



# Novel Prevention Technologies: Lessons Learned and a Glance at the Horizon

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Women's Global Health Imperative

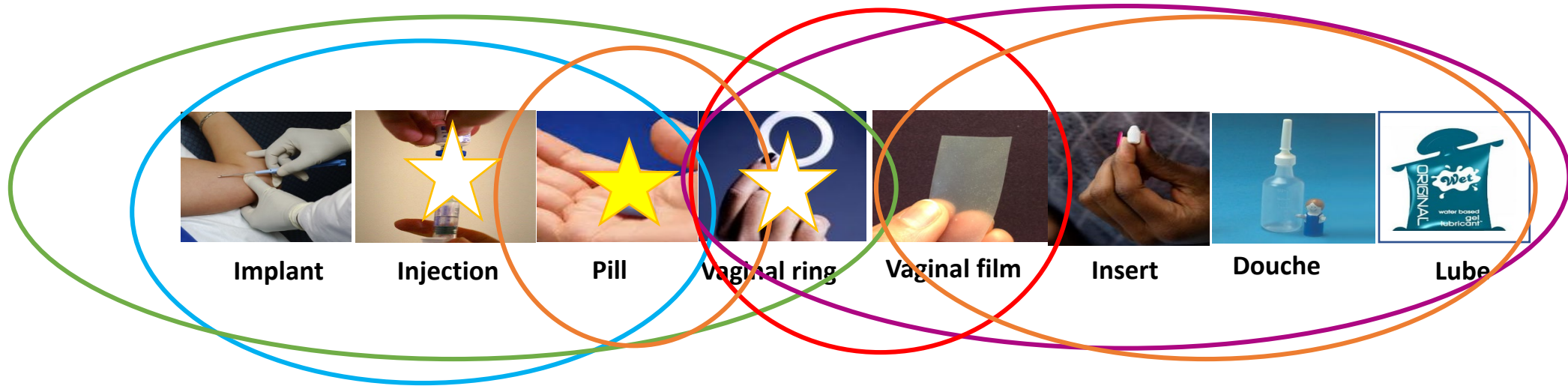
# Agenda

1. The toolbox of biomedical prevention options
2. Novel Technology by Product Pipeline Stages
  - Discovery
  - Development
  - Delivery
  - @ The Horizon
3. Conclusion- the Science of Choice



**Lessons learned**

# 1. The expanding toolbox of biomedical prevention



Options → choices → coverage → impact

**Aqua**= systemic methods

**Green**= Long acting

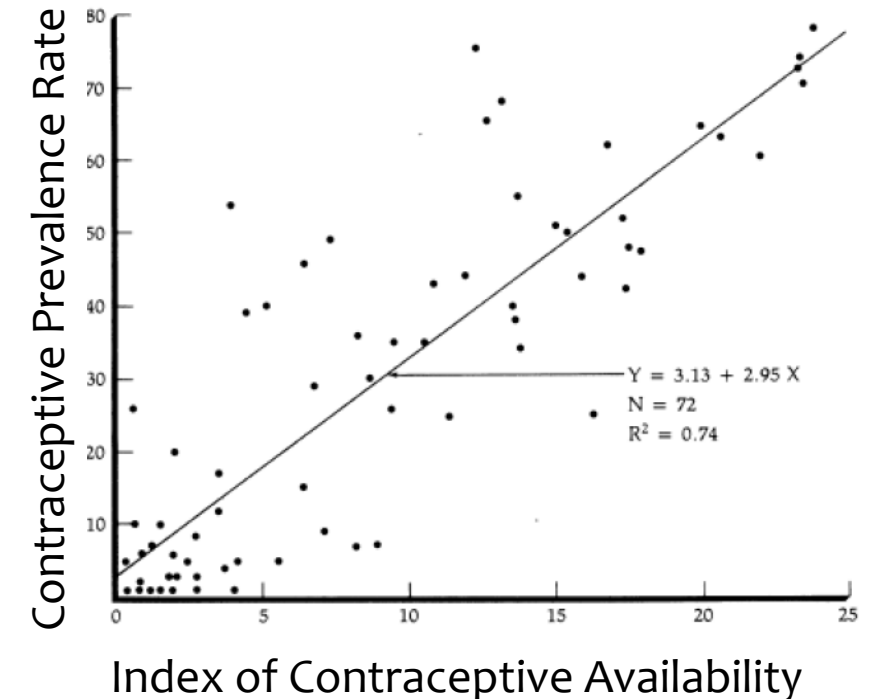
**Pink**= topical

**Red**= vaginal compartment only

**Orange**= on demand

# Benefits of Product Choice: E.g. for Contraception

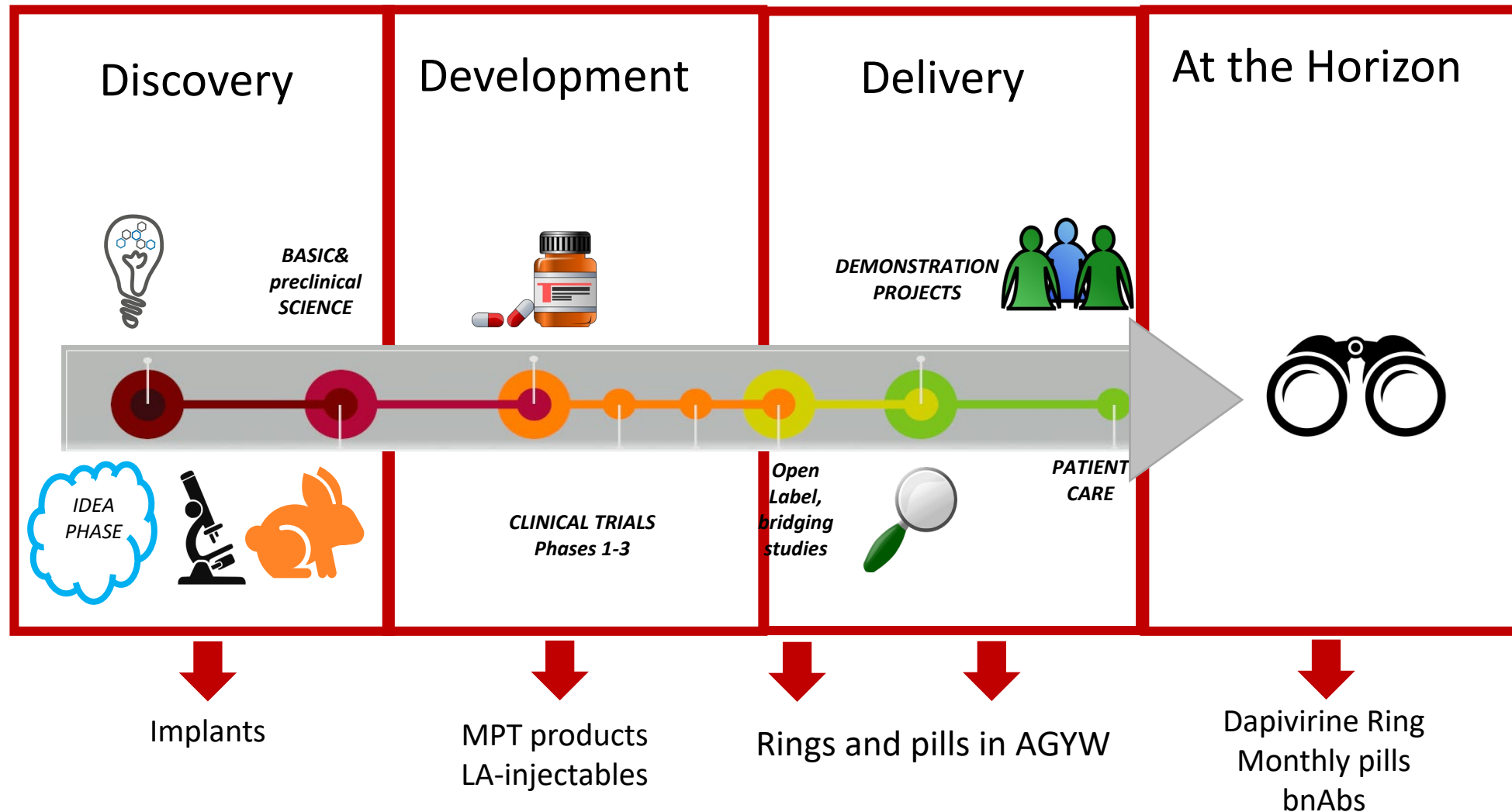
- WHO Systematic Review
- 231 articles, limited high quality evidence
- **Increased choice** associated with:
  - Increased contraception uptake
  - Better health outcomes (fewer pregnancy, STIs)
- Women given contraceptive choice continue their chosen method to a greater degree than those denied choices
- Contraceptive **needs and choices vary over a women's reproductive life**



12% increase contraceptive prevalence for EACH additional method

**How much will it be for PrEP?**

## 2. Novel Technologies by Product Pipeline Stages



# Discovery Stage



**It is never too early to engage end-users in the research**



# HIV PrEP and MPT implants:

## Implant Capabilities:

- Sustained, long-acting delivery of API
  - Capable of dual delivery (ARV + Hormone)
- Biodegradable
- Reversible
- Subcutaneous inserted via commercially available trocar
- Discrete
- User-Independent

## Milestones:

- Demo'ed > 1 year drug release in vitro
- Demo'ed > 6 months constant release in animals
- Demo'ed vaginal efficacy in NHP
- Demo'ed: co-release of hormone and ARV

## **Other implants at clinical stage (non biodegradable):**

- TAF implant (OCIS)
- Islatravir implant (Merck)
- Cabotegravir implant (NW U/ ViiV) [www.rti.org](http://www.rti.org)





# Preferred User Characteristics (PUC):

## Study populations for PUC component



- Young cis-women and men/male partners, health care providers



- Reproductive aged cis-women (aged 18-30 years)



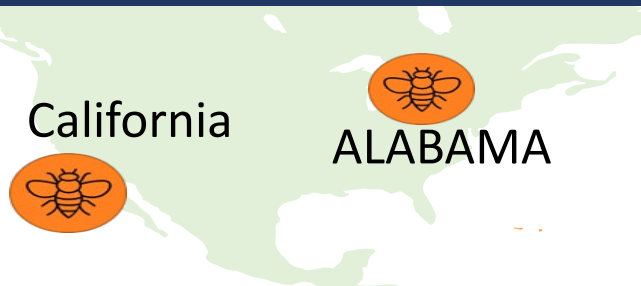
- Men-who-have-sex-with-women-only (MSW)
- Men-who-have-sex-with-men (MSM)
- Cis-women



- Male youth MSM and MSW (aged 18-24 years)



- MSM, TGW, and cis-women at risk for HIV

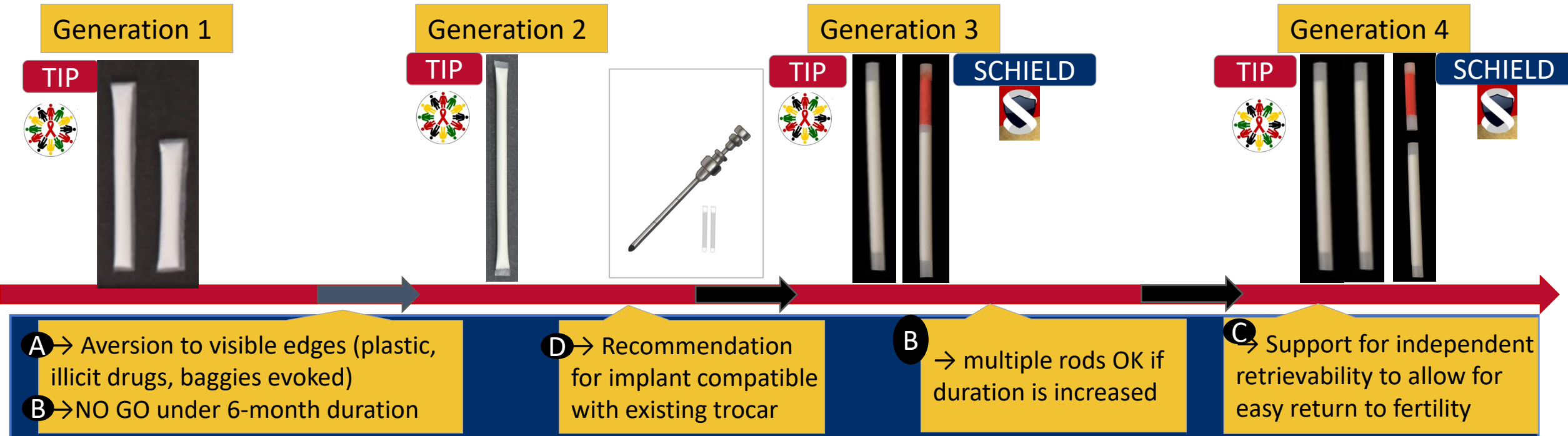


### Methods Used:

- In-Depth-Interviews
- Focus Group Discussions
- Discrete Choice Experiment (DCE)
- Questionnaire surveys

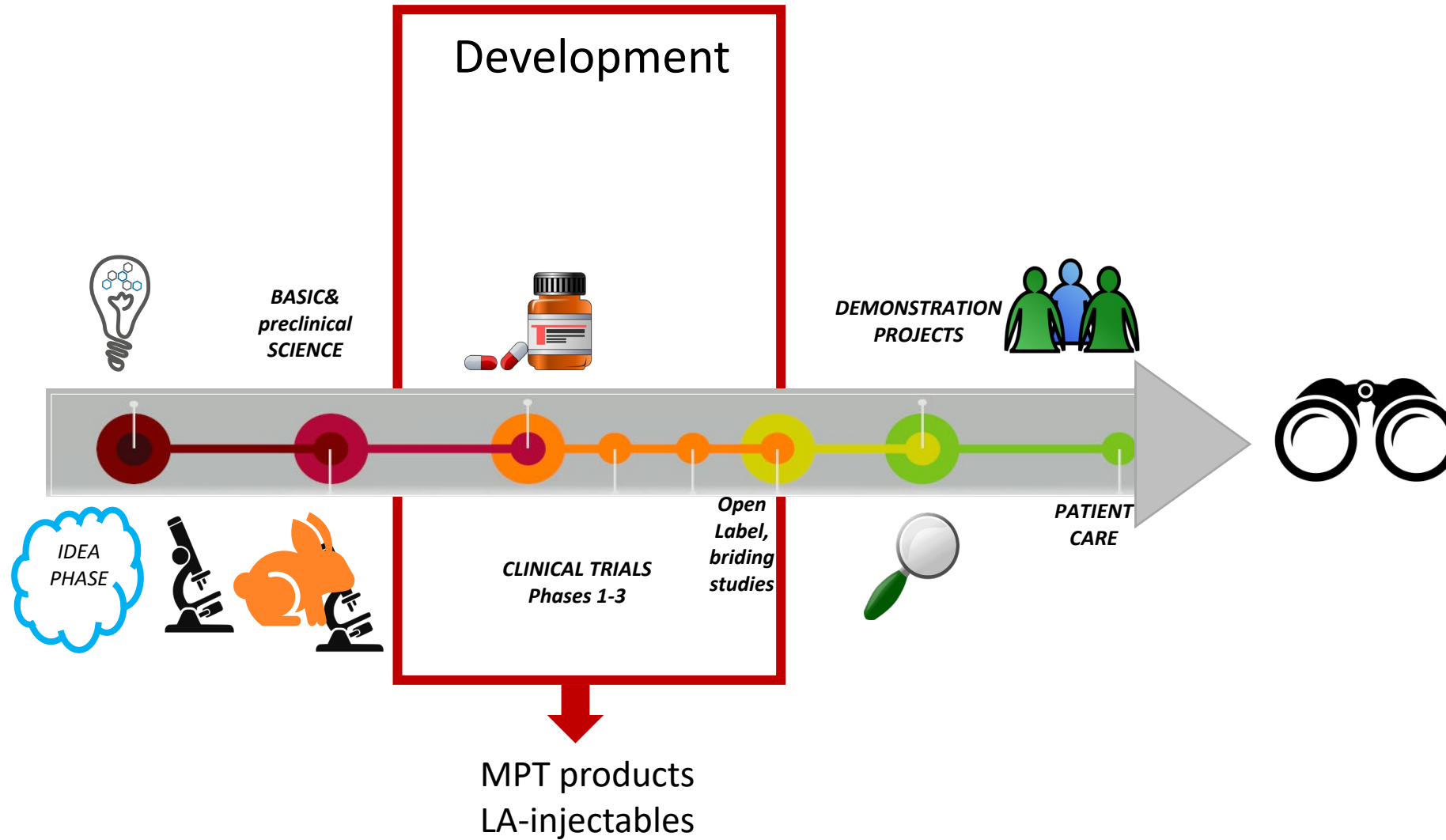











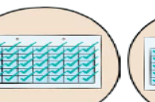
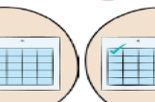
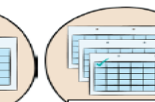


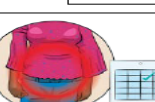
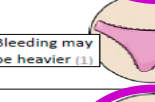

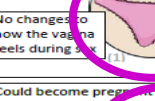
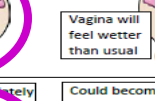
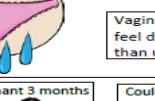
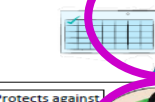


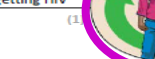

	Question	Who we asked	What the change was
<b>A</b> Appearance	What do you think about these physical characteristics?	Subject matter experts, health care providers, key stakeholders, women aged 18-30	Removal of side seam from Gen1, removal of top and bottom seam from Gen2
<b>B</b> Duration	How long should this implant last?		NO GO for implants that last <6 months Multiple rods OK if duration is increased
<b>C</b> MPT	How should two indications be delivered?		Easily removable contraceptive implant component
<b>D</b> Inserter	How should the implant be inserted?	Subject matter experts, health care providers	Implant developed to be compatible with Jadelle trocar (for cost and training reasons)

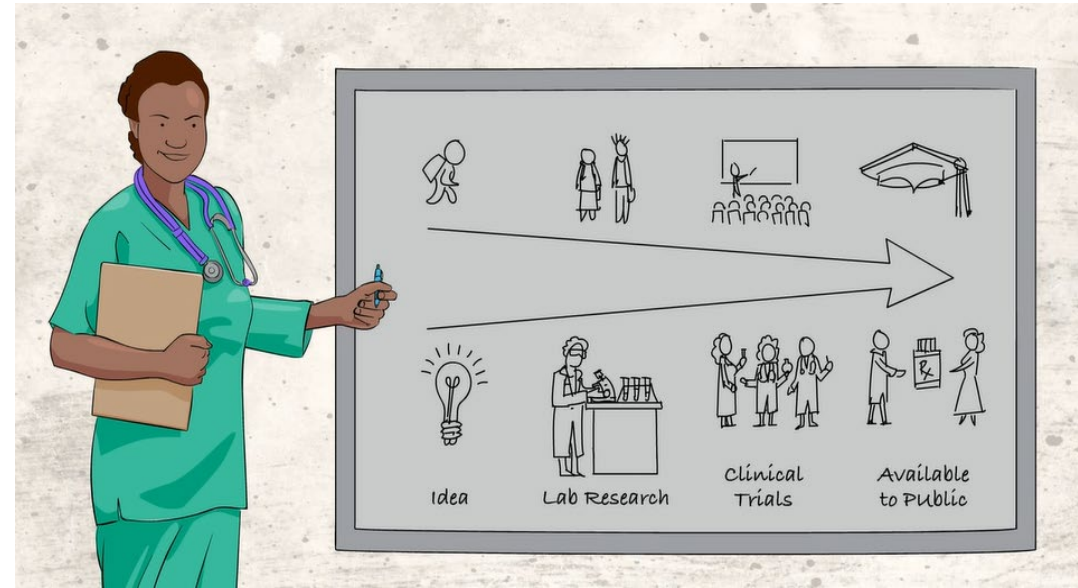
# Development Stage



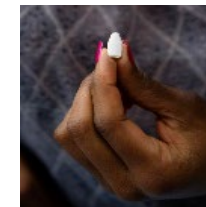
# CUPID/MTN-045: a 400 couples preference study for MPTs

- 400 couples from Uganda and Zimbabwe
- Discrete Choice Experiment (DCE) with 7 attributes
- Subset of qualitative interviews
- DCE done first individually, then jointly by both
- Ideal product activity for couples under D.O

Product	 (1) Oral tablet  (2) Vaginal ring  (3) Vaginal insert  (4) Vaginal film
Duration/ Frequency	 (1) Use before sex  (2) Use every day  (3) Use once a week  (4) Use once a month  (5) Use once every 2-3 months
Side effects	 (1) Headaches/dizziness  (2) Stomach cramps/nausea
Effect on Menses	 (1) Bleeding may be heavier  (2) Spotting or bleeding between menses
How vagina feels during sex	 (1) No changes to how the vagina feels during sex  (2) Vagina will feel wetter than usual  (3) Vagina will feel drier than usual
Return to fertility	 (1) Could become pregnant immediately after stopping use  (2) Could become pregnant 3 months after stopping use  (3) Could become pregnant 6 months after stopping use
Type of protection	 (1) Protects against all ways of getting HIV  (2) Only protects against HIV during vaginal sex



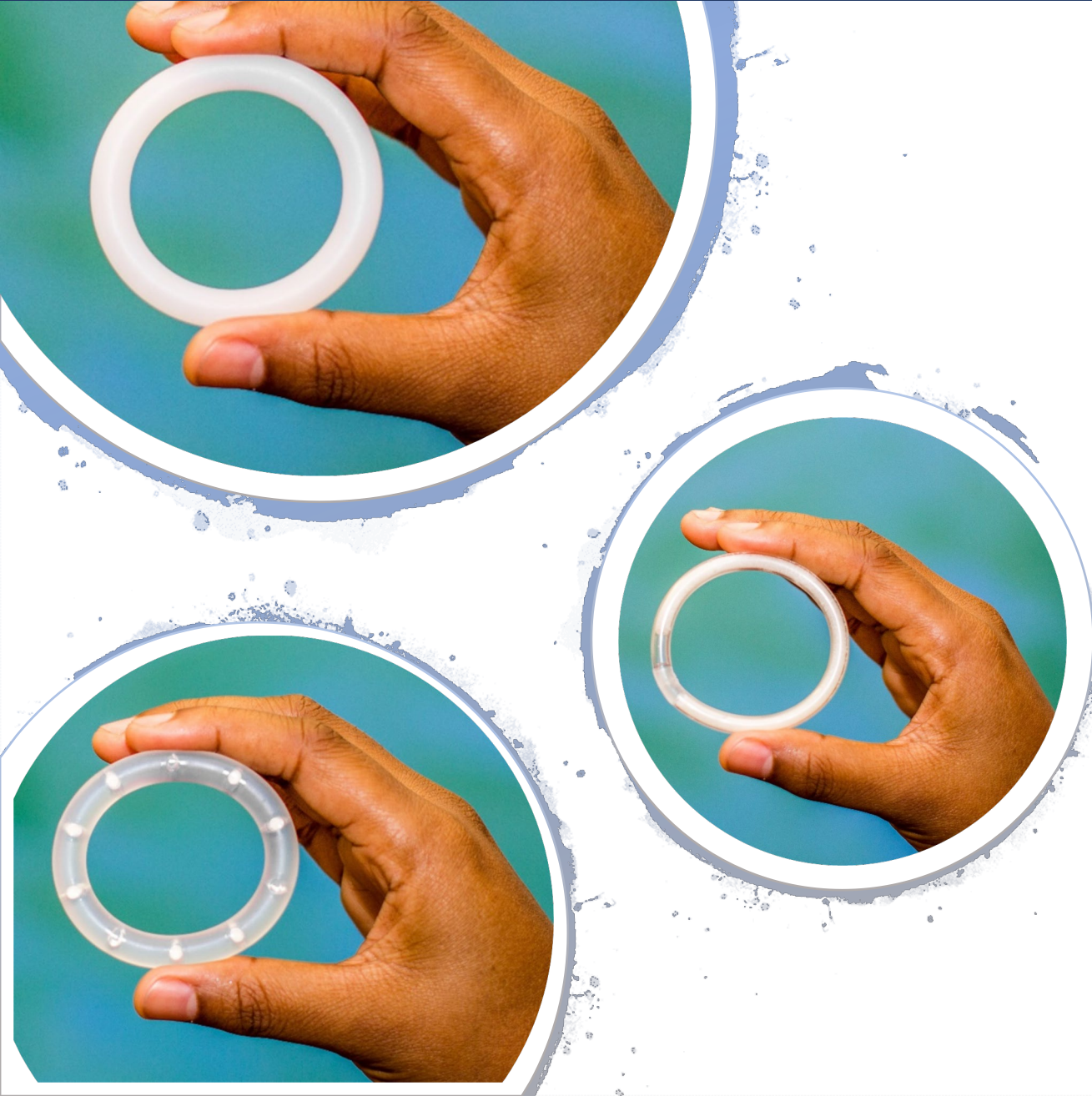
Informational video (product pipeline)



4 Delivery Forms are evaluated:  
Vaginal Ring; Film; Insert and Oral Tablet



# MPT Rings



## International Partnership for Microbicides (IPM)

- HIV PrEP & contraceptive ( LNG/DVR) 3-month ring
- MTN-044: Open label Phase 1 with continuous or monthly removal for approximately 90 days (N=24)

## CONRAD-128

- TFV/LNG ring for HSV2, HIV & contraception
- **CONRAD-128:** Placebo-controlled RCT phase I trial assessing TFV, TFV/LNG ring for 2 weeks (N=51)

## OCIS

- Pod ring delivering TAF/ACV/ENG+EE to prevent HIV, HSV2, contraceptive
- Evaluated in pigtailed macaques (N = 6) over 35 days

# MULTIPURPOSE PREVENTION TECHNOLOGIES (MPTs)

ARE NEW METHODS **IN DEVELOPMENT** THAT COMBINE FAMILY PLANNING, HIV & STI PREVENTION

**89 MILLION**  
**UNINTENDED**  
**PREGNANCIES**  
**AROUND THE WORLD**  
**EVERY YEAR**

**EVERY 4 MINUTES**

**WOMEN**  
**NEED**  
**BETTER**

**FOR WOMEN'S HEALTH**

**HIV**  
**PREVENTION**

**STI**  
**PREVENTION**

**MPTs**

**CONTRACEPTION**



**When you can, bundle your indications**

**1 MILLION PEOPLE**  
**CONTRACT AN**  
**STI EVERY**  
**DAY**

- **EFFICIENT**
- **FEMALE INITIATED**



**RINGS & ONE-SIZE-  
FITS-ALL  
DIAPHRAGMS**



**GELS  
& FILMS**



**MULTIPURPOSE  
VACCINES &  
INJECTABLES**



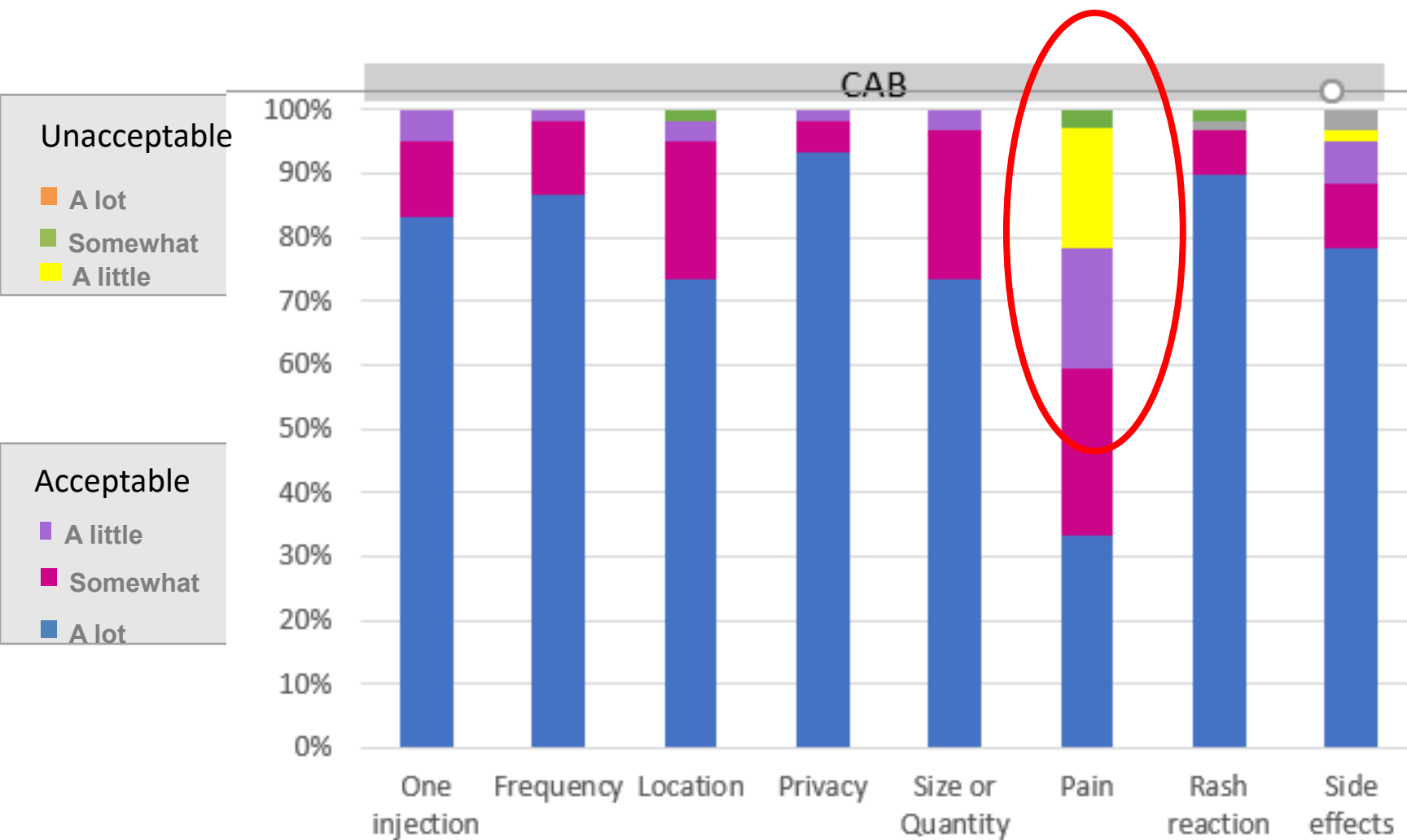
**DRUG  
COMBINATIONS**




**SUPPORT MPT RESEARCH**

**[WWW.MPTs101.ORG](http://WWW.MPTs101.ORG)**

# HPTN 077: Acceptability of CAB-LA



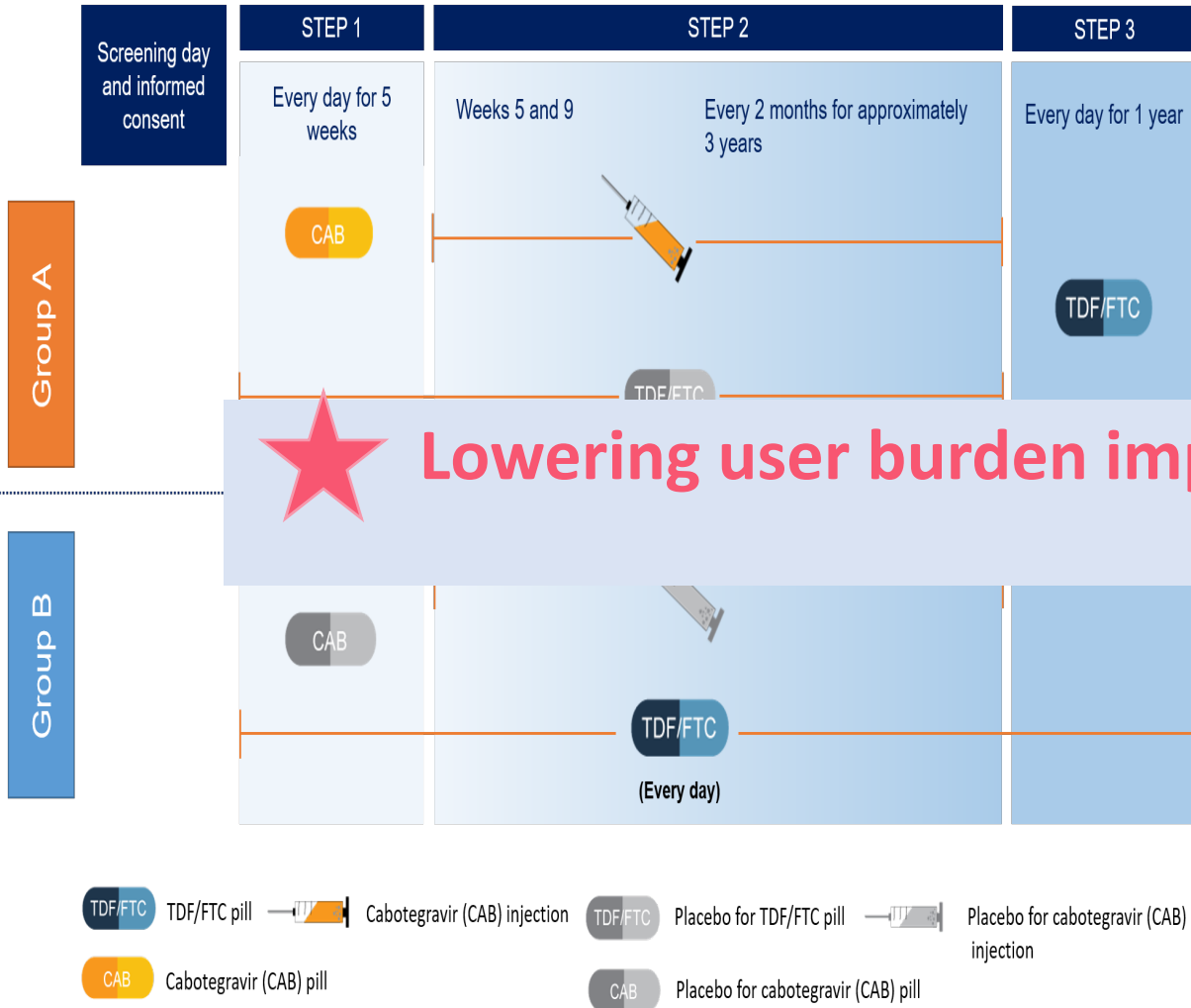
**Cohort 2**



600 mg per 1 injection

**1<sup>st</sup> 2 injections 4 weeks apart, then every 2 months, 3 cycles**

# HPTN 083/084: Efficacy of CAB-LA



**Lowering user burden improves product effectiveness**

## HPTN 083:

- N=4570 MSM/TGW
- CAB-LA provided **high efficacy** compared to TDF/FTC
- CAB LA was found to be **statistically superior** to daily oral TDF/FTC for PrEP
  - 50 incident HIV infections occurred

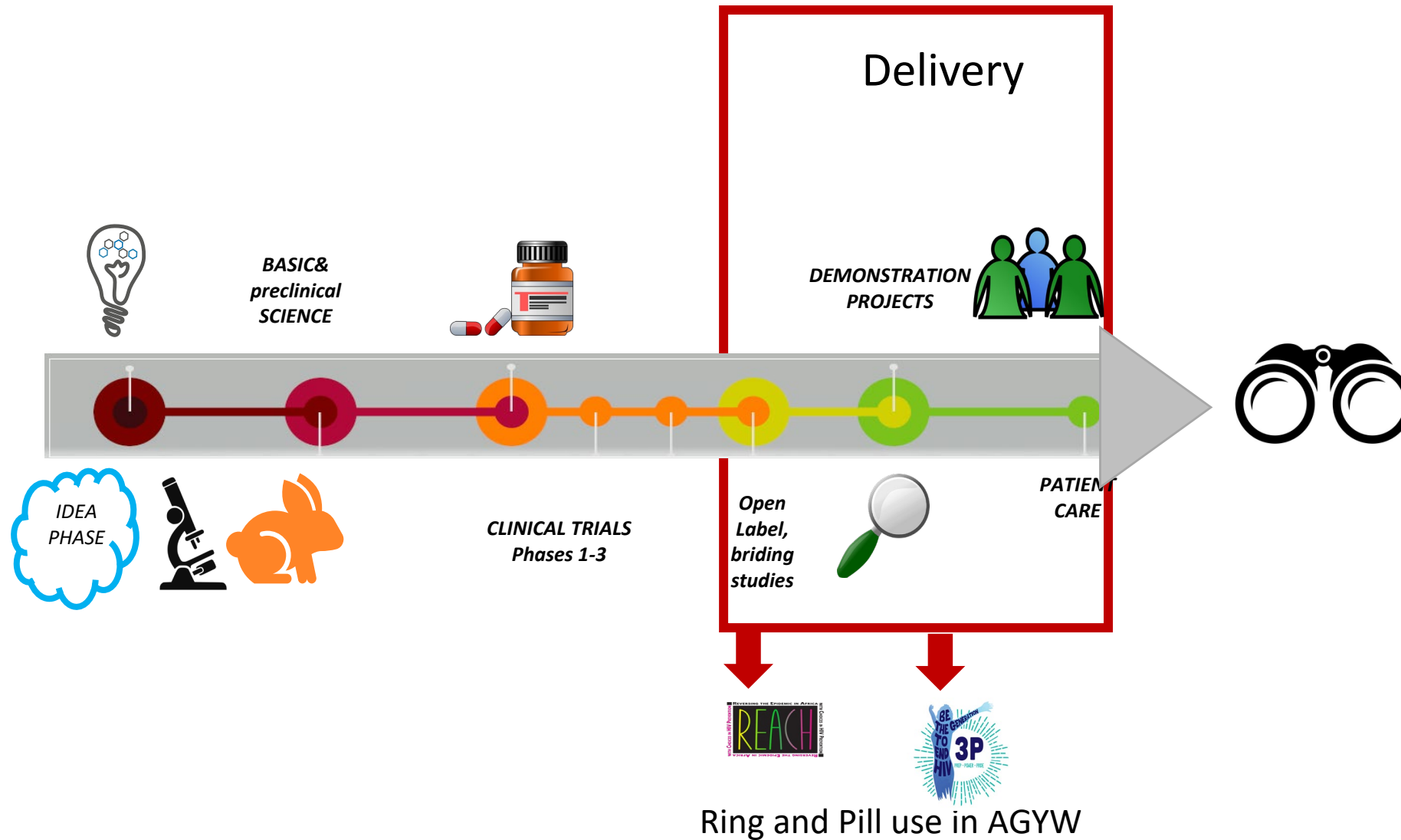
➤ TDF/FTC 50 incident HIV infections (0.38% incidence rate)

- Status: **Halted early for efficacy.** Moving into OLE

## HPTN 084

- N=~ 3,200 women (aged 18-45 years) in sub-Saharan African who are at risk for acquiring HIV
- Status: **ONGOING**

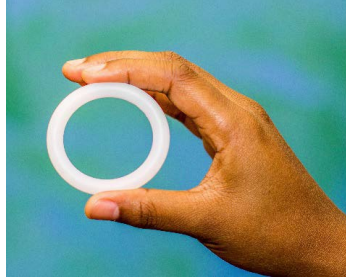
# Delivery Stage



Ring and Pill use in AGYW



# MTN-034/REACH: Cross-over open label phase IIa trial



Choice, Preference and Use  
N=300 AGYW aged 16-21

4 Locations

Status: c



**Providing choice is empowering and increases autonomy**

**All participants use PrEP and the ring – each for 6 months – and then they can *choose* which to use for another 6 months**

ACASI/CRFS

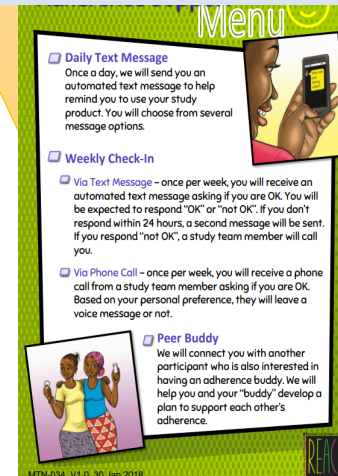
Stated  
preference;  
Willingness to

Product  
choice

Qualitative

To explore  
preference,

Drug level  
feedback





# 3P for PrEP Among AGYW Aged 16-25 N=200



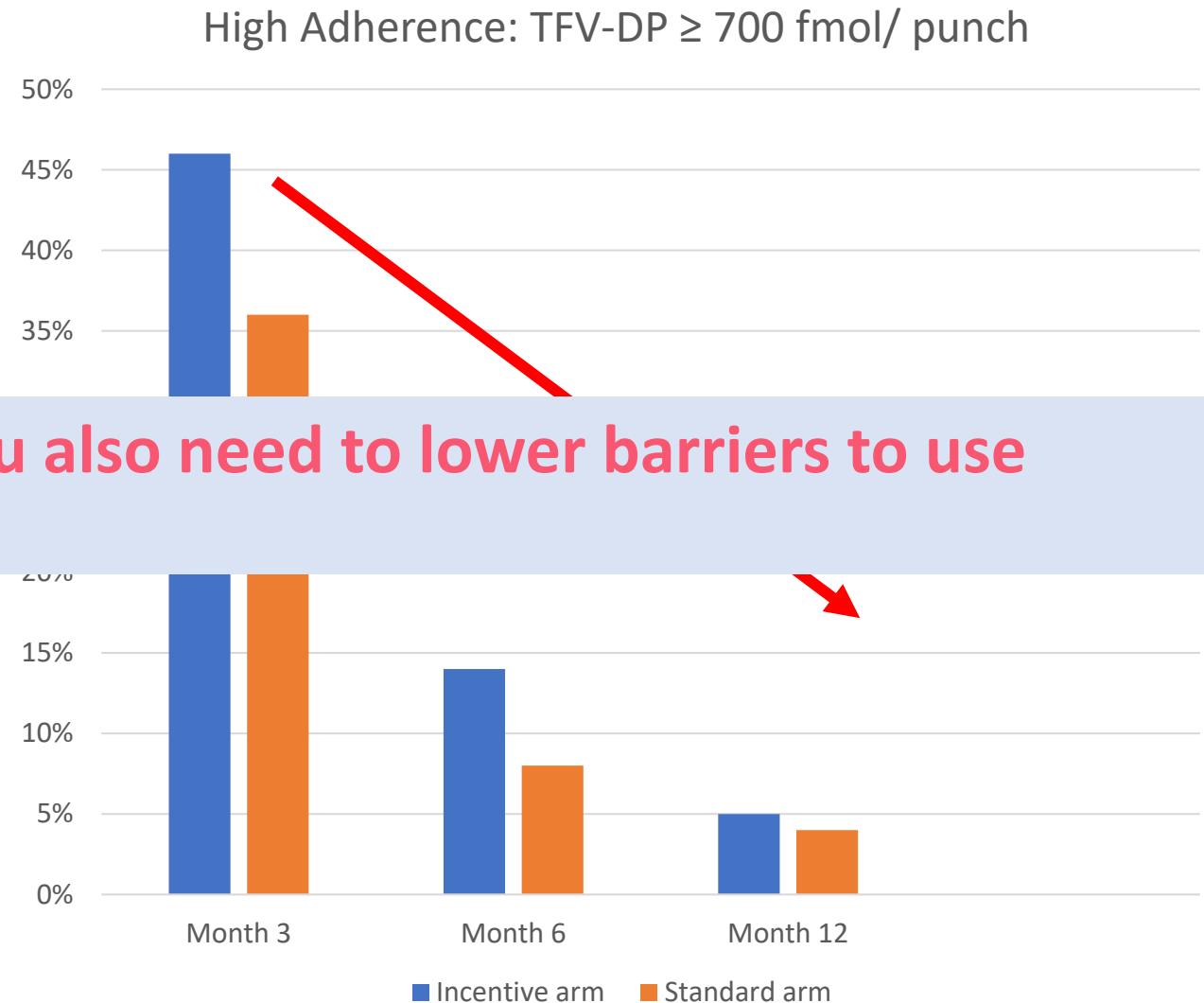
- Median age:19 (IQR 17-21)
- 78%  $\geq$  secondary education
- $\frac{1}{2}$  randomized to **incentive arm** (counseling at months 2 and 3 about the prior month's drug level with a



**Incentives can help, but you also need to lower barriers to use**

2 and 3 about the prior month's drug level without an incentive).

- At 3 months, < half had high adherence (TFV-DP in DBS  $\geq 700$  fmol/punch)
- The proportions with high adherence decreased from M3 to M6 and M12

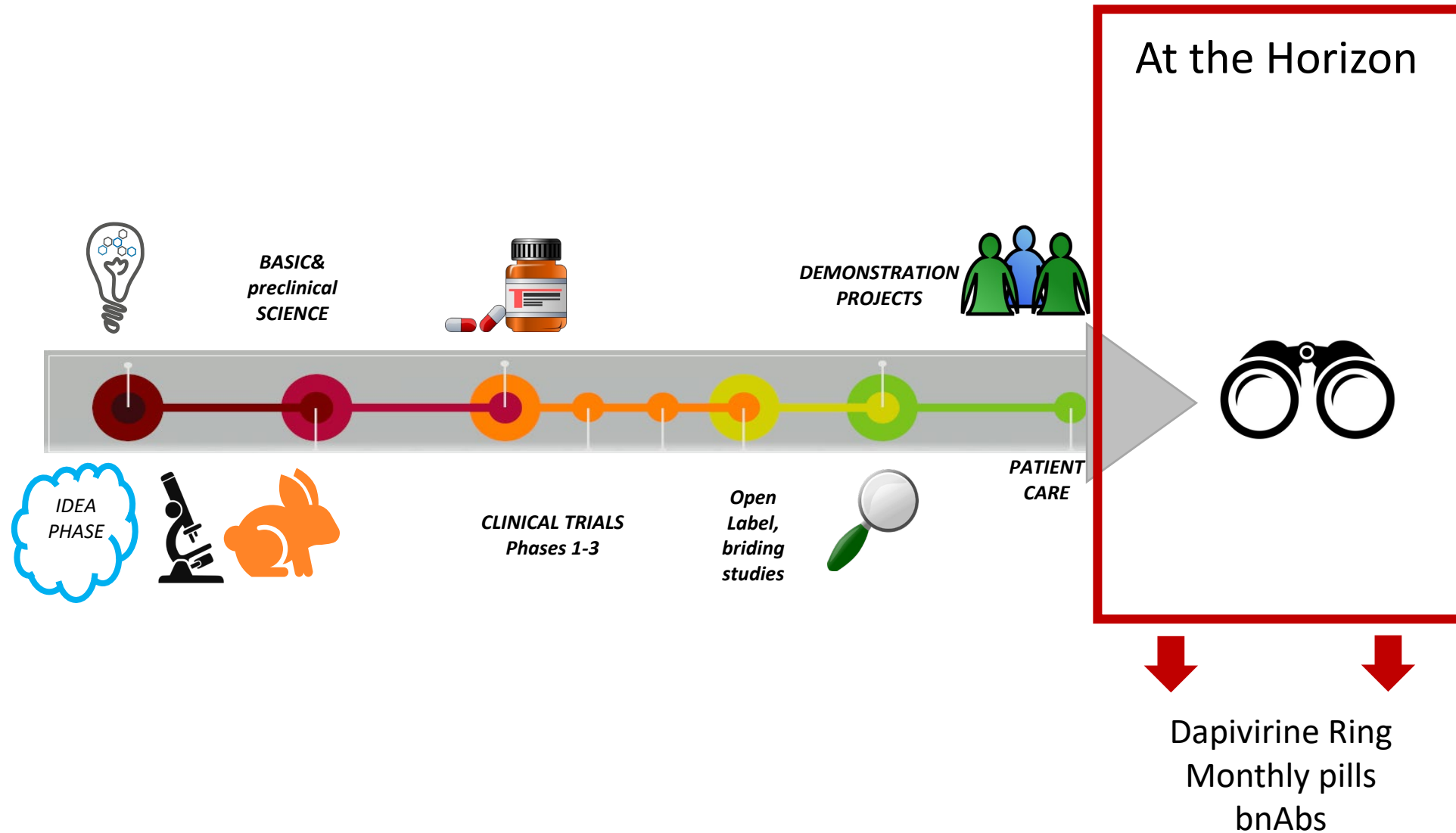




## Lessons learned

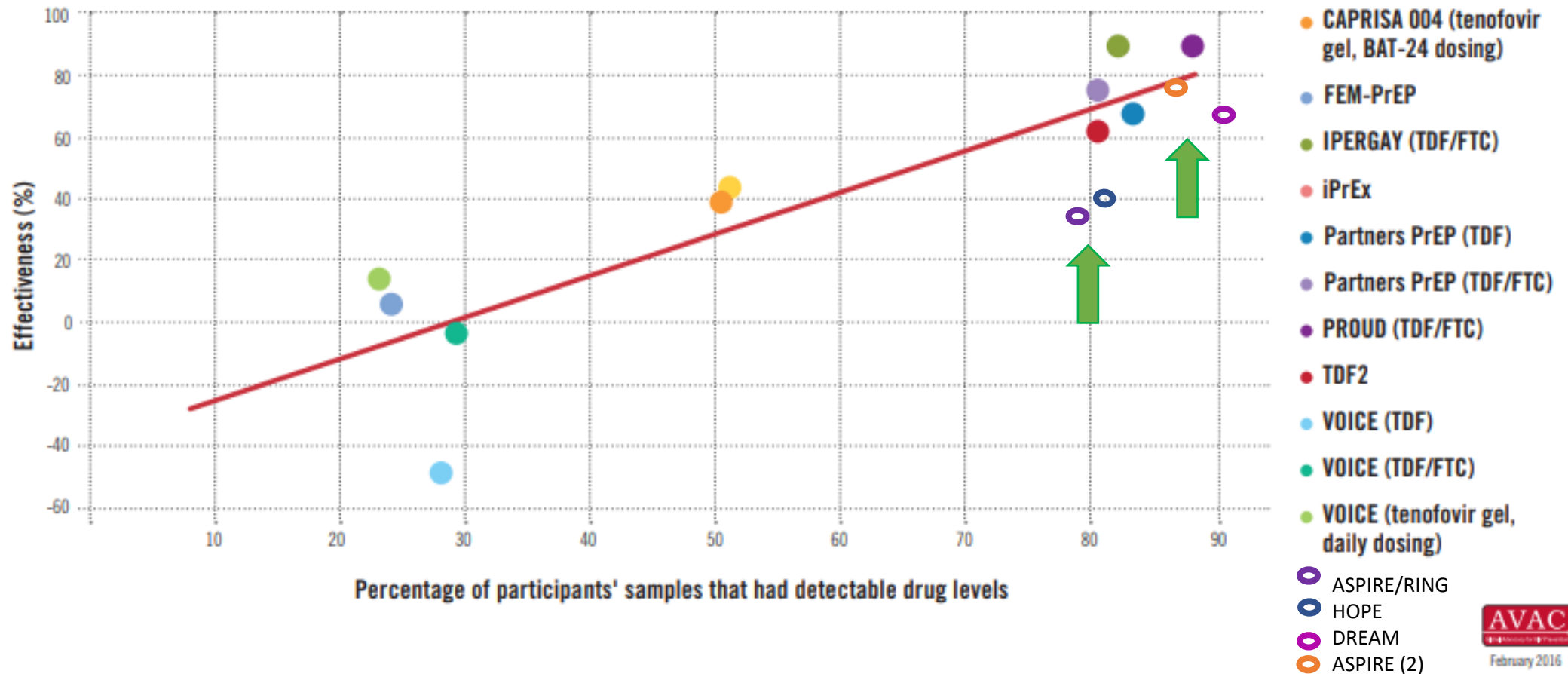
1. It is never too early to engage end-users in the research
2. When you can, bundle your indications
3. Strategies that help lower user burden improve effectiveness
4. Providing method choice is empowering and increases autonomy
5. Incentives can help, but you also need to lower barriers to use

# Product Development Pipeline: At the Horizon



# @ The Regulatory Horizon: The Dapivirine Vaginal Ring

## PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



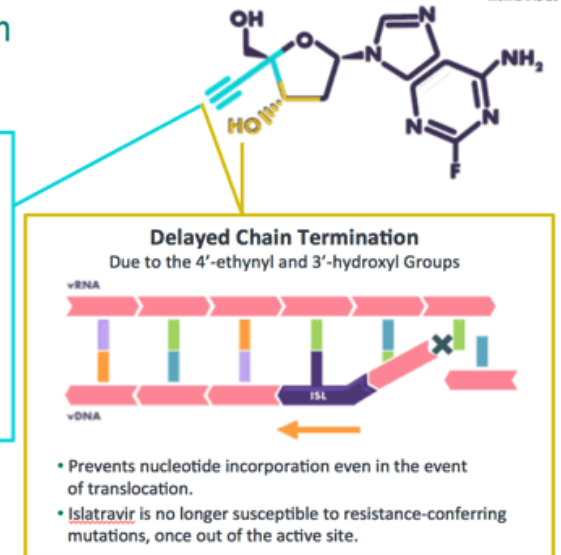
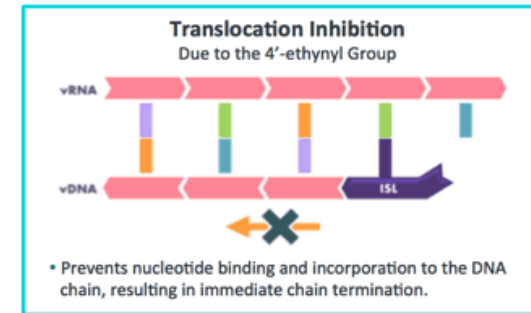
# @ Clinical Horizon: Islatravir Multiple Dosages & Indications

## Islatravir, NRTTI

formerly known as MK-8591 and EFdA, halts construction of new viral DNA by acting as a defective building block and acting at a later step in the viral replication process

- Can be dosed once a week
- Under investigation as a potent form of post-exposure prophylaxis (PEP), for monthly oral dosing as PrEP, or for even longer which will be given in an implant form (1 year)

Islatravir, a First-in-Class NRTTI with Multiple Mechanisms of Action



## TAKING PrEP TO PREVENT HIV

People who use PrEP must commit to **taking it every day** and seeing their health care provider **every 3 months for follow-up**.

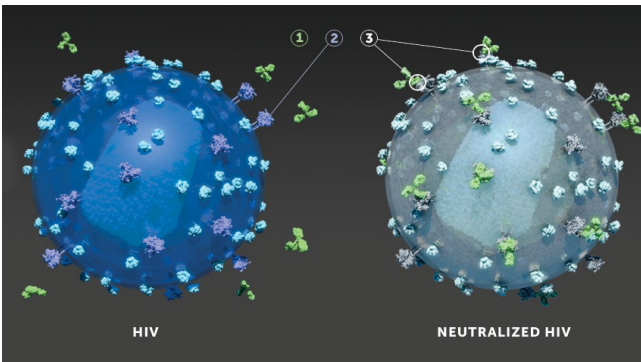
Week or Month



HIV.gov







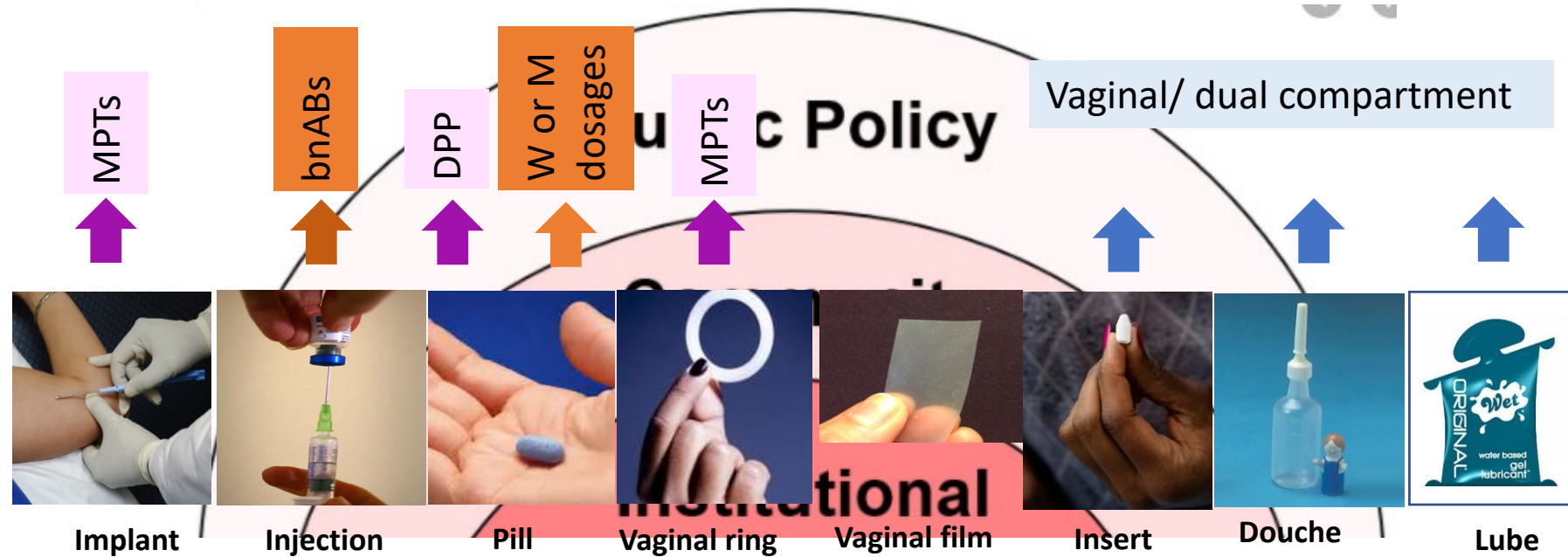
## Antibody Mediated Prevention (AMP) Study (HPTN 081 and 085)

- Giving people antibodies to see if the antibodies will protect them from getting infected with HIV
- AMP study (phase IIB trial) is the first study testing if antibodies can prevent HIV infections in people

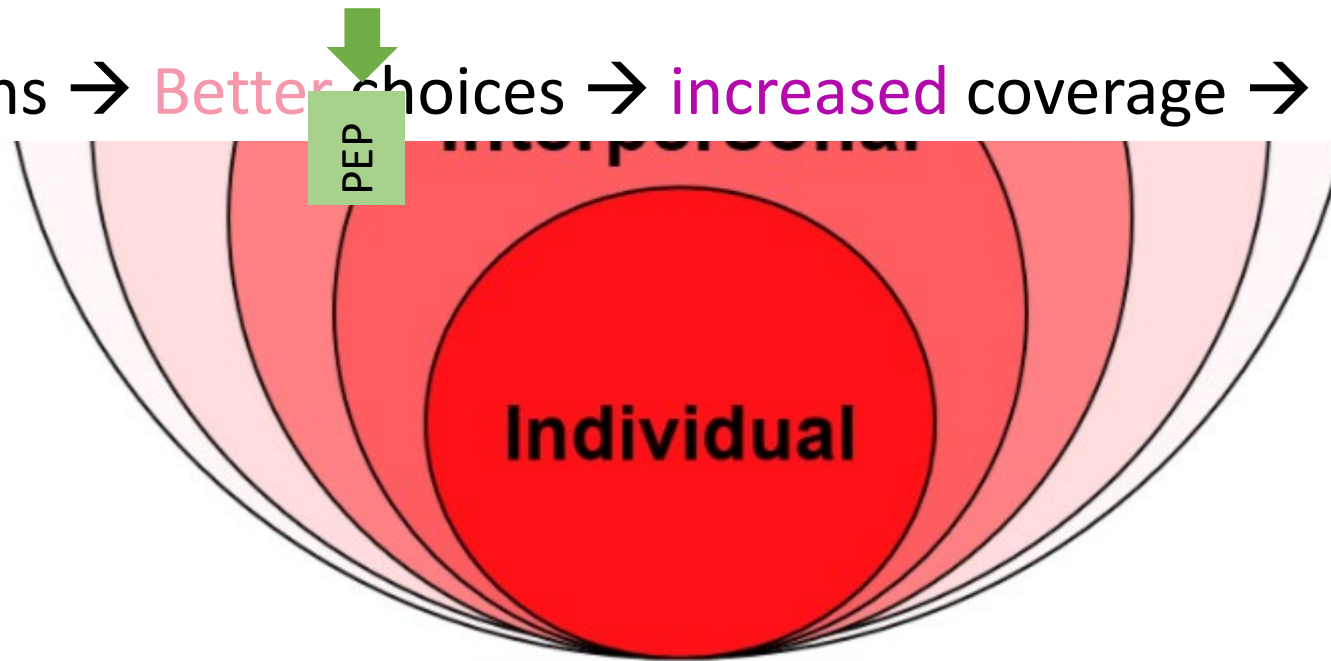
## bnAbs

- Rare antibodies that latch on to HIV virus and hinders the virus from attaching to human cells, neutralizing different forms of HIV virus from around the world
- In AMP, a bimonthly infusion of a bnAb called VRCO1 is evaluated as an HIV preventative strategy (N=4,625)
- The goal is to use these antibodies to create new ways to combat HIV infection
- A new phase I trial (HVTN127/HPTN 087) evaluates VRC07-523LS (a longer lasting and more potent bnAB) via infusion, SubQ injection and IM injection

### 3. More Options → Better Choices: The science of informed choice

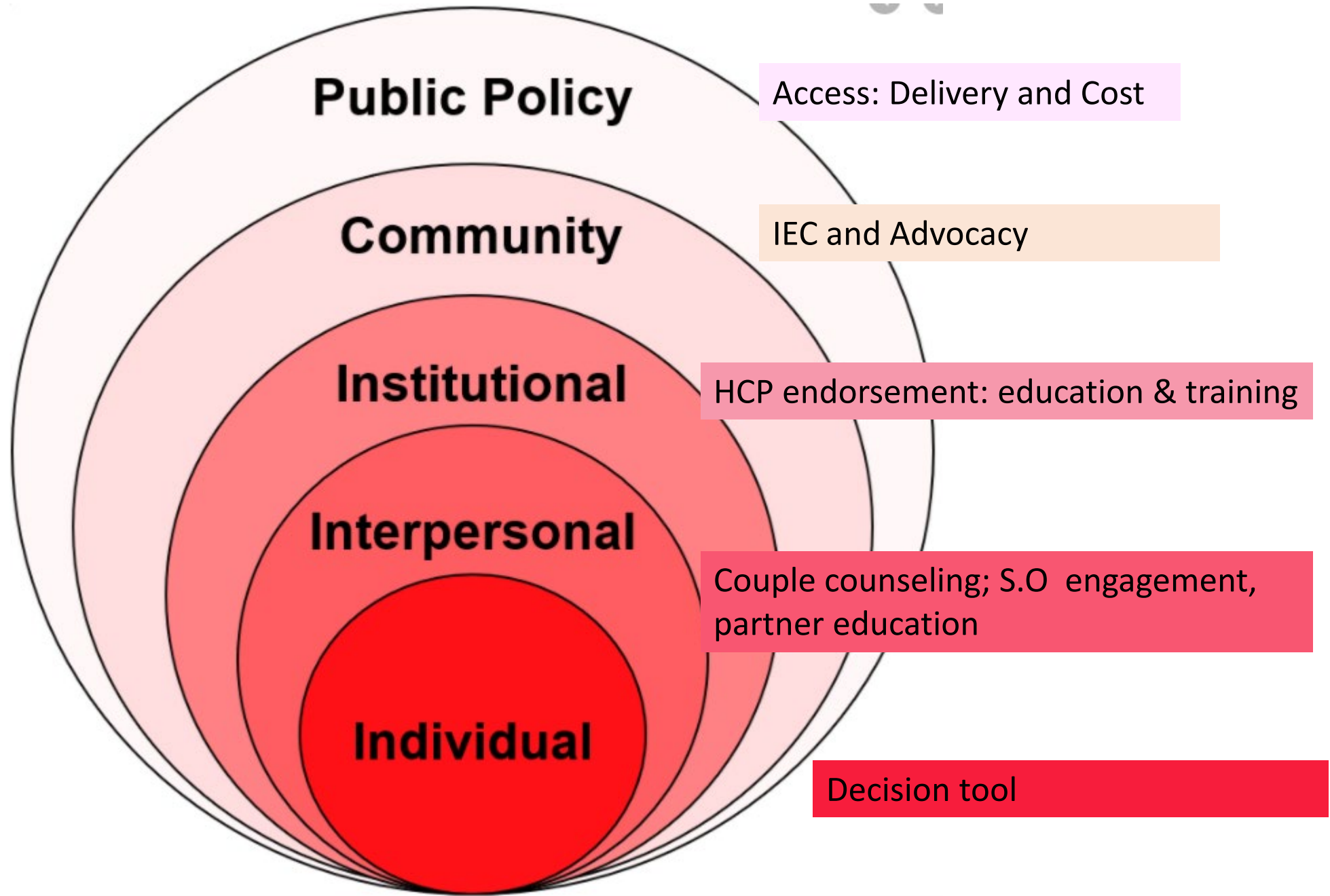


More Options → Better choices → increased coverage → higher impact





# The science of informed choice



# Studies, Collaborators and Funders

SAMURAI



Desmond Tutu HIV Centre  
Masibambane Ngezandla



BILL & MELINDA  
GATES foundation



# Thank you!!













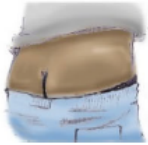


# Questions?

Contact: [ariane@rti.org](mailto:ariane@rti.org)

EXTRA SLIDES

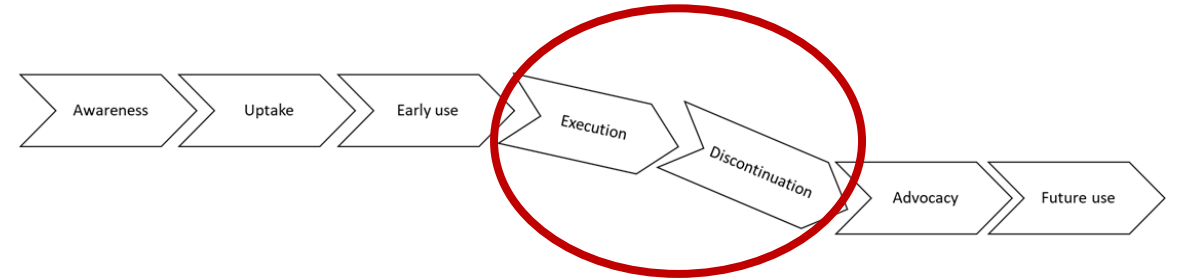


## DCE Characteristics

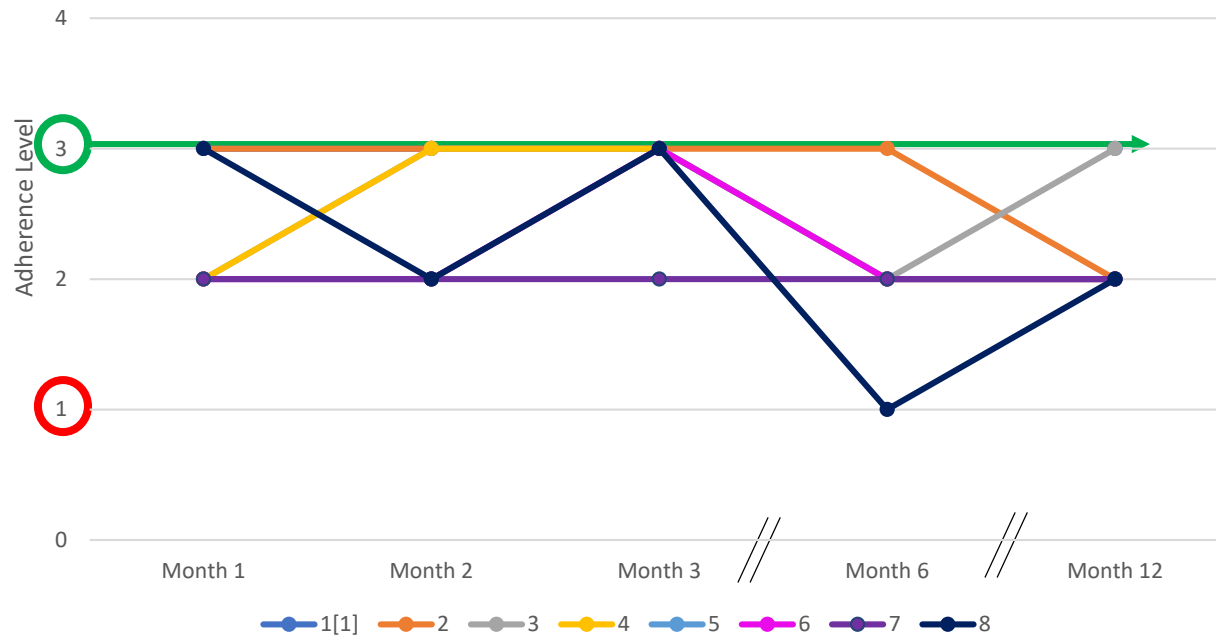
Attribute	Levels			
<b>Product form</b>	Implant 	One Injection 	Two Injections 	
<b>Duration</b> – how often you will need to get a dose	One dose every 2 months 	One dose every 6 months 	One dose every year 	
<b>Where it is available</b>	Pharmacy 	Health clinic 	Mobile clinic (like Tutu Testers) 	Community site (like a library or community hall) 
<b>Soreness after injection/implant</b>	Mild 	Moderate 		
<b>Location of injection/implant</b>	Bum 	Thigh 	Upper Arm 	

- DCE is designed to elicit product preferences by examining trade-offs individuals make when choose between alternate product designs
- iPrevent enrolled youth (MSW, MSM, females) in a DCE to determine their preferences for an HIV-prevention products
- Key Finding:** Duration was the major driver of preference

# 3P Adherence Level (Persistors and Non-Persistors): an end-user journey



Adherence Heat Map of Persistors in 3P Study over 12 Months (n=8)



Adherence Heat Map of Non-Persistors in 3P Study over 12 Months (n=14)

