

New Product Delivery Options for RAI



DESIRE

**Developing and Evaluating Short-acting
Innovations for Rectal Use**

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WITS RHI

Outline

- HIV in young SGM communities
- Current prevention approaches
- Beyond pills and gels: MTN-035
- What will we learn?

Background

- SA PrEP rollout priorities + T&T
- TRANSFORM conducted at Wits RHI
 - Qualitative phase
 - Observational study
 - RDS = 300 MSM
 - HIV prevalence
 - STI rates high
 - Condom use inconsistent
 - aware of PrEP but low uptake , PEP access a challenge
 - stigma associated with ART uptake



HIV in young SGM communities

- MSM remain vulnerable to HIV infection
 - stigma, shame, violence, criminalization, provider bias, discrimination
- Limited relevant and responsive resources and services
 - Comprehensive sex education and HIV prevention services
- Willing to test new interventions
- Malleable in their willingness to test and adopt new behaviours
- SGM may benefit the most from rectal microbicide products - Important to include cis and transgender people

Unprotected RAI

- Globally, TGW and MSM are 19 times more likely to be living with HIV compared with the general population.
- RAI is associated with the highest probability for sexual acquisition of HIV infection, conferring ~ 10 to 20 times more risk than unprotected receptive vaginal intercourse (RVI).

What works ?

- Oral PrEP works for prevention of HIV transmission through RAI, yet it may not be accessible, available or desired among certain population segments.
- Topical prophylaxis may have buy-in among young 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

What has been learned ?

PrEP “Acceptability”

- Half of YMSM discontinued PrEP.
 - Access to continued care
 - Change 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

Lessons Learned from MTN-017

- Oral PrEP works, but not everyone likes it.
- Least Preferred:
 - 28% oral PrEP
 - 28% Before/After Sex RM gel
 - 43% rated daily RM gel
- Geographical differences observed in terms of product acceptability
 - Non-US participants more favorable to gels than pills when compared to US participants.

New approaches are needed

- Beyond efficacy considerations, users may also select products based on:
 - Behavioral congruence
 - Different protection windows
 - Youth friendliness
 - Ease of use
 - Autonomy
 - Access

Multi-site, randomized-sequence, 1:1:1:1:1:1, three-period, open-label crossover study.

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

Sample size : 210 participants, 18-35 years

Study Duration: Approximately 3.5 months of follow-up with a projected accrual period of 9-12 months



- Peru
- Thailand
- South Africa
- Malawi
- USA

MTN- 35

Study Products: Placebo rectal insert, Placebo rectal douche, Placebo rectal suppository



- Compare/contrast modalities based on product characteristics and participants' characteristics and contexts.
- Assess modality acceptability and tolerability, including best practices learned from participants' experiences

MTN-035

- MTN-035 will evaluate the acceptability of three potential rectal microbicide formulations that could be used prior to RAI and could potentially deliver enough anti-HIV drug locally to prevent HIV infection during RAI.
- It is believed these drug delivery mechanisms would be congruent with cleansing practices and behaviours regarded as normal preparations prior to engaging in RAI or participating in activities where the probability of engaging in RAI is high



Design

MTN-035 is a multi-site, randomized-sequence, 1:1:1:1:1:1, three-period, open-label crossover study.

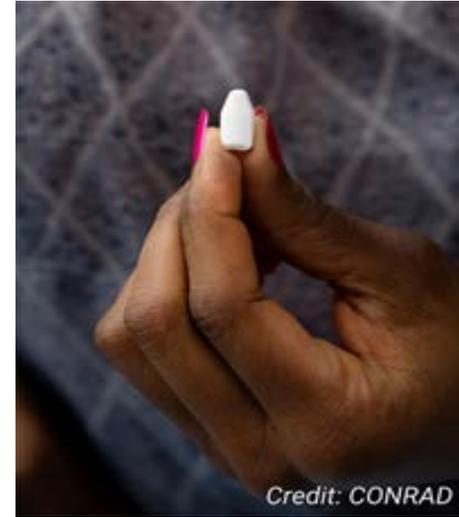
Sequence	N	Period 1 (4 weeks)	Washout period (~1 week)	Period 2 (4 weeks)	Washout period (~1 week)	Period 3 (4 weeks)
A	35	Rectal insert	--	Rectal douche	--	Rectal suppository
B	35	Rectal douche	--	Rectal suppository	--	Rectal insert
C	35	Rectal suppository	--	Rectal insert	--	Rectal douche
D	35	Rectal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

Why a placebo study?

- Learn how to promote the 3 A's of our products before investment in a product that contains drug
 - Awareness
 - Acceptability
 - Adherence

Why a placebo study?

- Understand participants' acceptability and 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.



Behavioural Congruence

- As past PrEP and microbicide studies have shown, drug efficacy translates to drug effectiveness only when people use the drug based intervention as intended
- It is crucial for products to be designed so that they can deliver drugs via mechanisms that not only deliver enough drug to block HIV transmission, but are also a good behavioural fit with the drug's intended end-users.

Behavioural Congruence & Douching

- In a global review of rectal douching, up to 88% of MSM who practice anal sex had douched.
 - 43–64% reported douching.
 - 87–97% douche before RAI.

MTN 017 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	

Inserts and suppositories

- Studies are needed to assess acceptability of a smaller/differently shaped and formulated fast-dissolving inserts and suppositories.
- Limited data on acceptability, tolerability and adherence of **suppository** and **insert** modalities.
 - Rectal Rocket Study: Suppository (8g) used was much larger than one to be used in MTN-035 (2g).



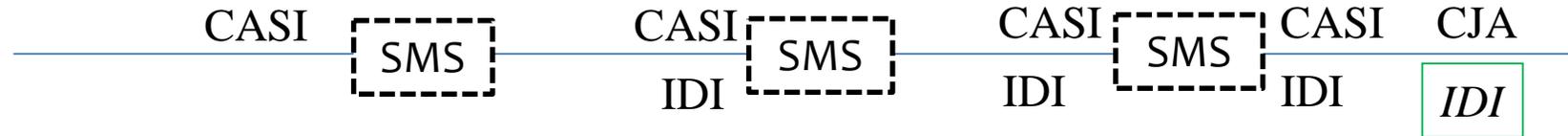
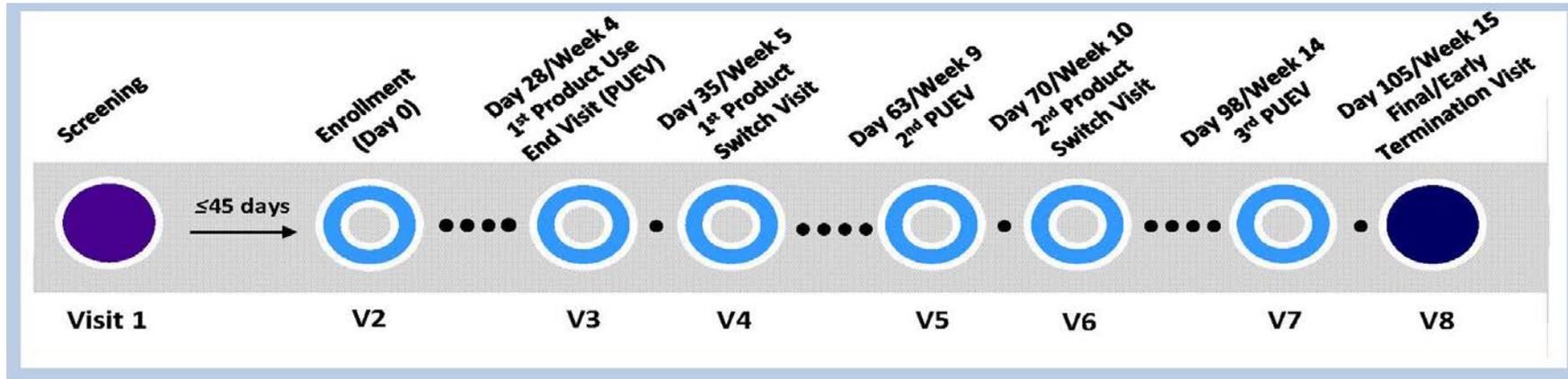
“The final frontier...”



Credit: CONRAD

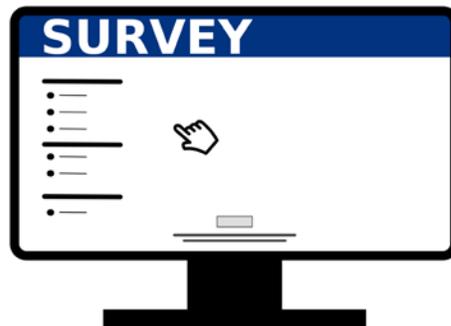
Size matters!

MTN 035 PROCEDURES



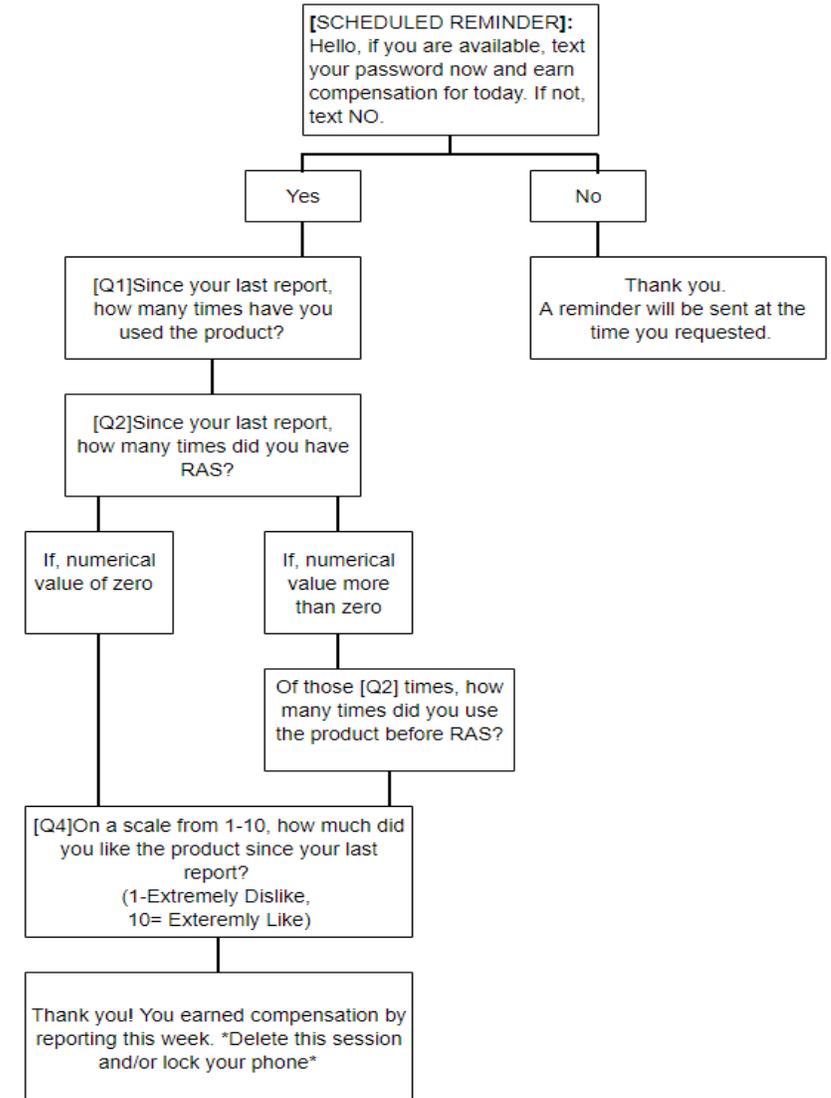
CASI & IDI Domains

- 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



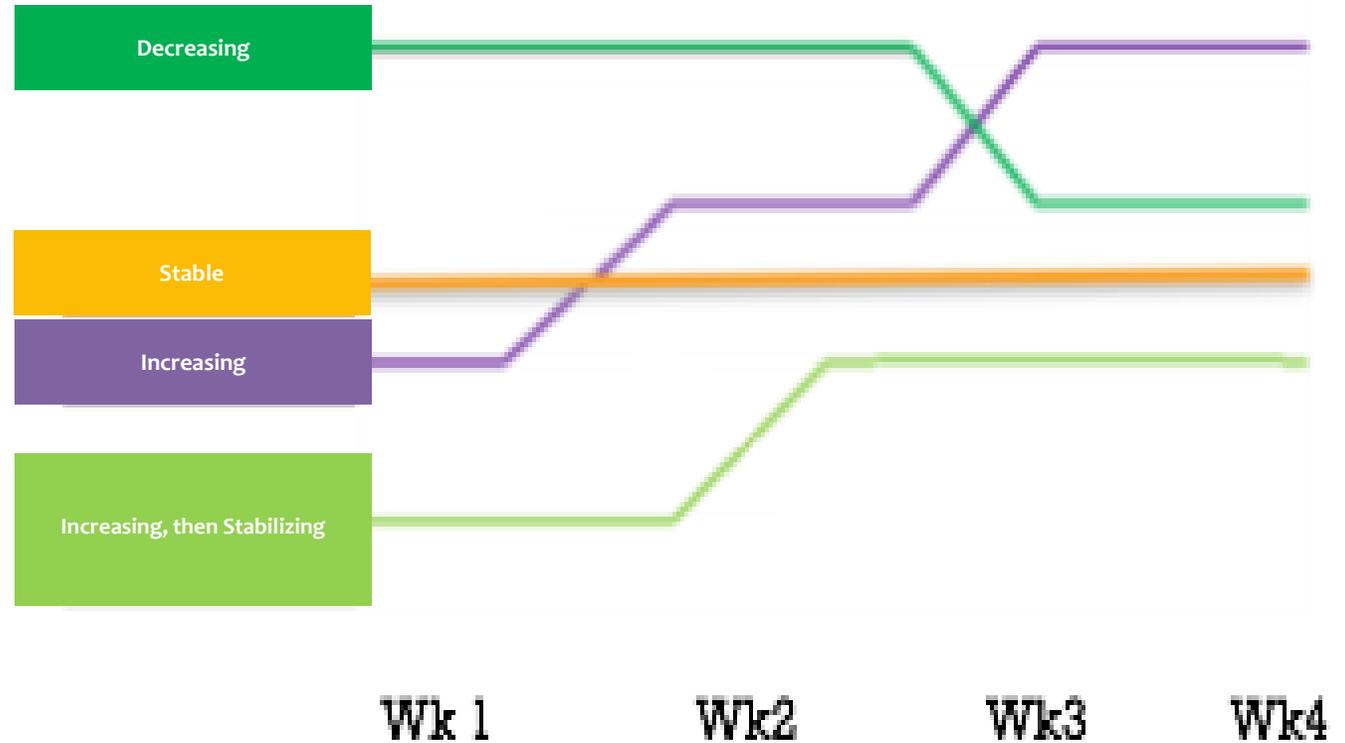
SMS

- Sent on a weekly basis.
- Text answers in relation to product use since previous report.
- Used to tailor IDIs.



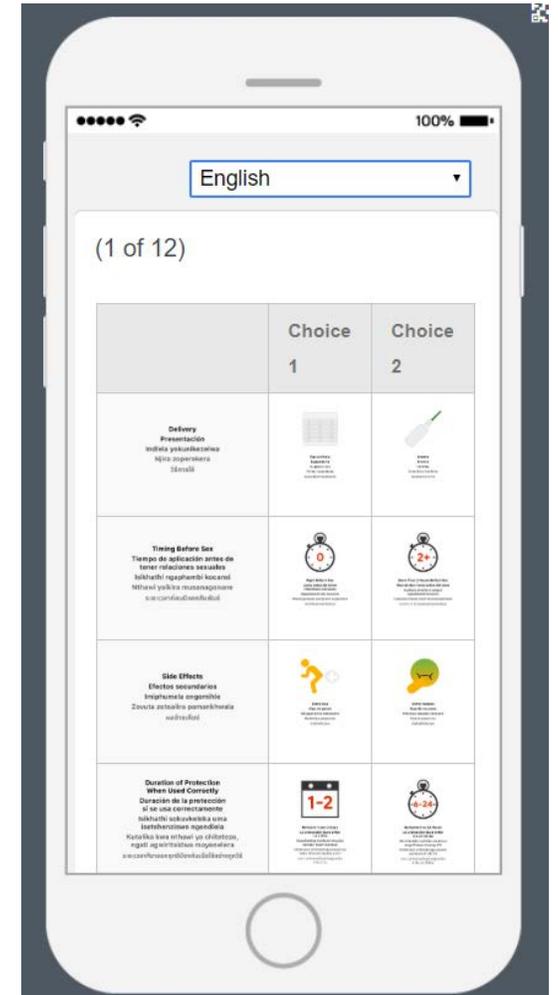
SMS & Use Trajectories

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



End of Trial Choice Experiment

- Use of Conjoint Analysis (CJA) to examine participants' value of different attributes between modalities.
- Use CASI data to create predictive models of participants' choice.
- Triangulate CJA and IDIs to develop an understanding of population segments and desire of product features.



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"/>

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.

Conclusion

- Drug efficacy translates to drug effectiveness only when people use the drug based intervention as intended
- Products needed that not only deliver enough drug to block HIV transmission, but are also a good behavioural fit with the drug's intended end-users.
- MTN 035 aims to inform the pipeline of work related to choices for SGM

We have a great team!

Some people spend their whole lives wondering if they have made a difference we don't have that problem!



Acknowledgments

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