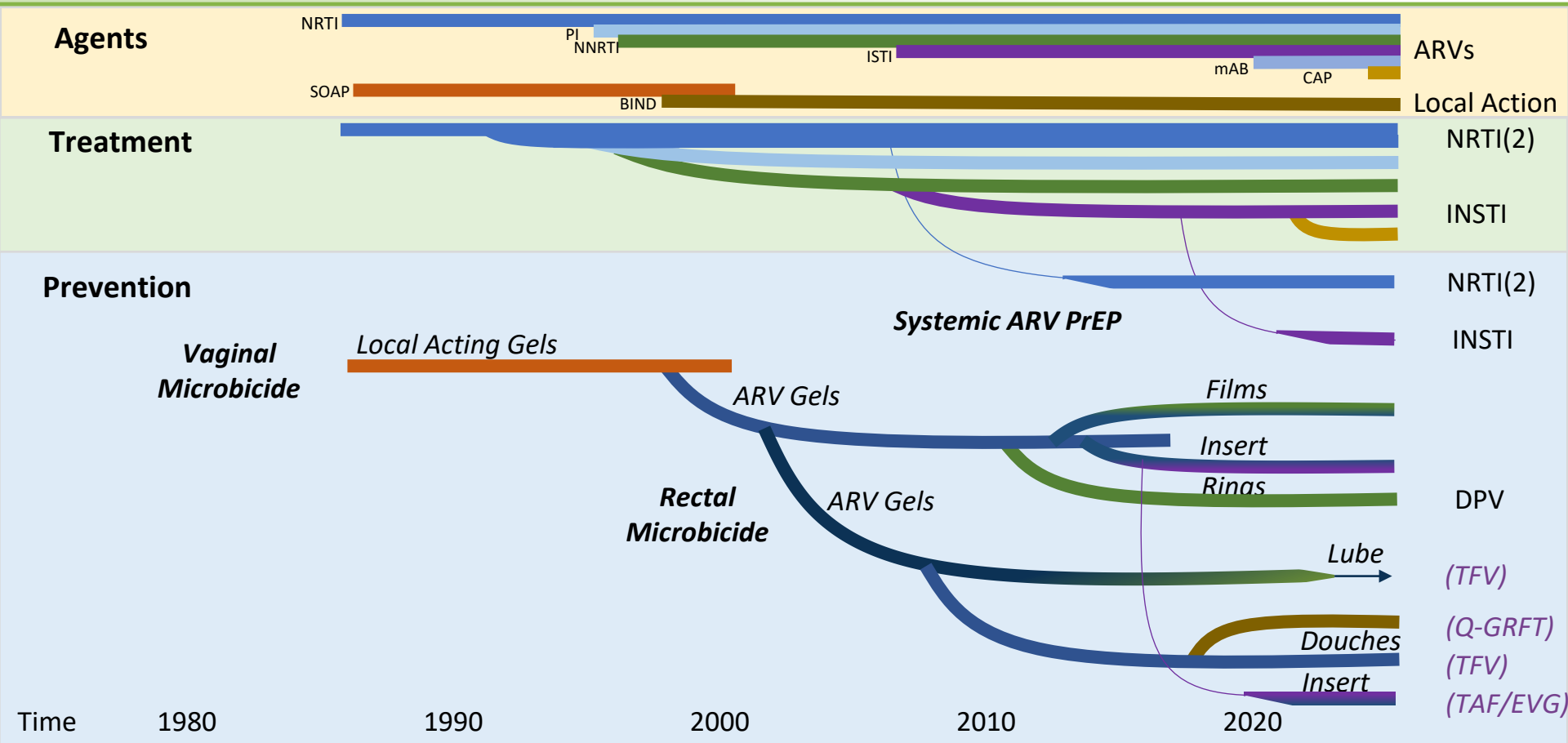
# Disclosures

- Research grants
  - Gilead, Merck
- US Patents
  - 10,092,509; 10,646,434; Hypotonic microbicides
- Prionde Biopharma, LLC
  - Rectal microbicide product development
  - Founder, manager, no fiduciary or financial role
  - Conflict managed by Johns Hopkins University

# Objectives

- PrEP development history
- Behaviorally-Congruent RM Candidates
  - Lubricant TFV
  - Douche Q-GRFT
  - Douche TFV
- Rectal Microbicide Future – *Never More Exciting!*

# PrEP Development History



# Rectal Microbicide Candidates

Drug	Formulation	NHP SHIV Challenge	Clinical PK	Ex Vivo HIV Challenge	Toxicity	Acceptability	BHVR-CONG	Status
TFV	VF gel	Rect/Vag	Sustained	0.5 log <sub>10</sub>	AE's	Modest		End
TFV	RGVF gel	Rectal	Sustained	0.8 log <sub>10</sub>	none	Modest		End
TFV	RF gel	-	Sustained	1.0 log <sub>10</sub>	none	High	<i>lube?</i>	<i>More?</i>
TFV	liquid	Rectal	Sustained	1.6 log <sub>10</sub>	none	High	douche	Phase 2
DPV	gel	-	Brief	1.0 log <sub>10</sub>	none	High		End
DPV	gel	-	Brief	0.3 log <sub>10</sub>	none	High	lube	End
PC-1005	gel	Rect/vag	Brief	0.5 log <sub>10</sub>	none	High		End
IQP-0528	gel	-	Brief	1.6 log <sub>10</sub>	minor	High		End
MVC	gel	Rectal	Brief	NR	none	High		End
OB-002H	gel	Vaginal		ND	none	High		?

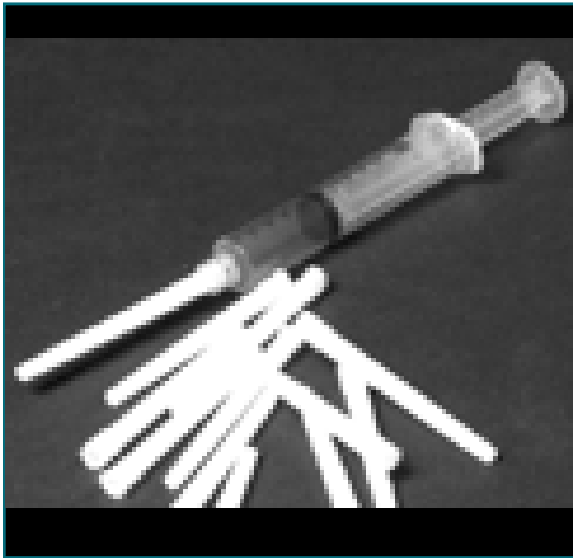
NR not relevant; ND not done

# Behaviorally-Congruent Options

- *Behaviorally-congruent*: medicate products commonly used
- Common health fortification of existing products
  - Fluoridated drinking water & toothpaste
  - Vitamin A & D fortified 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%)

# Behaviorally-Congruent Feasibility

## Applicator (gel)



- Dose Delivered: ?
- Behavioral: ?

## Lube



- ? ?
- ? ?

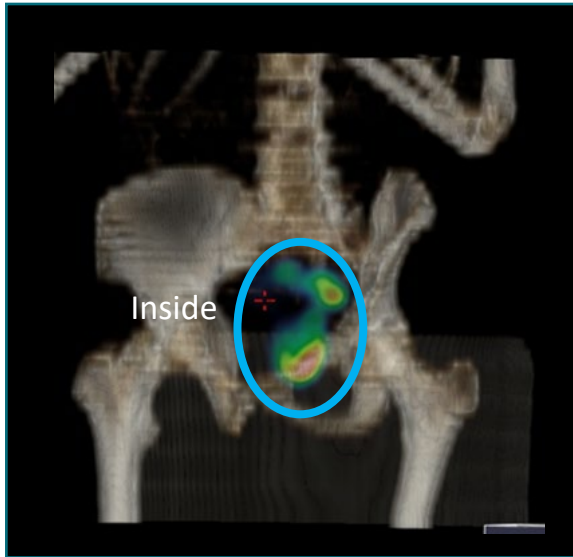
## Douche



- ? ?
- ? ?

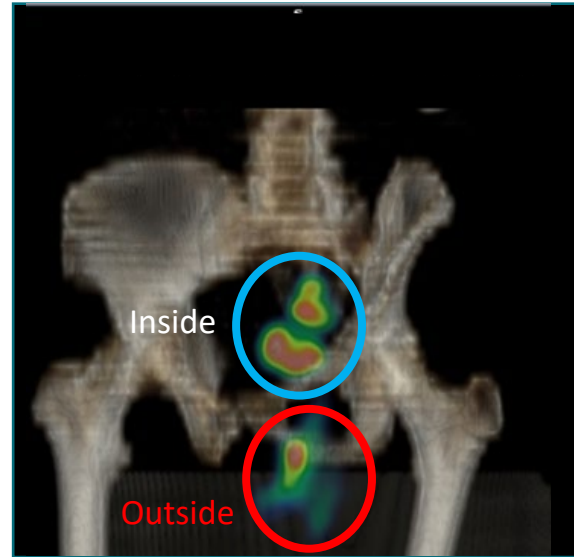
# Behaviorally-Congruent Feasibility

## Applicator (gel)



- Dose Delivered: 95%
- Behavioral: Disliked

## Lube



10%  
Commonly Used

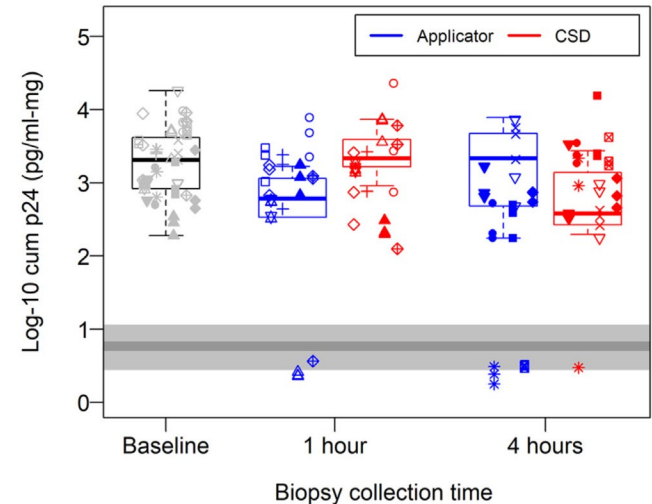
## Douche



60%  
Commonly Used

# Lube as Microbicide – Part 2

- Goal: Assess feasibility of lubricant RM
- Design: Compare DPV gel delivery with applicator vs. as lube
- Results
  - 41-50% of dose delivered
  - HIV suppression modest/brief (figure)
- More drug loading with longer half-life drug  
*lube as RM could be feasible!*



MTN-033: Ken Ho, et al. AAC. 2022

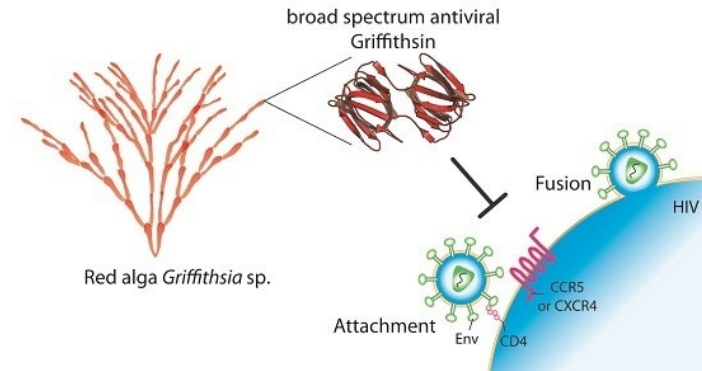


# Douche Rationale

- Single Agent Proven Efficacious
  - Oral TDF, CAB-LA, DPV VR
- On Demand Proven Efficacious
  - Oral F/TDF MSM/TGW; vaginal TFV women
- Topical Proven Efficacious
  - DPV VR (75-91% adh) & TFV Vaginal gel (73-81% adh)
- Behavioral-congruence untested
  - Leverage existing behaviors to increase adherence

# Q-Griffithsin Douche

- Q-GRFT
  - Modified algae protein
  - Prevents HIV binding to CD4+ (gp120)
  - MPT potential
- Vaginal SHIV protection in macaques
- Vaginal Gel Phase 1 Safety & PK
  - GRFT & carrageenan
  - No safety signal, no systemic absorption
  - CVL activity against HIV, HPV
- Rectal Douche Phase 1 Safety & PK
  - Single dose colorectal safety established
  - Modest PK (24h duration) & Antiviral activity (0.4 log<sub>10</sub> decrease)



Derby Nat Commun 2018; Teleshova PLoS One 2022; Boger Sci Reports 2023; Brand (pers comm)

# TFV Douche Safety & Acceptability

- Phase 1 Experience:
  - 36 participants, 102 total doses (median 3 doses per participant)

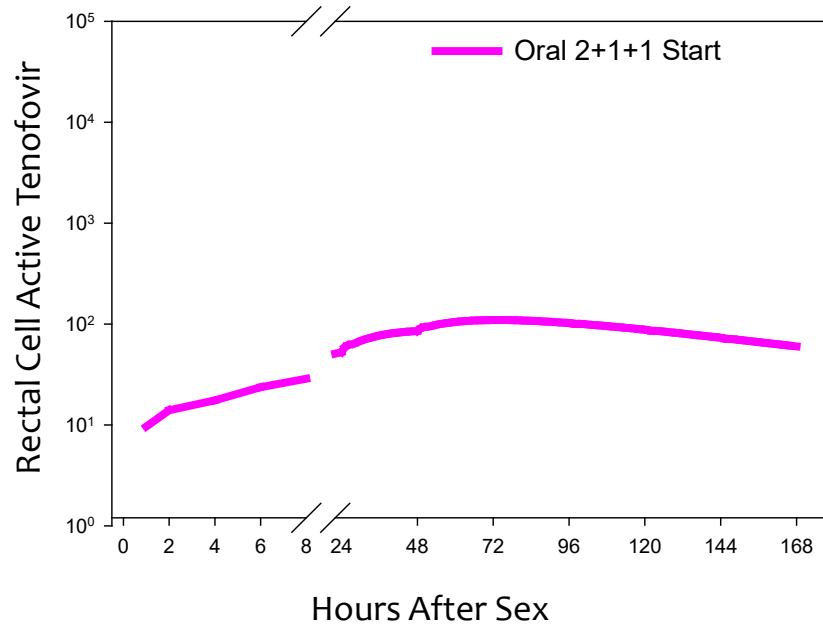
- Safety

Study	N	Grade 1	Grade 2	Grade 3	Attrib.	SAE
DREAM-01	21	56	2	3	2	1
DREAM-02	9	5	6	0	1	0
DREAM-03	6	27	12	0	2	0
<b>Total</b>	<b>36</b>	<b>88</b>	<b>20</b>	<b>3</b>	<b>5</b>	<b>1</b>

- 5 AEs attributed to TFV douche: all grade 1, reversible
  - Histology – no change from baseline
- Acceptability
  - High degree of acceptability
  - High degree of likelihood of future product use

# Oral vs. Douche Colon Cell TFV-DP

Oral 2+1+1 Start

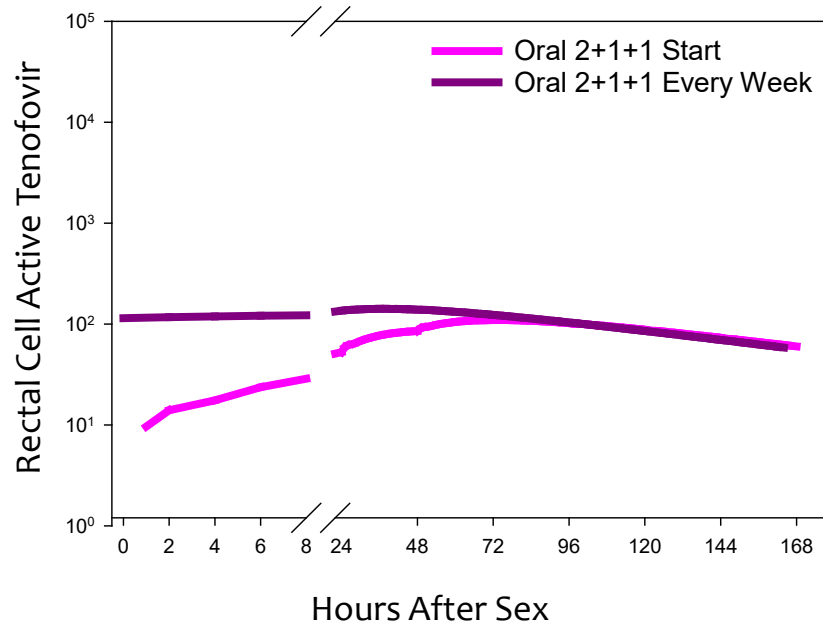


# Oral vs. Douche Colon Cell TFV-DP

Oral 2+1+1 Weekly



Oral 2+1+1 Start



# Oral vs. Douche Colon Cell TFV-DP

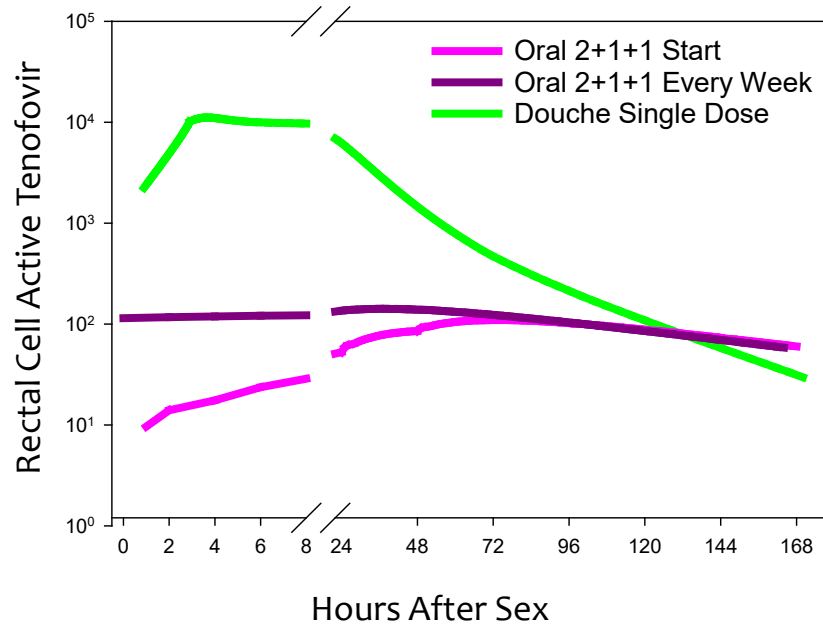
Douche Single Dose



Oral 2+1+1 Weekly



Oral 2+1+1 Start



# Oral vs. Douche Colon Cell TFV-DP

Douche Triple Dose



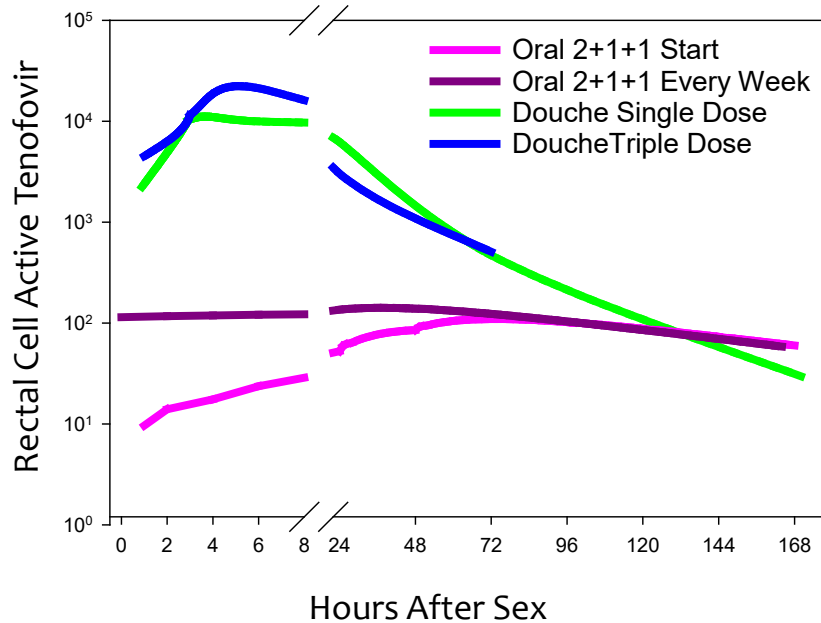
Douche Single Dose



Oral 2+1+1 Weekly

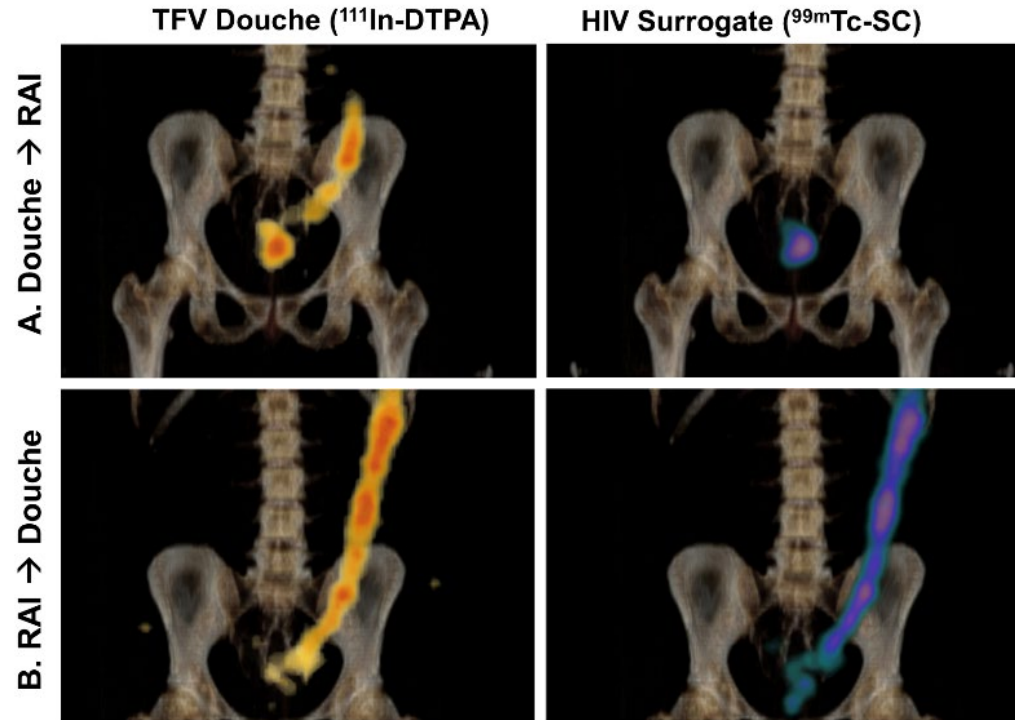


Oral 2+1+1 Start



# Product Sex-Compatibility Essential

- Sex
  - Insertive sex *displaces & dilutes* (semen) products in rectum or vagina
- Sex-Related Behaviors
  - Lubricants, douches
  - Interact, dilute, displace



**SPECT/CT Images 1 hr after TFV douche (J205).** A (TOP). TFV douche preceded simulated RAI. B (BOTTOM). Simulated RAI preceded TFV douche. LEFT TFV douche <sup>111</sup>In-DTPA; RIGHT HIV surrogate <sup>99m</sup>Tc-SC. Amber scale CT (spine, pelvis); color scale indicates isotope signal intensity.



# Sachet: Flexible Delivery



# *HPTN 106 “REV UP”*

Rectal Versus Oral Use of  
On-Demand PrEP

Phase 2 TFV Douche



HPTN



# HPTN 106 Phase 2 TFV Douche

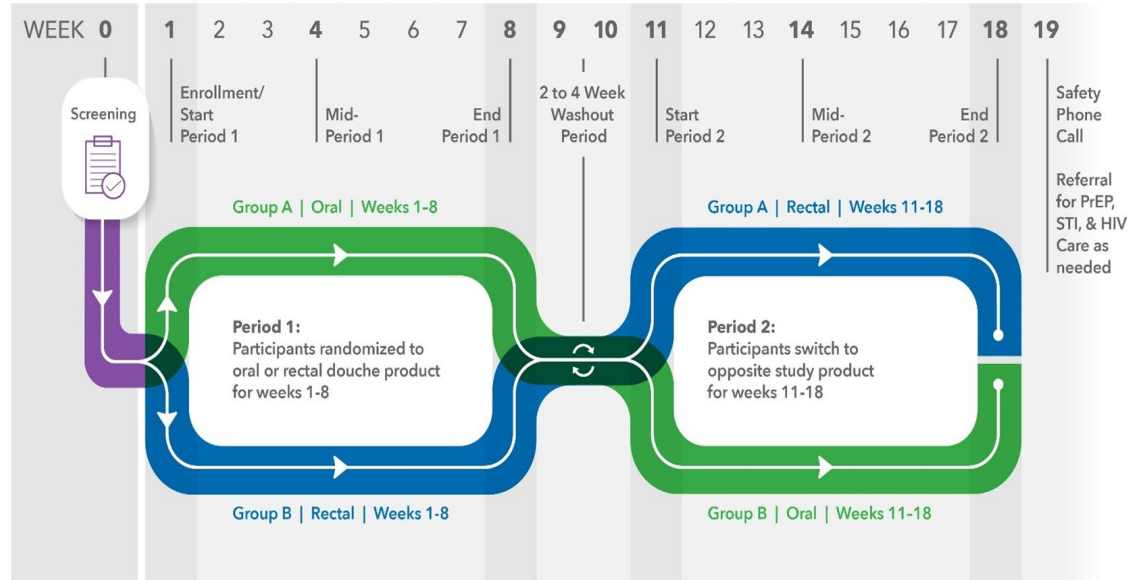
- Objective
  - Compare weekly TFV douche vs. oral F/TDF 2+1+1
- Outcomes
  - Safety
  - Acceptability
  - Product Preference
  - Pharmacokinetics (sub-study)
  - Antiviral Effect ex vivo (sub-study)



Prototype Sachet 3-1/8 in.

# HPTN 106 Phase 2 TFV Douche

- On demand PrEP
  - ❑ TFV rectal douche
  - ❑ F/TDF oral 2-1-1
- 2 Period cross-over
  - ❑ 2 months weekly for each
  - ❑ 2 week washout between
- 150 MSM & TGW



# HPTN 106 Sites

Alabama CRS

Chapel Hill CRS

Fenway Health CRS

Hope Clinic CRS

Johns Hopkins University CRS

UCLA CARE Center CRS

University of Pittsburgh CRS

Weill Cornell Chelsea CRS



# Essential Community Input

- 2015-2022 – DREAM Program: Jim Pickett, AIDS Foundation Chicago, iRMA, AVAC
- 04/08/22 – Protocol writing begins
  - Weekly leadership calls (Chair, Co-chair, HPTN LOC [community representative])
  - Weekly team calls (HPTN LOC, clinical, behavioral, community, pharmacy, stats, ethics)
- 05/06/22 – HPTN CWG Steering Leadership call
- 05/23/22 – HPTN CWG Steering Committee call
- 06/05/22 – HPTN Annual Meeting HPTN 106 Team Meeting invited Community
- 10/27/22 – HPTN Global Community Working Group
- 06/04/23 – HPTN Annual Meeting Community Working Group
- 06/06/23 – HPTN 106 Team Meeting – Community Invited
- 08/24/23 – Johns Hopkins CTU Community Advisory Board

# What the Future Could Look Like

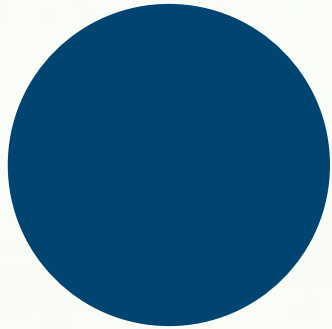


...with apologies for the obvious commercial appropriation.

# Rectal Microbicide Future – *Bright!*

- TAF/EVG Fast-Dissolving Insert
  - MPT, rectal & vaginal, potent, durable
  - *Impact of douche & sex?*
- TFV Douche
  - Behaviorally-congruent
  - MPT, potent, durable
  - *Vaginal formulation feasible?*
- TFV Lube
  - Feasible
  - *Who will fund?*
- MPT (HIV, STI) potential





**Thank You**