

---

# MTN-035: What It Will Teach Us

José Bauermeister PhD, MPH  
University of Pennsylvania  
MTN BRWG Member  
MTN-035 Protocol Chair



# “SCORECARD” FOR PREVENTION MODALITIES



Modality	Efficacy	Low user burden	Low Cost	Low systemic side effects	Reversibility	Low risk of Resistance	Increases sexual pleasure	MPT
Daily oral PrEP								
On demand PrEP								
Injectable PrEP								
PrEP implant								
Vaginal ring								
Rectal lube or insert								
Rectal douche								
bNAbs/HIV Vaccine								

\*Adapted from original slide courtesy of Dr. Liu.

# NEW APPROACHES ARE NEEDED



- Oral PrEP may not be accessible, available or desired among certain population segments.
- Topical prophylaxis may have buy-in among vulnerable populations who:
  - Have complex lifestyles
  - Experience risk seasonally
  - Find daily adherence challenging
  - Have poor/limited health access
  - Can't access/afford systemic prevention
  - Associate stigma with the use of ARV pills

# EMPHASIS ON YOUNG SGM COMMUNITIES



- Youth need to be front and center of our agenda.
  - Greatest vulnerability for HIV infection
  - Greatest innovators
  - Malleable in their willingness to test and adopt new behaviors
- Sexual and gender minorities may benefit the most from rectal microbicide products.

# PREP-RELATED DISPARITIES IN THE US



- Daily oral PrEP works, yet requires successful adherence and retention to PrEP care.
- Between 2012-15, Gilead Sciences reported nearly 50,000 new PrEP prescriptions in the US.
  - Only 7.5% of new users were under the age of 25
  - Only 10% were Black
- Among men who have sex with men (MSM), 6% of 18– 24 year-olds had ever used PrEP compared to 18% of those in the 30+ age group.

# PREP USE



## ■ Almost half of PrEP users discontinued use in a cohort of YMSM in Chicago.

- Access to continued care
- Changes in insurance
- Changes in perceived risk
- Perceived side-effects
- Self-management difficulties
- Stigma

**Table 1** Participant reasoning for discontinuation of PrEP use, RADAR, Chicago 2015–2017 (N = 65)

	Total	
	n	%
I had trouble getting to doctor's appointments	14	21.5
My insurance would not cover it, or I lost my insurance	13	20.0
I didn't think that I was at risk for HIV anymore	12	18.5
I just didn't feel like taking it anymore	8	12.3
Side effects from the medication	6	9.2
I couldn't afford the medication anymore	6	9.2
I had trouble remembering to take the medication	5	7.7
People reacted negatively when they found out I was taking PrEP (like friends or family)	4	6.2
Other	4	6.2
I was getting it as part of a research study and the study ended	3	4.6

Participants were able to select more than one category

# CAN WE REALLY CLOSE THE PIPELINE?



Modality	Youth Friendly	Behaviorally congruent	Easy to Use	Promotes Autonomy	Accessible without Rx	Accessible without insurance
Daily oral PrEP						
On demand PrEP						
Injectable PrEP						
PrEP implant						
Vaginal ring						
Rectal lube or insert						
Rectal douche						
bNAbs/HIV Vaccine						

# RM OPPORTUNITIES



- Many people remain enthusiastic about the idea of rectal products that would prevent HIV.
  - Several RM candidates currently being tested in MTN protocols as Phase I.
- People often report using other rectal products before/after anal sex.
  - In a review of douching practices among MSM who practice RAI:
    - 88% report ever douching before RAI
    - 43-64% report douching in past year before RAI
    - Average age of onset is mid to late 20s
  - In a study assessing rectal health and behaviors in Los Angeles and Baltimore, 38% of male and 40% of female participants reported ever using a rectal suppository.



# DOUCHING



- Douching behavior is highly popular among sexual and gender minorities who are particularly vulnerable to HIV infection.
- Given the popularity of rectal douching, if an effective microbicide could be delivered via a rectal enema, it might have high acceptability and uptake.
- Ongoing RM safety trials for a douche-delivered candidate underway.



# BEHAVIORAL CONGRUENCE WITH DOUCHING BEHAVIOR



- MTN-017 found high rectal douching in preparation for receptive anal sex among MSM and Transgender Women.

Study Site	Mean Frequency of RD in prep for RAI (1=Never – 5= Always)
Bangkok, Thailand	4.38
Boston, Mass, USA	4.00
Cape Town, South Africa	3.33
Chiang Mai, Thailand**	4.10
Lima, Peru**	3.83
Pittsburgh, Pennsylvania, USA**	3.81
San Juan, Puerto Rico	2.00
San Francisco, California, USA**	3.65
**= MTN-035 Study Site	

# WHAT ABOUT INSERTS AND SUPPOSITORIES?



- Limited data on acceptability, tolerability and adherence of suppository or insert modalities.

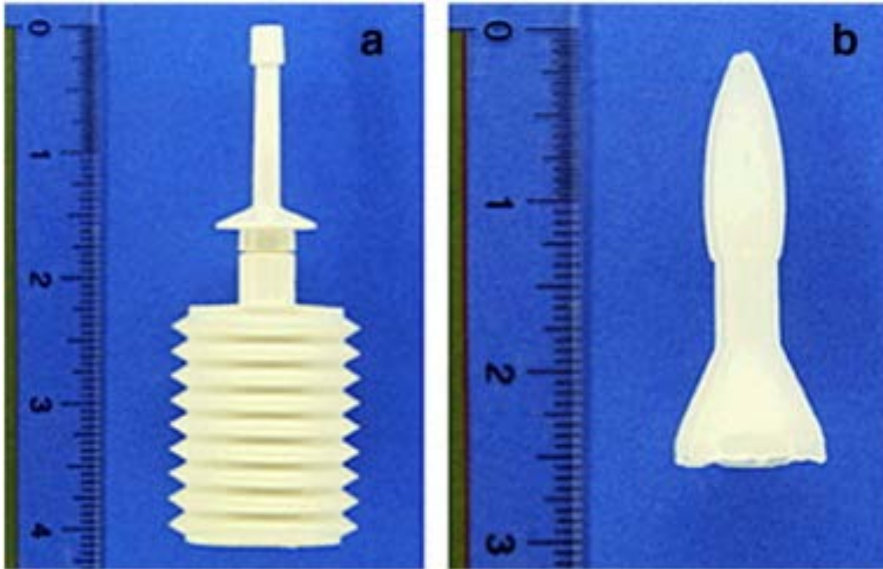


Fast-dissolving insert



Suppository

# FRONTIERS IN PREVENTION



35 ml placebo gel and 8 g placebo rectal suppositories used on up to three RAI occasions each.

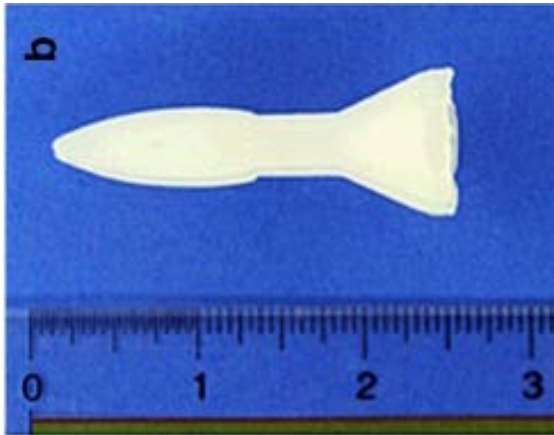
- Participants preferred the gel over the suppository (75% versus 25%,  $p < 0.001$ )
- Participants also reported that their partners also preferred the gel over the suppository (71% versus 29%,  $p < 0.001$ ).

*Sex Transm Infect.* 2008 November ; 84(6): 483–487. doi:10.1136/sti.2008.030478.

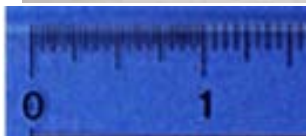
**Preference for gel over suppository as delivery vehicle for a rectal microbicide: Results of a randomized, crossover acceptability trial among men who have sex with men**

A. Carballo-Diéguez<sup>1</sup>, C. Dolezal<sup>1</sup>, J.A. Bauermeister<sup>1</sup>, B. O'Brien<sup>2</sup>, A. Ventuneac<sup>1</sup>, and K. Mayer<sup>2,3</sup>

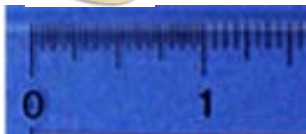
# WHAT A DIFFERENCE A DECADE MAKES!



2.5 inches and 8 g  
(6.35 cm)



1.2-1.5 inches and 2 g  
(3-3.8 cm)



2/3 of an inch  
(1.5 cm)

---

# Acceptability, Tolerability, and Adherence of Three Rectal Microbicide Placebo Formulations among HIV Seronegative Cisgender Men, Transgender Men And Transgender Women Who Engage In Receptive Anal Intercourse

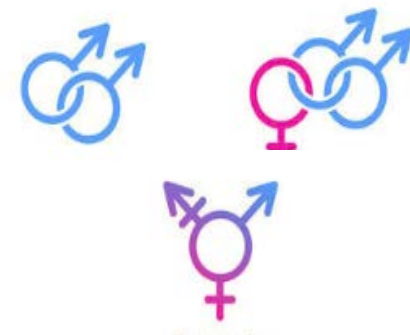
MTN 035



# MTN 035



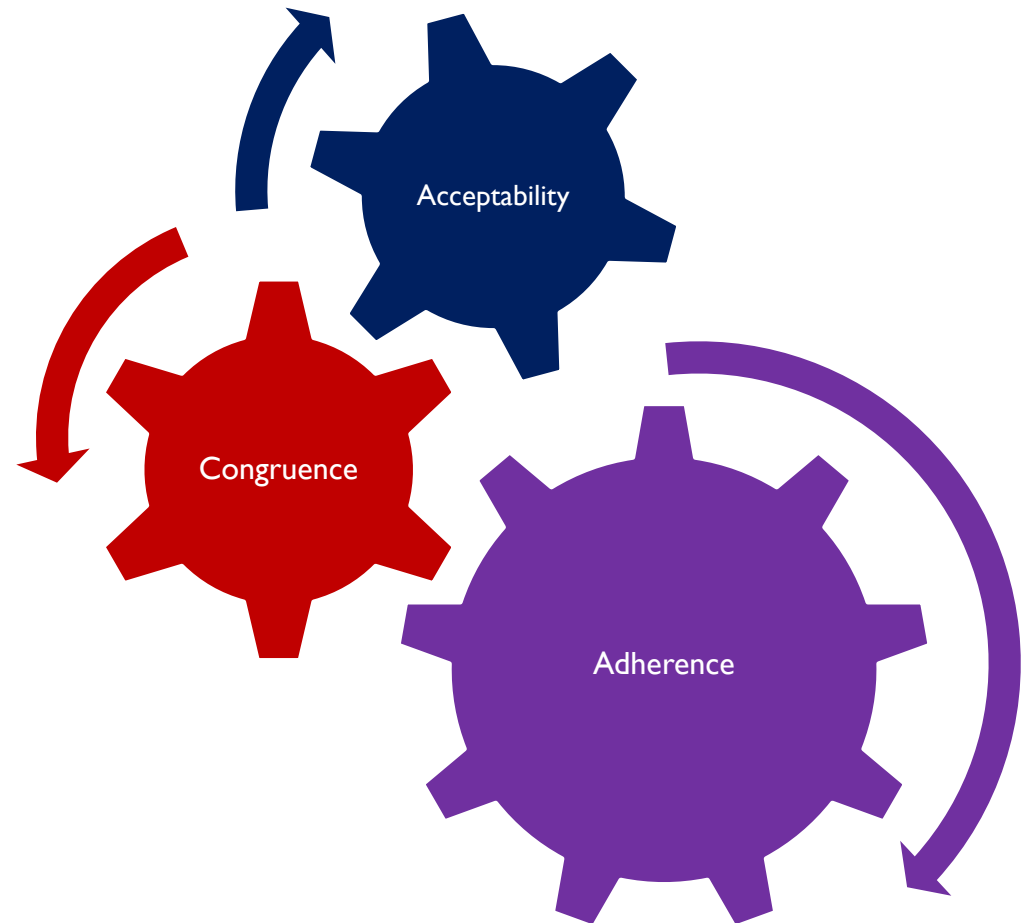
- First study to systematically examine the acceptability, tolerability and adherence of three **placebo** formulations in a sample of young MSM and Transgender People in 5 countries.
- Compare/contrast modalities based on products' and participants' characteristics and contexts.
- Assess modality acceptability, adherence and tolerability, including best practices learned from participants' experiences, as MTN explores formulations.



# WHY A PLACEBO STUDY?



- Understand participants' experiences with non-gel delivery vehicles (e.g., douche, insert, suppository).
- Learn from users about their experiences with these products in order to develop intervention strategies that promote adherence within a future drug trial.
- Plan and address foreseeable barriers and opportunities.



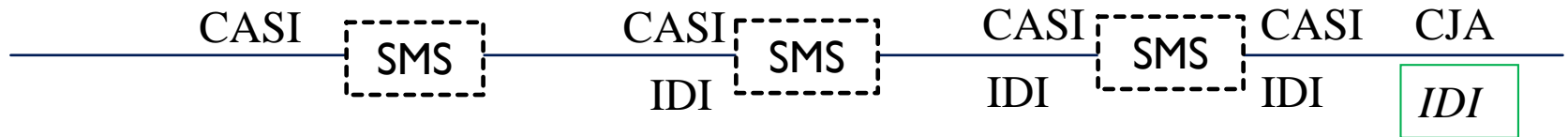
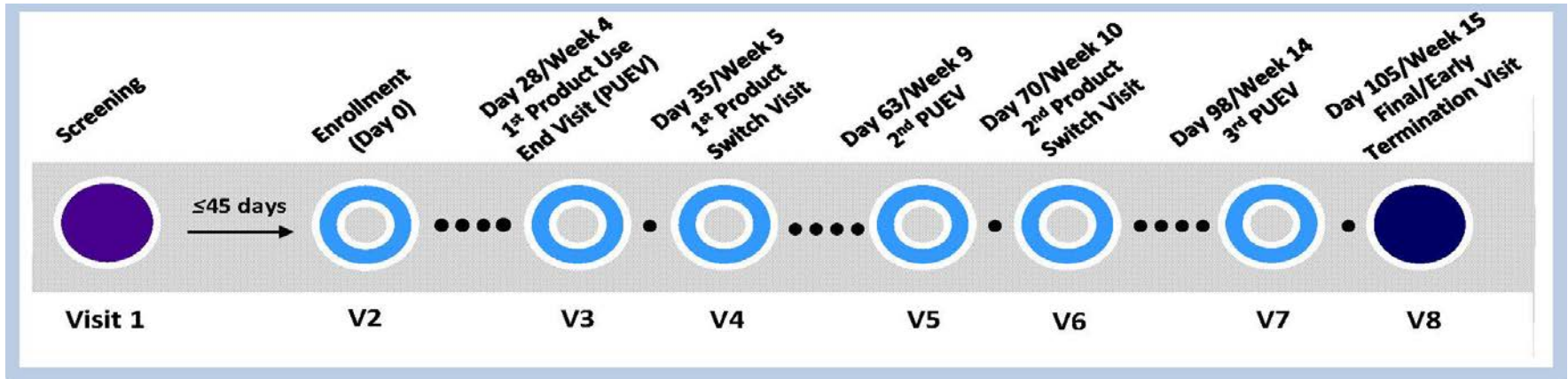


# MTN 035



Sequence	N	Period 1 (4 weeks)	Washout period (~1 week)	Period 2 (4 weeks)	Washout period (~1 week)	Period 3 (4 weeks)
<b>A</b>	35	Rectal insert	--	Rectal douche	--	Rectal suppository
<b>B</b>	35	Rectal douche	--	Rectal suppository	--	Rectal insert
<b>C</b>	35	Rectal suppository	--	Rectal insert	--	Rectal douche
<b>D</b>	35	Rectal insert	--	Rectal suppository	--	Rectal douche
<b>E</b>	35	Rectal douche	--	Rectal insert	--	Rectal suppository
<b>F</b>	35	Rectal suppository	--	Rectal douche	--	Rectal insert

# MTN 035 PROCEDURES



# CASI & IDI DOMAINS



## Enrollment

- Microbicide Acceptability
- Mental Health & Drug Use
- Prior Rectal Product Use
- Rectal Behaviors and Practices
- Mental Health & Drug Use

## Product Use End Visits

- Psychosocial Traits
- Product Use, Adherence, Acceptability, and Problems
- Sexual Behavior
- Substance Use
- Social Influence



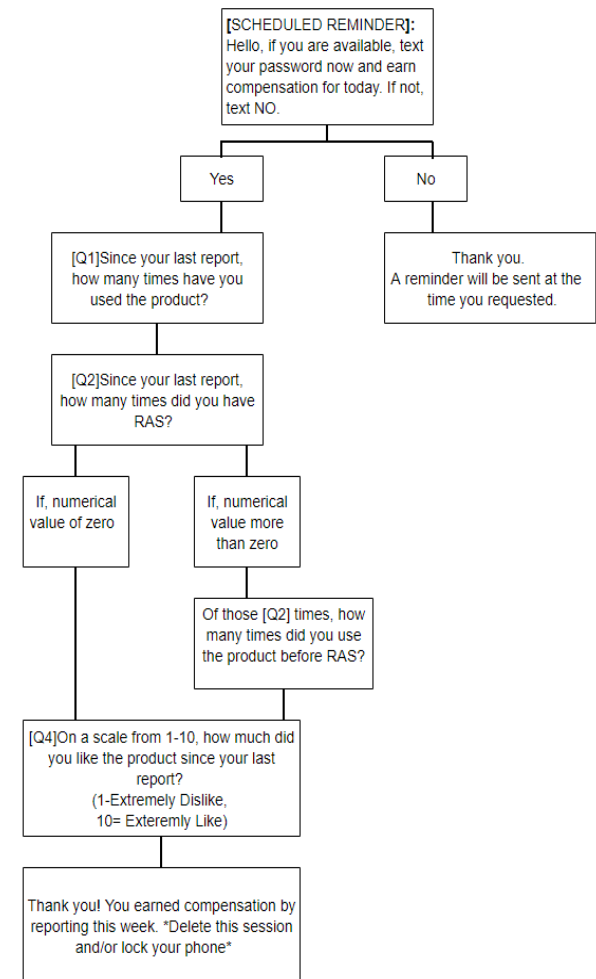
# SMS

- Sent on a weekly basis.



- Text answers in relation to product use since previous report.

- Used to tailor IDIs.



# SMS & USE TRAJECTORIES



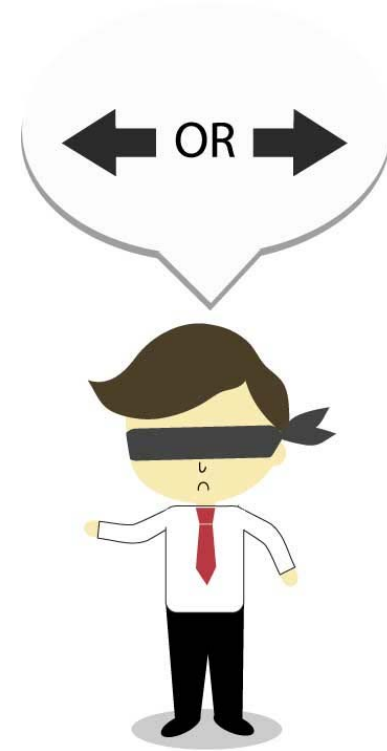
- SMS data used to map trajectories to understand how participants' acceptability and adherence patterns vary over time.
  - What are users' product journey during the trial?
  - What is the stability of their product acceptability over 4 weeks?
- Trajectories used to tailor IDIs.



# END VISIT: WHICH IS THE BEST PRODUCT?



- Random Utility Theory
  - A product is  $>$  than the sum of its parts.
- Participants weigh product traits differently based on their lived experiences.
  - Gender
  - Sexual Behaviors
  - Geography
  - Formulation
  - Efficacy
  - Timing
  - Dosage
  - Need for a Prescription



# CONJOINT ANALYSES



- Analysis of perceived and enacted attributes on choice and decision-making.
  - Helps determine how people value different attributes of a modality.
- Develop an understanding of different population segments and their choices about product features.

	Choice 1	Choice 2
Delivery	Suppository	Enema
Timing before sex	Right before sex	Right before sex
Side effects	No side effects	Some gas
Duration of protection when used correctly	Less than 6 hours	Between 3-5 days
Effectiveness	65%	80%
Frequency of Use	Every day, once a day	Every day, once a day
Prescription Needed	Prescription only	Available over the counter without a prescription
	<input type="radio"/>	<input type="radio"/>

WE ARE A NETWORK OF SCIENCE



Why not just ask participants in a survey to answer hypothetical use instead of a complicated trial?

"Nothing ever becomes real 'til it is experienced."  
— John Keats



# WHAT WILL MTN 035 ACCOMPLISH?



- Assess participants' **CHOICE** for a rectal delivery device after they've had an opportunity to use it, and, importantly, before specific products have been developed.
- Important to have data that systematically examines the acceptability, tolerability and adherence of three **placebo** delivery vehicles in a sample of young sexual and gender minorities (e.g., MSM and transgender people).
- Compare/contrast modalities based on delivery characteristics and participants' characteristics and contexts in order to inform future formulations.

THE WAY FORWARD!



We have an **AMAZING** MTN 035 Protocol Team & Study Sites



# ACKNOWLEDGMENTS



The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UMIAI068633, UMIAI068615, UMIAI106707), 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 content is solely the responsibility of the author and does not necessarily represent the official views of funding agencies.*