

# DESIRE

Developing and Evaluating Short-acting  
Innovations for Rectal Use

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# Agenda

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- Lessons learned from the “rectal road”
- Choice matters: Who, When, How & Why
- Beyond pills and gels: MTN 035
- Where should we be going next after 035?

# HIV in young SGM communities

- Youth need to be front and center of our prevention agenda.
  - Greatest vulnerability for HIV infection
  - Greatest innovators
  - Open & willing to test and adopt new behaviors
- Sexual and gender minorities may benefit the most from rectal microbicide products.
  - Important to include cis and transgender people

# Lessons learned from the “rectal road”

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# New approaches are needed

- Oral PrEP works for Receptive Anal Intercourse (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 pills

# PrEP “Acceptability”

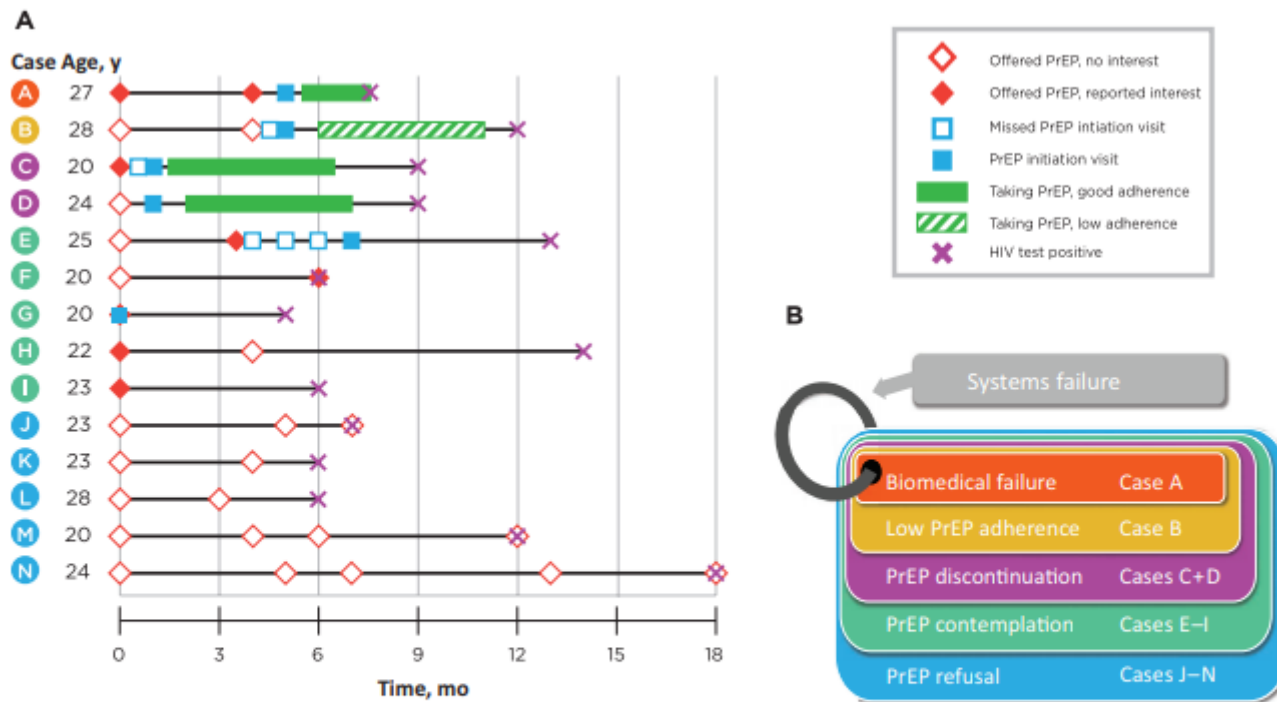
- Half of YMSM discontinued PrEP.
  - Access to continued care
  - Change in insurance
  - Changes in perceived risk
  - Perceived side-effects
  - Self-management difficulties
  - Stigma

**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

# PrEP “Acceptability”



**Figure 1.** A, Timelines in 14 participants (A–N) with human immunodeficiency virus (HIV) seroconversion occurring after preexposure prophylaxis (PrEP) was offered in the EleMENT cohort. B, Proposed framework of PrEP failure typologies, beginning with biomedical failures (case A) and expanding to include low PrEP adherence (case B), PrEP discontinuation (cases C and D), PrEP contemplation (cases E–I), and PrEP refusal (cases J–N). Systems failures are represented as a ring joining the other 4 typologies, given the cross-cutting nature of this barrier to PrEP effectiveness.

# Lessons Learned from MTN-017

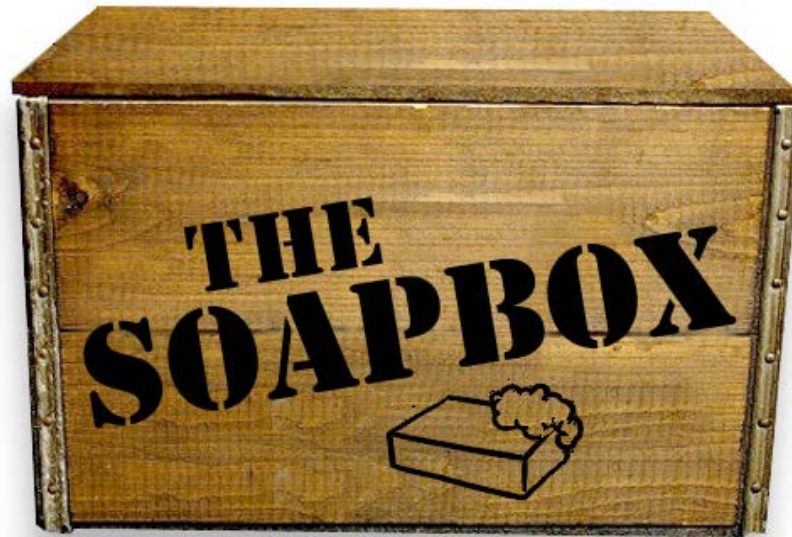
- Oral PrEP works, but not everyone likes it.
- Least Preferred:
  - 28% oral PrEP.
  - 28% Before/After Sex RM gel.
  - 43% rated daily RM gel.
- Geographical differences observed in terms of product acceptability
  - Non-US participants more favorable to gels than pills when compared to US participants.



# New approaches are needed

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- Beyond efficacy considerations, users may also select products based on:
  - Behavioral Congruence
  - Different protection windows
  - Youth Friendliness
  - Ease of Use
  - Autonomy
  - Access



We need to expand the prevention toolbox and recognize that “choice” and “acceptability” may vary across populations and contexts.

# We are a network of science

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*Why not ask them what they would prefer to use rather than having a complicated trial?*

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

# What choice matters? To whom? When?

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Choice and decision-making is not static

# Trajectories in Project Gel

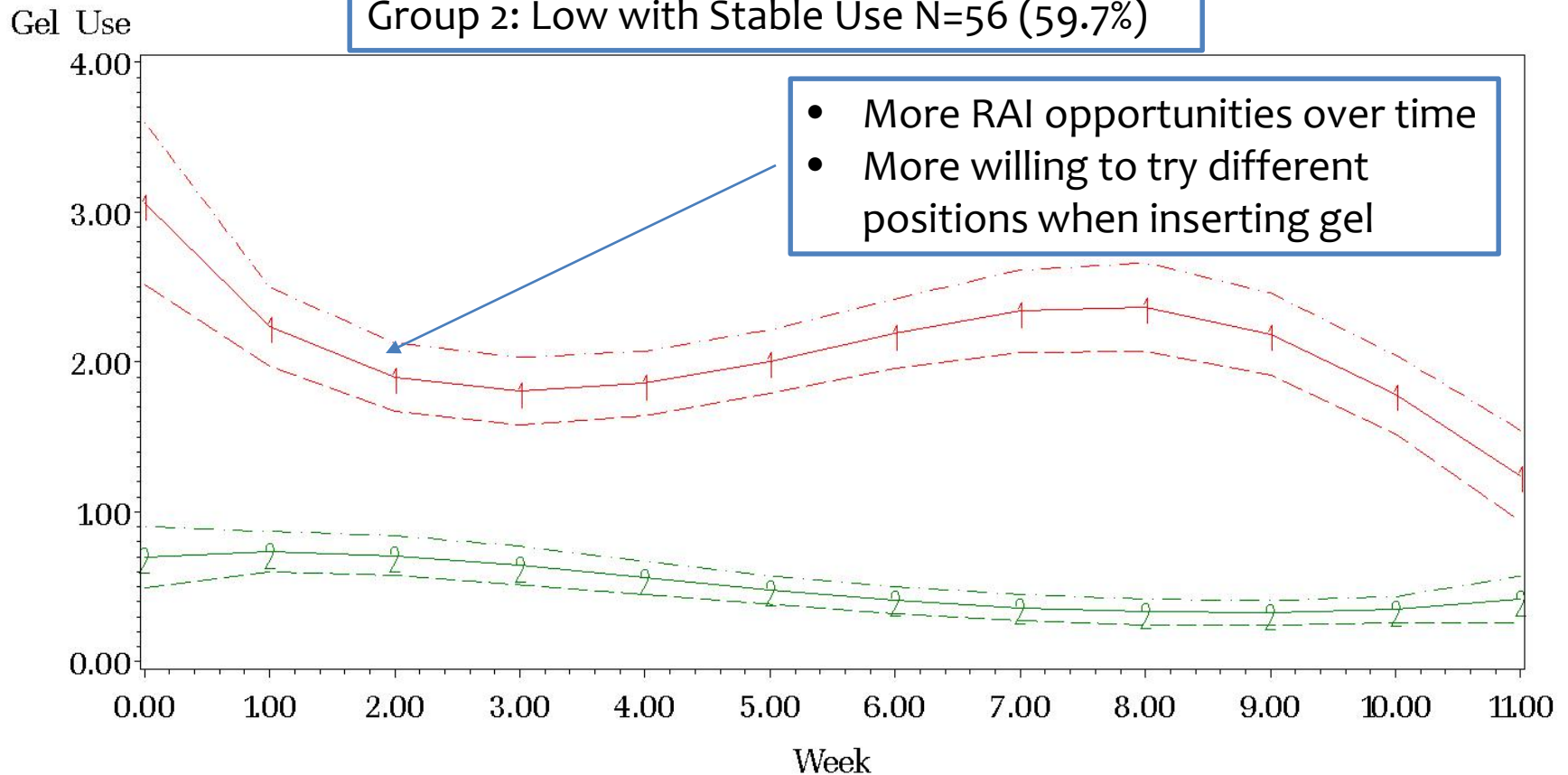
- An ethnically diverse sample of 94 YMSM (aged 18 to 30 years) were asked to insert HEC placebo gel rectally before RAI during 12 weeks.
- Using data from the Interactive Voice Response System, we used trajectory analyses to characterize participants' use of the rectal gel over the 12 weeks.



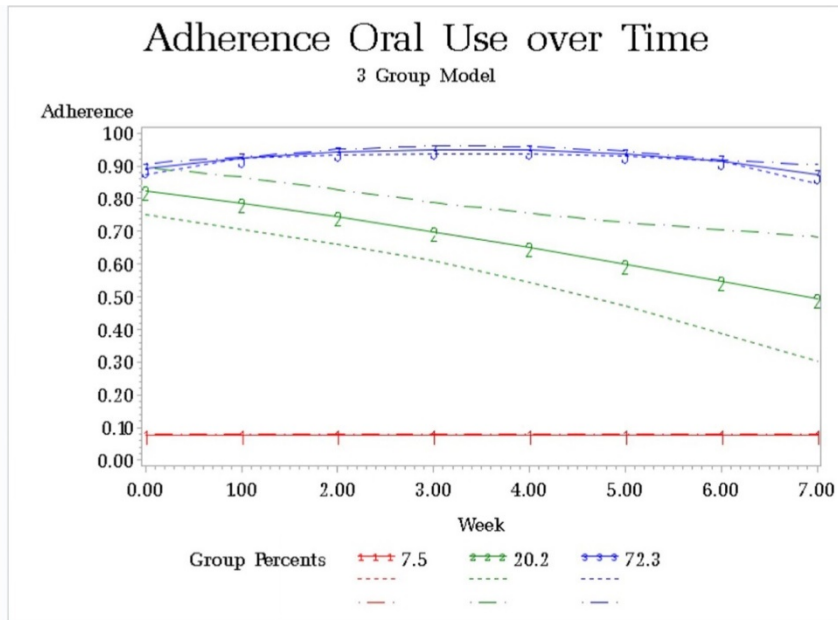
# Trajectories in Project Gel

## Gel Use over Time

Group 1: High with Varying Use N=38 (40.3%)  
Group 2: Low with Stable Use N=56 (59.7%)



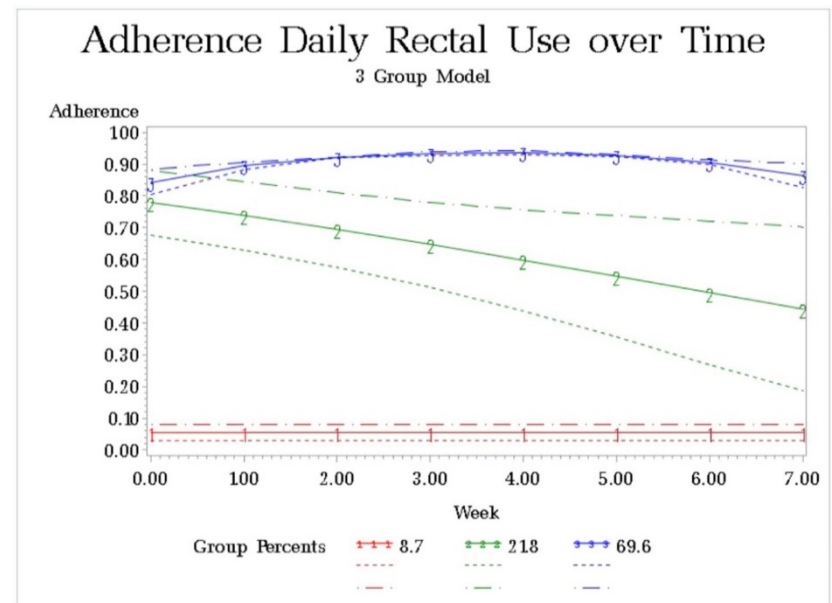
# MTN 017



Group	Parameter	Estimate (SE)	t	p
1: Low-adherers	Intercept	-0.19 (0.05)	-3.65	<.001
	Linear	-0.07 (0.01)	-5.55	<.001
2: Decreasing-adherers	Intercept	0.95 (0.05)	18.80	<.001
	Linear	-0.07 (0.01)	-5.55	<.001
3: High-adherers	Intercept	1.10 (0.04)	31.09	<.001
	Linear	0.11 (0.02)	4.72	<.001
	Quadratic	-0.02 (0.00)	-5.05	<.001

*Probability of Group Membership:*  
 1: Low-adherers: N=14 (8%); 2: Decreasing-adherers: N=38 (20%); 3: High-adherers: N=135 (72%).

*Model Fit Statistics:*  
 BIC = -932.67 (N=1496); BIC=-923.31 (N=187); AIC=-908.77.



Group	Parameter	Estimate (SE)	t	p
1: Low-adherers	Intercept	-0.26 (0.07)	-3.61	<.001
	Linear	-0.06 (0.01)	-4.68	<.001
2: Decreasing-adherers	Intercept	0.87 (0.05)	16.69	<.001
	Linear	-0.06 (0.01)	-4.68	<.001
3: High-adherers	Intercept	0.99 (0.03)	28.57	<.001
	Linear	0.13 (0.02)	5.77	<.001
	Quadratic	-0.02 (0.00)	-5.58	<.001

*Probability of Group Membership:*  
 1: Low-adherers: N=16 (9%); 2: Decreasing-adherers: N=41 (22%); 3: High-adherers: N=130 (70%).

*Model Fit Statistics:*  
 BIC = -957.13 (N=1496); BIC=-947.77 (N=187); AIC=-933.23.

Leu, C.S. et al. (2019). Trajectory of use over time of an oral tablet and a rectal gel for HIV prevention among transgender women and men who have sex with men. *AIDS Care*, 31, 379-387.

# Differences between trajectories

**Table 3.** Potential predictors of participant characteristics based on trajectory of adherence to daily rectal regimen in MTN-017 – polytomous logistic regression.

Regimen: Daily Rectal

Potential predictors	High-adherers vs. Low-adherers*			High-adherers vs. Decreasing-adherers*		
	OR**	95% CI	p-value	OR**	95% CI	p-value
Age	<b>1.16</b>	<b>1.05, 1.28</b>	<b>0.002</b>	<b>1.04</b>	<b>1.01, 1.09</b>	<b>0.042</b>
Number of Partners	1.39	0.98, 1.96	0.065	0.99	0.93, 1.05	0.803
Overall liking of the product	1.82	0.98, 3.23	0.056	<b>1.75</b>	<b>1.18, 2.50</b>	<b>0.005</b>
Ease of applying the gel	1.67	0.79, 3.57	0.175	<b>1.61</b>	<b>1.00, 2.63</b>	<b>0.050</b>
Ease of applying the gel the last few times	<b>2.27</b>	<b>1.01, 5.00</b>	<b>0.048</b>	<b>2.04</b>	<b>1.20, 3.45</b>	<b>0.009</b>
Overall liking of the gel applicator	1.69	0.93, 3.03	0.090	<b>1.72</b>	<b>1.16, 2.44</b>	<b>0.006</b>
Reason preventing from using the gel – don't have privacy needed to use the product	0.20	0.04, 1.12	0.067	0.37	0.10, 1.33	0.127
Reason preventing from using the gel – don't like the gel	<b>0.10</b>	<b>0.02, 0.59</b>	<b>0.011</b>	0.40	0.11, 1.52	0.178
Reason preventing from using the gel – there was change in regular routine	<b>5.26</b>	<b>1.23, 100</b>	<b>0.031</b>	0.95	0.40, 2.27	0.908
Likelihood of using the gel knowing it provides protection against HIV	1.28	0.75, 2.22	0.361	<b>1.47</b>	<b>1.05, 2.08</b>	<b>0.023</b>

\*The high-adherers (maintaining high adherence throughout the 8-week study period) represented 72% of participants; the decreasing-adherers (adherence decreased consistently over time) represented 20% of participants; the low-adherers (having low adherence throughout the 8-week study period).

\*\*OR: Odds ratio.

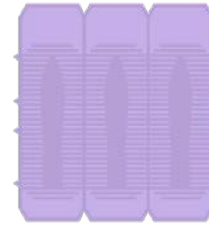




Insert  
Inserto  
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Piritsi laufa  
แบบสอดทางทวารหนัก



Enema  
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Zotsukira kobibira  
อุปกรณ์สวนทวาร



Suppository  
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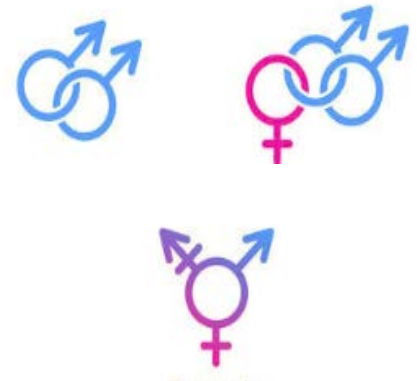
# Beyond pills and gels: MTN 035

# DESIRE

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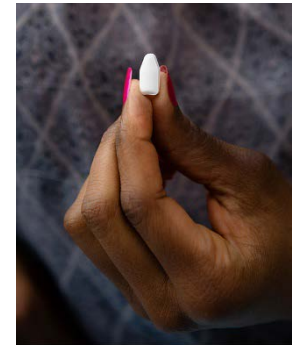
# MTN 035

- First study to systematically examine the acceptability, tolerability and adherence of three placebo formulations in a sample of young cisgender men and transgender people who have sex with men in 5 countries.
- Compare/contrast modalities based on product characteristics and participants' characteristics and contexts.
- Assess modality acceptability and tolerability, including best practices learned from participants' experiences, as MTN explores formulations.



# 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.



Credit: CONRAD



# Behavioral 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).

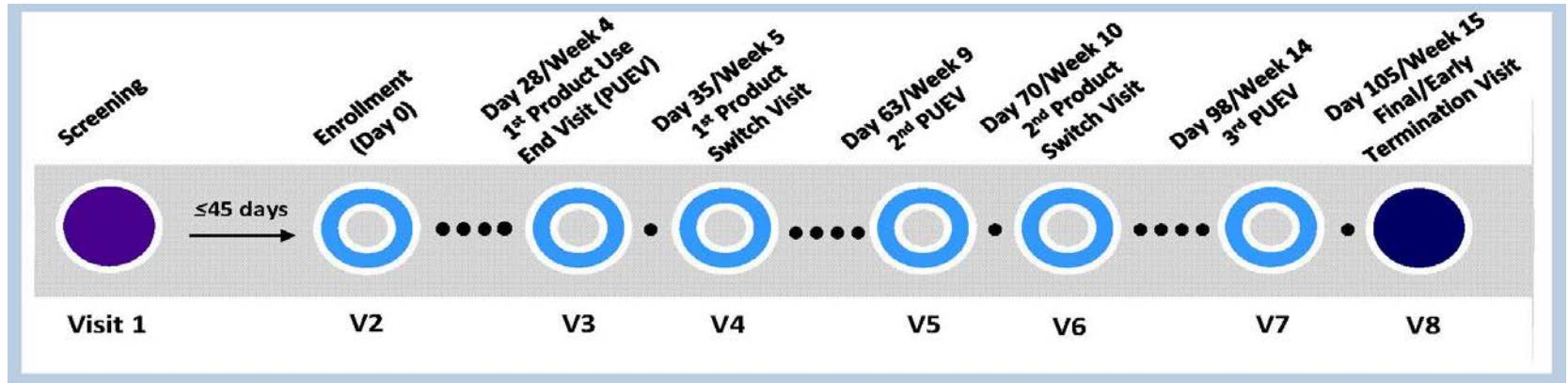


“The final frontier...”

# Proposed Design

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

# How will we accomplish it?

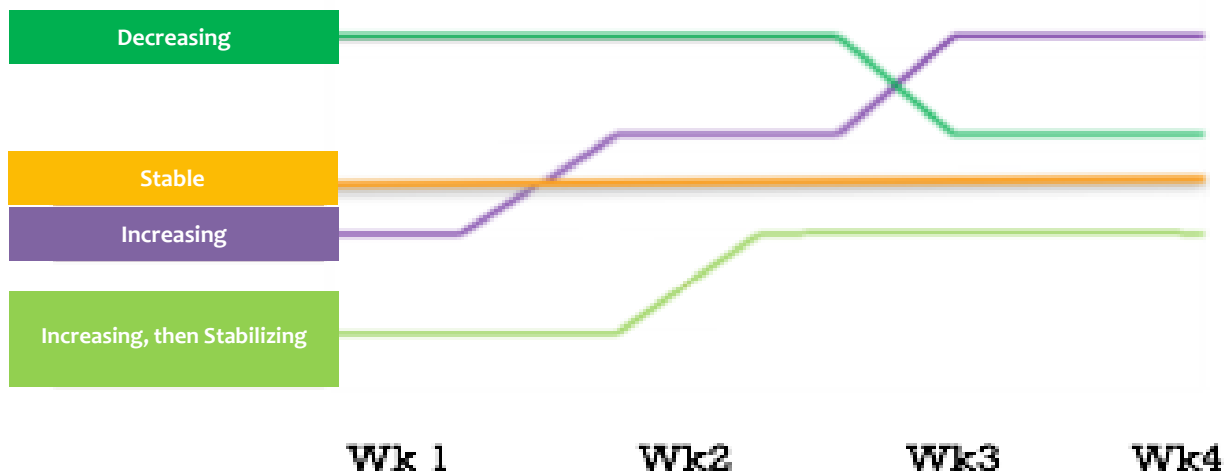


CASI SMS CASI SMS CASI SMS CASI CJA  
 IDI IDI IDI IDI IDI



# SMS & Use Trajectories

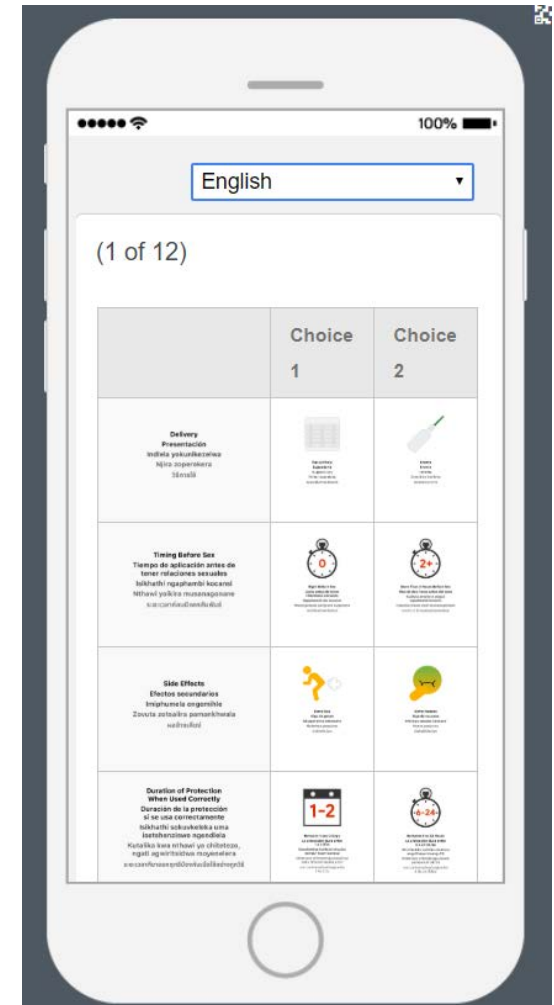
- SMS data used to map trajectories and understand participants' use and acceptability patterns of each product.
- SMS data used to tailor IDI interviews.






# 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.



Where should we be going next  
after 035?



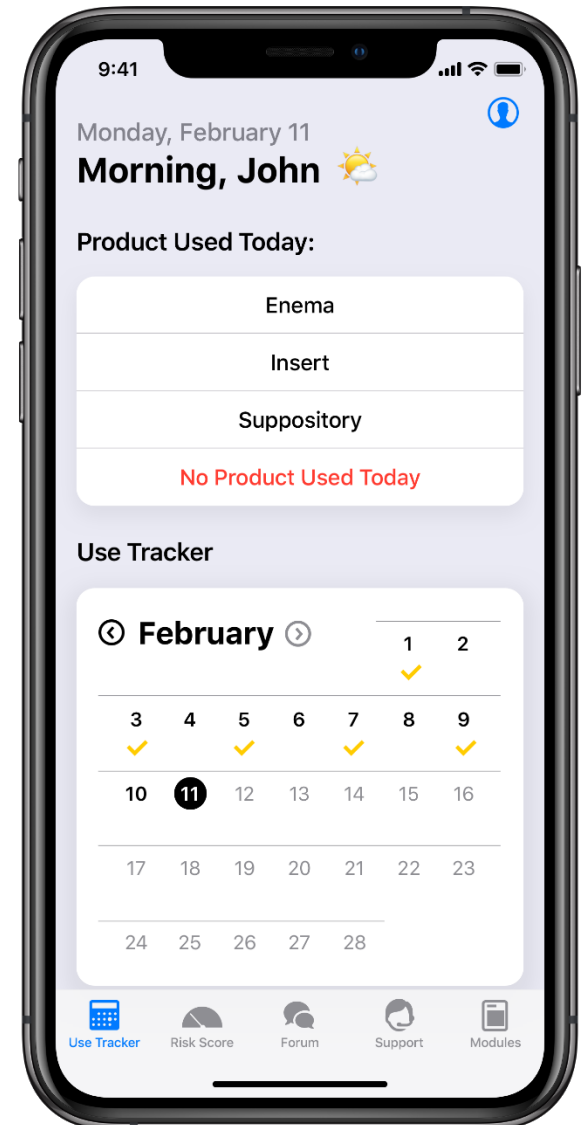
# Where Next?

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- Create opportunities for user-engineer partnerships during formulation design.
- Extend the socio-behavioral platform within clinical trials to include the pilot testing and implementation of behavioral “just-in-time” interventions.
- Leverage trajectory data to support participants with real-time intervention strategies.

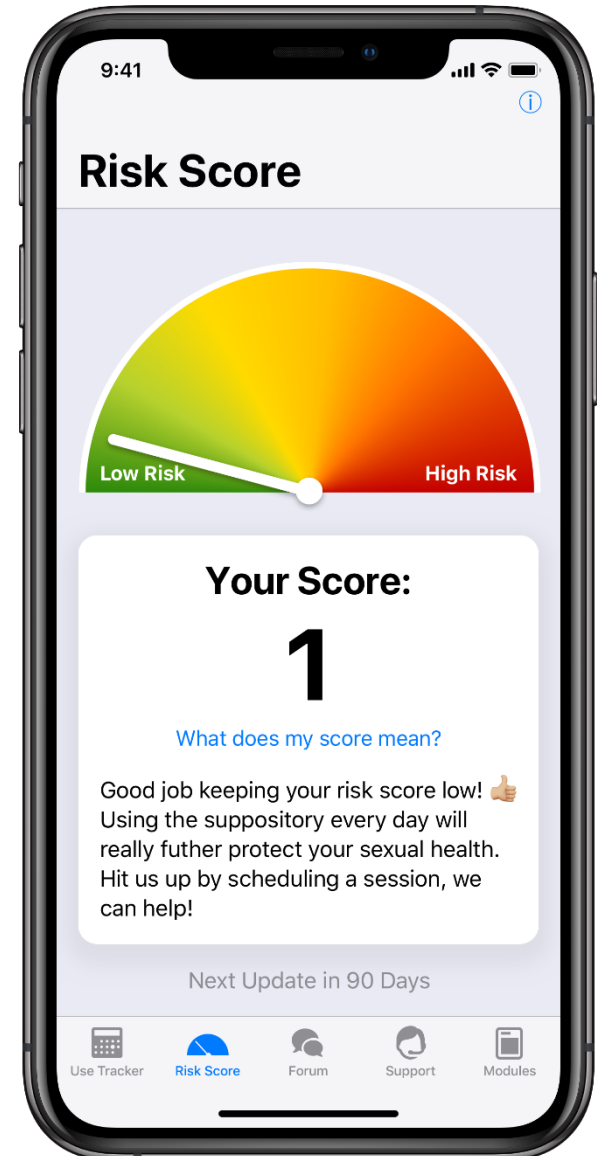
# Behavioral Support in Real-Time

- What if users could...
  - Track their use in real-time



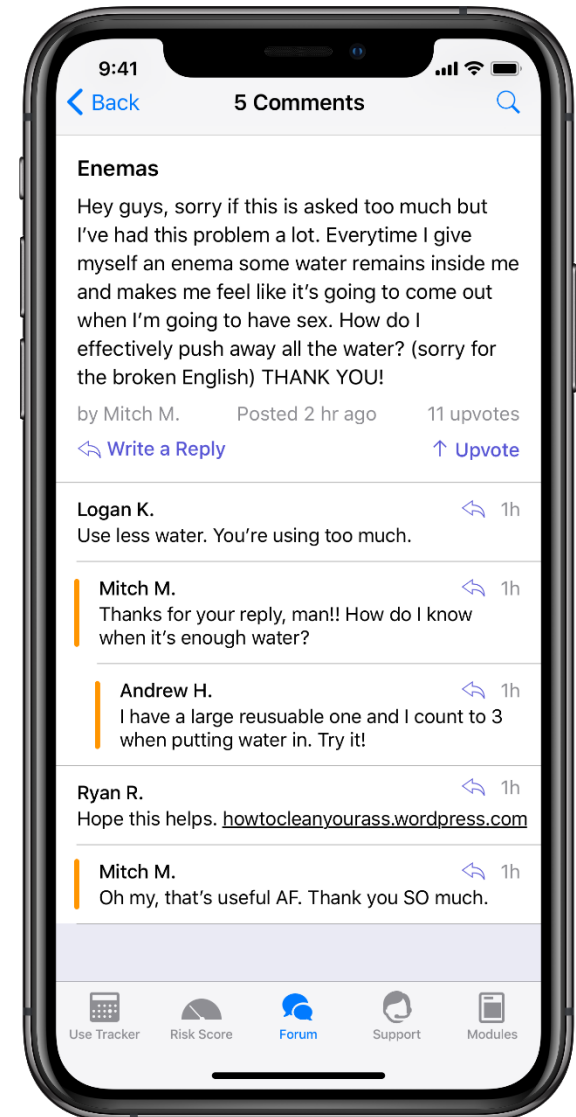
# Behavioral Support in Real-Time

- What if users could...
  - Track their use in real-time
  - Verify their risk over time



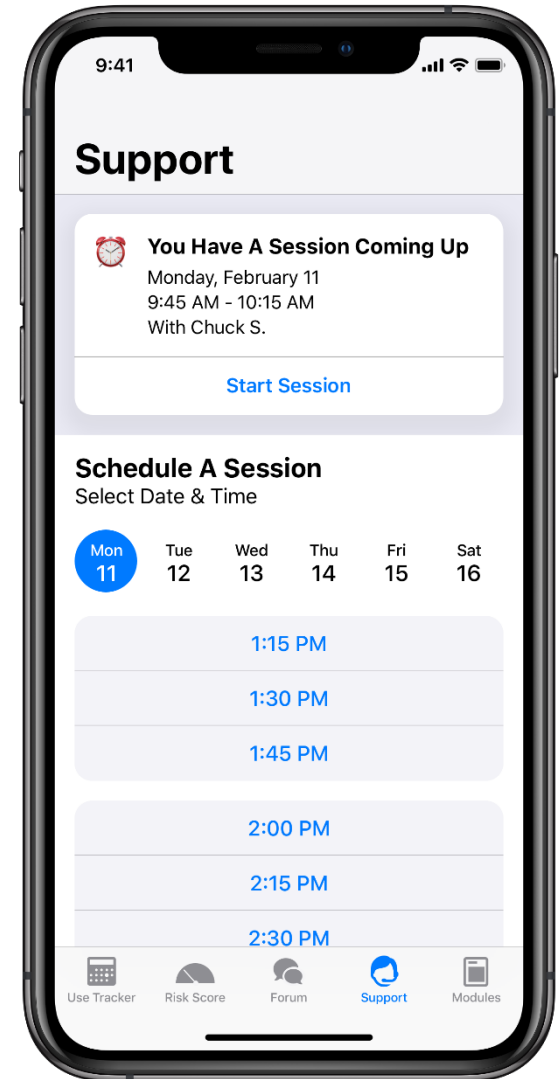
# Behavioral Support in Real-Time

- What if users could...
  - Track their use in real-time
  - Verify their risk over time
  - Create community and garner social support through forums



# Behavioral Support in Real-Time

- What if users could...
  - Track their use in real-time
  - Verify their risk over time
  - Create community and garner social support through forums
  - Access telehealth support and counseling in real-time



# Behavioral Support in Real-Time

- What if users could...
  - Track their use in real-time
  - Verify their risk over time
  - Create community and garner social support through forums
  - Access telehealth support and counseling in real-time
  - Review product-related FAQs







# Acknowledgments



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