



# MTN 034/IPM 045: REACH

## Rings and PrEP in Young Women

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On behalf of MTN 034 protocol team

MTN Annual Meeting: 2017

Bethesda North Marriott Hotel and Conference  
Centre

# CAN A PILL A DAY PREVENT HIV?

FOR INFORMATION ON THIS NEW AND  
EXCITING HIV PREVENTION STUDY

SMS "info" at no cost to 30060 or  
e-mail MCMHP@hiv-research.org.za

All participants will be compensated for their time and transport.



## MTN 034



## Safety and Adherence Study of the DPV (25 mg) VR and TDF/FTC Tablet in a Young African Female Population

- VR safety data will be provided by MTN 020, MTN 023 and other studies
- PrEP efficacy: iPrEx (44% effective), Partners PrEP (75% effective) TDF-2 (62% effective)
- MTN 034: safety and tolerability among **African adolescents and young women**

# OVERVIEW

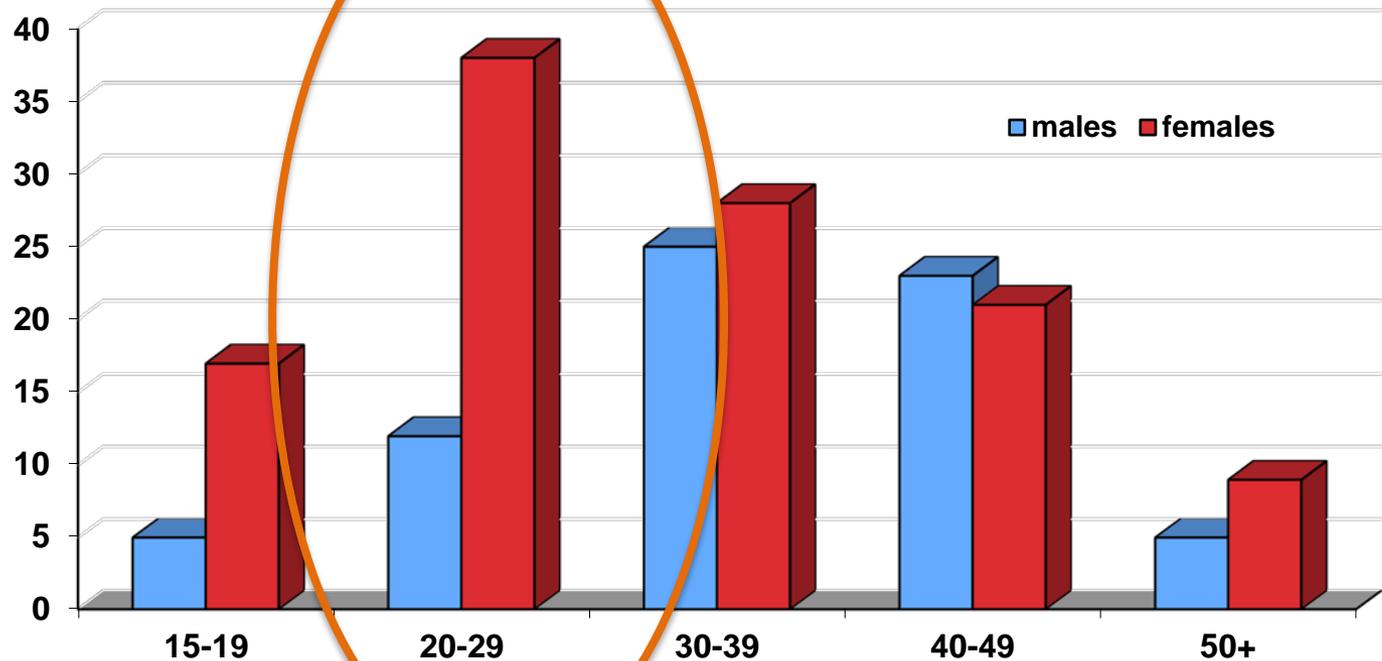
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- Rationale for REACH implementation
- Rationale for study design
- Timeline

# RATIONALE:

**AIDS is the #1 cause of adolescent deaths in Africa  
And the #2 cause of adolescent deaths globally.**

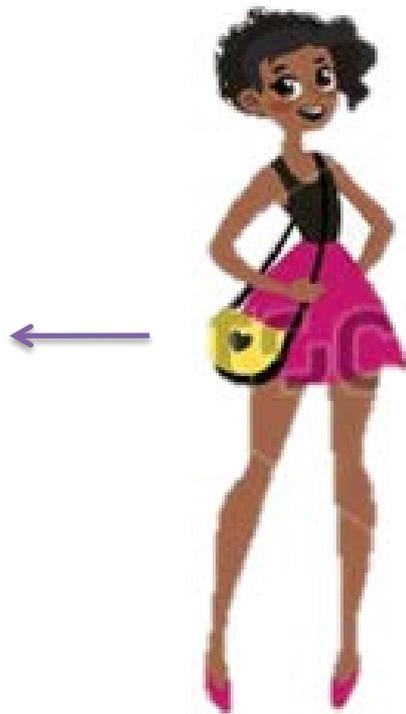
19-24 years: **4x** higher than  
male peers



15-19 years: **8x** higher than  
male peers

# Increased vulnerability associated with several factors:

Adolescence is a time of **high risk taking & experimentation**, with high susceptibility to peer pressure. Often unable to negotiate safe sex. (behavioral and decision making capabilities)



Relationship dynamics-  
Phylogenetic studies: new HIV infections in SA from heterosexual transmission **to young women from men on ave 8 years old** (de

Oliviera et al., 2016)

High rates of Gender-based violence

Social protection and Economic factors

(Cluver et al, 2015,2016)

**2000 new infections in young women in South Africa every week.**

# Risk for HIV acquisition

150 Healthy 15-19yo, Sexually active  
40:60 M:F Masiphumelele and Soweto

- 9% pregnant at screen
- 2% HIV infected at screen
- 40% reported condomless sex
- 27% concurrent partners
- 9% Intergenerational sex
- Median Sexual debut: 15ys

## STI Prevalence



Site and Organism	Overall (n=148) n (%)	Age (years)			Gender	
		15-17 (n=55) n (%)	18 (n=56) n (%)	19 (n=37) n (%)	Female (n=99) n (%)	Male (n=49) n (%)
Anysite, any organism	60 (41%)	19 (35%)	24 (43%)	17 (46%)	49 (50%)	10 (20%)
Herpes HSV(2)	24 (16%)	6 (11%)	13 (23%)	5 (14%)	20 (20%)	4 (8%)
Chlamydia	45 (30%)	15 (27%)	14 (25%)	16 (43%)	38 (38%)	7 (14%)
Gonorrhoea	8 (5%)	5 (9%)	2 (4%)	1 (3%)	6 (6%)	2 (4%)



50% of female participants  
had an STI



# PrEP and VR work

**BUT has to be on board when HIV attacks!!!**

- Sufficient evidence that adherence correlates with efficacy- **For VR as high as 75% protection with most consistent use** ( Brown, IAS 2016)
- Factors associated with low adherence:
  - Low risk perception & stigma (Partners PrEP/VOICE)
  - Not partnered (VOICE/FEM-PrEP)
  - Less sex (Partners PrEP/IPrEx)
  - Influence of peers (VOICE)
  - **Younger age** (Partners PrEP/VOICE/ASPIRE)

# Young Women can be adherent to PrEP and VR

## ASPIRE

- In women younger than 25 years with consistent ring use -HIV risk was reduced by about 84%.

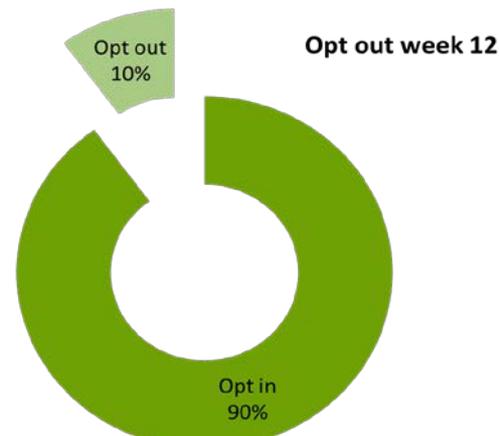
## HPTN 067

**HPTN 067:** An open label study of oral PrEP use by 179 women in Cape Town

- **Majority of women** took oral PrEP when made available, with **no difference** in drug levels between older and younger (<25 years) women
- Bekker CROI 2015

**PlusPills** – Reasons for PrEP opt out:

- Pill fatigue
- Side effects
- Tablets hard to swallow





# Unanswered Questions:

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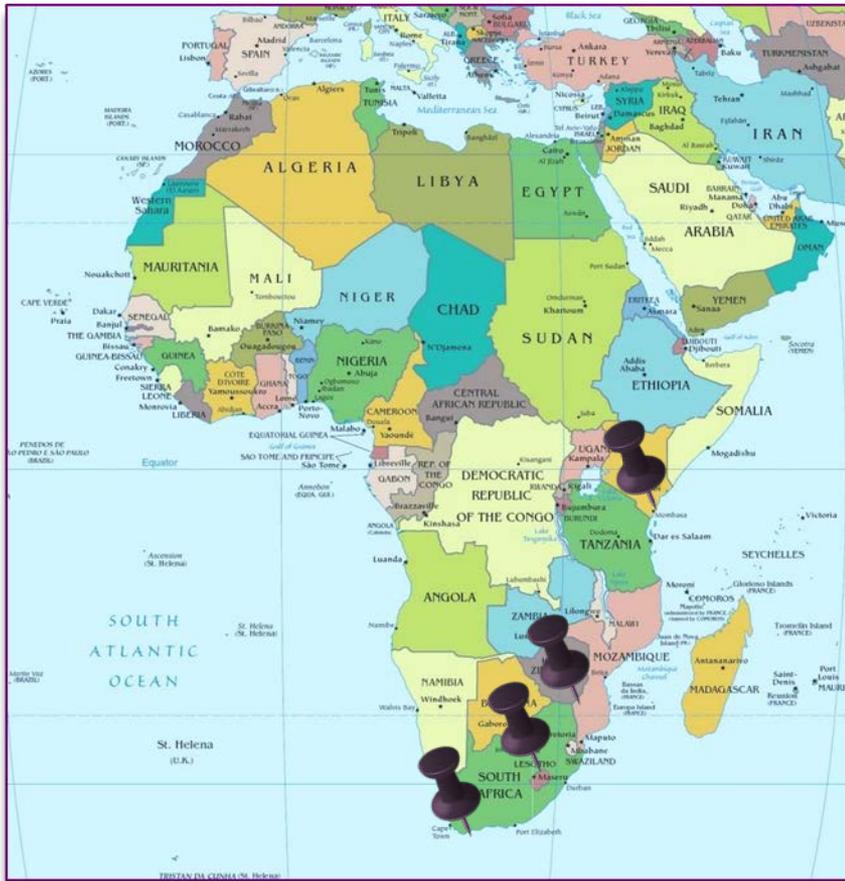
- in clinical trials, young women had difficulty with adherence - little or no HIV protection
- Unanswered questions about girls and young women:
  - Will adherence be better in “open-label” context (closer to real world)?
  - If given a choice what would be the preference
  - Do biological factors influence safety and efficacy in teen girls and young women
  - Are these methods generally safe? There is no data for either product among those under age18

# Participants

- **Sample Size:** 300 participants
- **Study Population:** Healthy, HIV-uninfected, adolescent females (16 - 17 years old) and young women (18-21 years old) on effective contraception

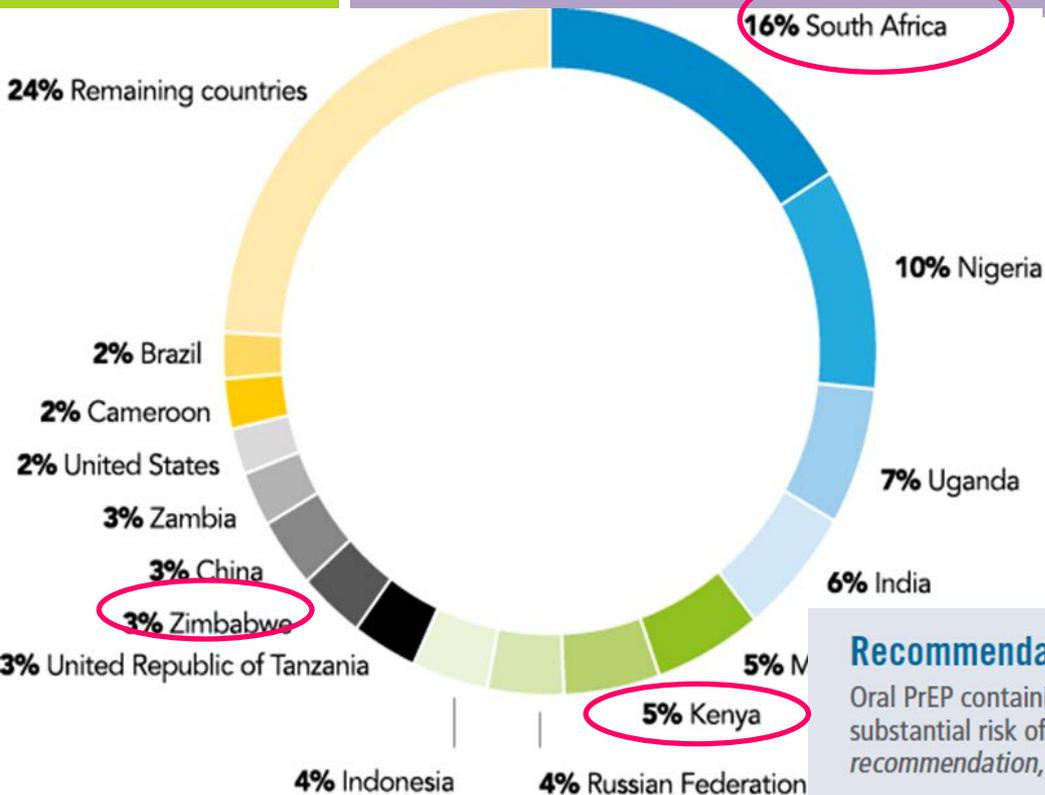


# Sites



- Desmond Tutu HIV Foundation (DTHV) Emavundleni clinical research site - Cape Town
- Wits Reproductive Health and HIV Institute – Johannesburg
- University of Zimbabwe-University of California San Francisco (UZ-UCSF) Clinical Trials Unit Spilhaus Site
- CDC/KEMRI CRS- Kisumu

# Burden of HIV infection in countries where the sites are located



**GUIDELINES**

**GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV**

SEPTEMBER 2015

## Recommendation

Oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (*strong recommendation, high-quality evidence*).

NEW

Proportion of new HIV infections by country -2013 (Source: UNAIDS)

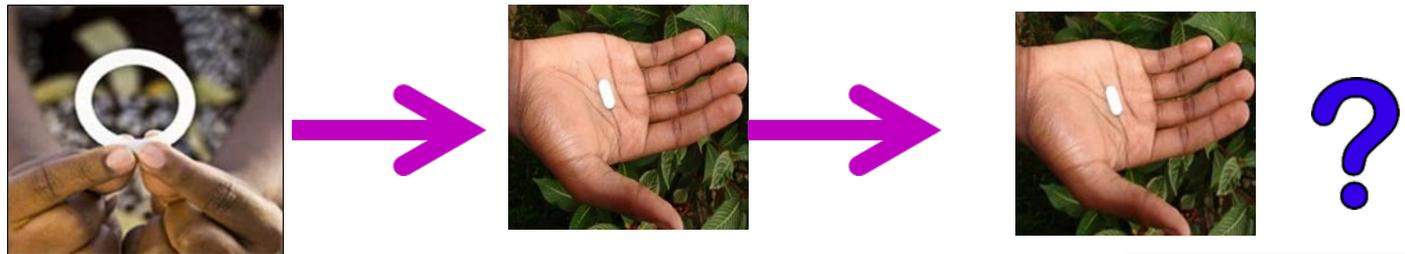
>3 per 100 person years

# Study Design: February 2017

- Protocol first reviewed by PSRC Dec 1, 2015, N = 300 adolescents ages 16-17
- Proposed changes based on ASPIRE results:
  - Include participants aged 18-21 (n 200)/adolescents 16-17 (n 100)
  - Add a third period during which young women will be allowed to select their preferred product

	Assigned Study Product Period 1 (24 Weeks)	Assigned Study Product Period 2 (24 Weeks)	Choice of product period 3 (24 Weeks)
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Sequence A



Sequence B



# Rationale for CHOICE option

**Available Now**



**Oral PrEP**

**Available 2018?**



**Vaginal ring**

**Results 2021?**



**Injectable**

**Results 2020?**



**Vaccine**

- PrEP is not a single solution, nor is it for everyone
- A product that best suits one's lifestyle and needs is more likely to be used
- Just as women have choices in contraception, they need choices for HIV prevention, too (average: 3,52 methods/woman – *J.Fam Prac.*2000)

# Response to Choice

*Stakeholder consultations with young women indicate support for product choice period*

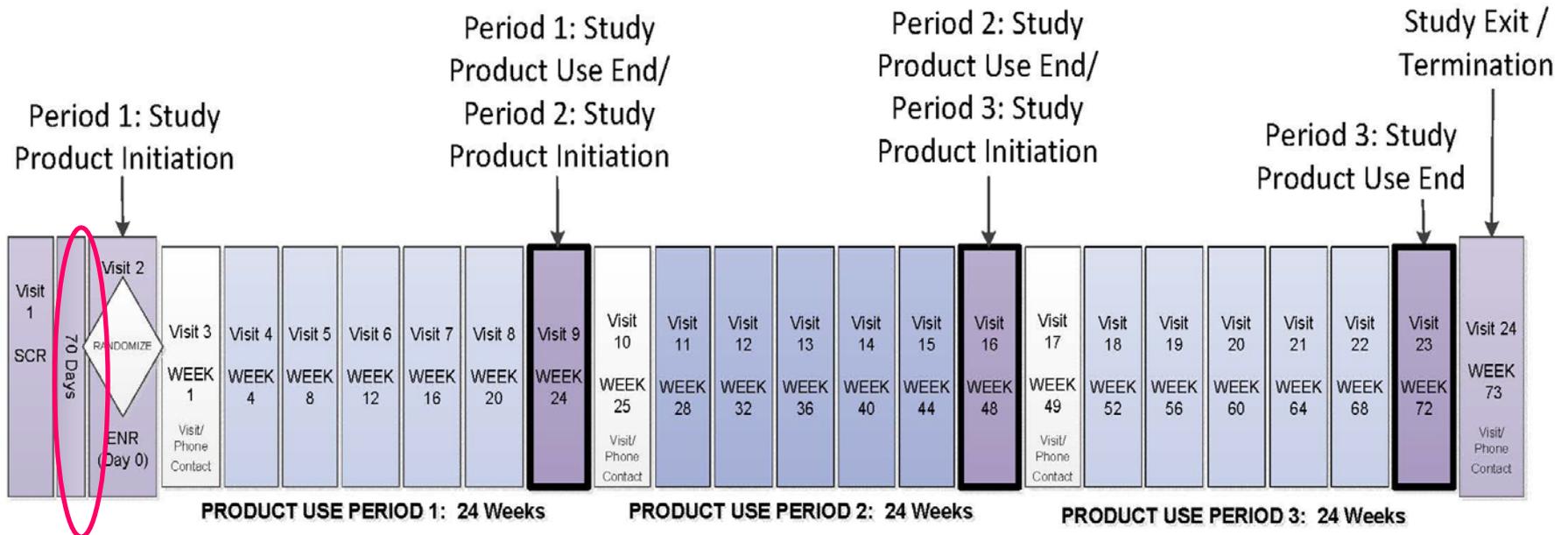
*Using condoms is not so easy. If you try and negotiate, it's like you're saying you're not being faithful. [The ring and PrEP] would give me ownership. I don't have to tell my partner I'm using them.*

*Trying two products is good, I support it. REACH helps young women to have control over their health, not to depend on her sexual partner, and to be under less risk.*



# Visit schedule

- Study Duration:** 73 weeks of follow-up per participant with a projected accrual period of approximately 12 months at each site

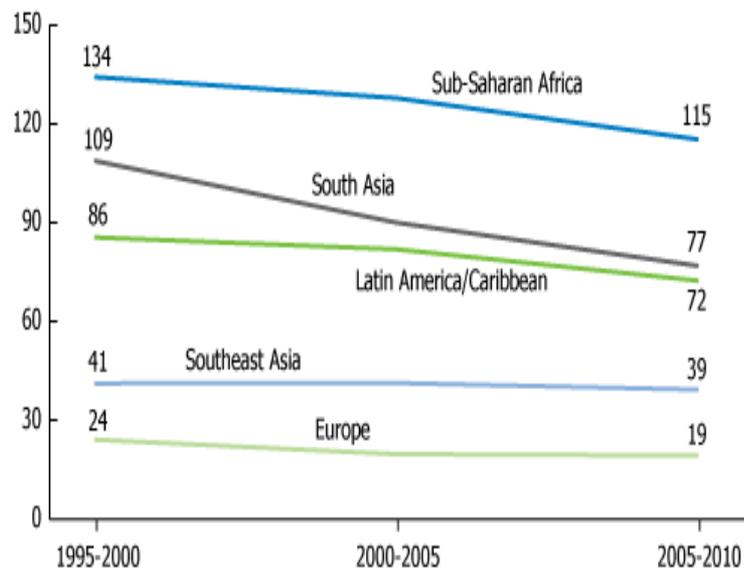




# Contraceptive Provision

- Long S:E window
- To allow for resolution of contraceptive related side effects prior to enrolment
- anticipated that majority will require contraception or be on injectable
- Provision to include LARCS/sanitary products
- Liking the idea of the contraceptive ring was associated with having had at least one pelvic exam and experience with vaginal product use.

Births per 1,000 Women, Ages 15-19



94 000 SA school girls: 2011  
77 000 Terminations: 2011

# Adherence support and counseling



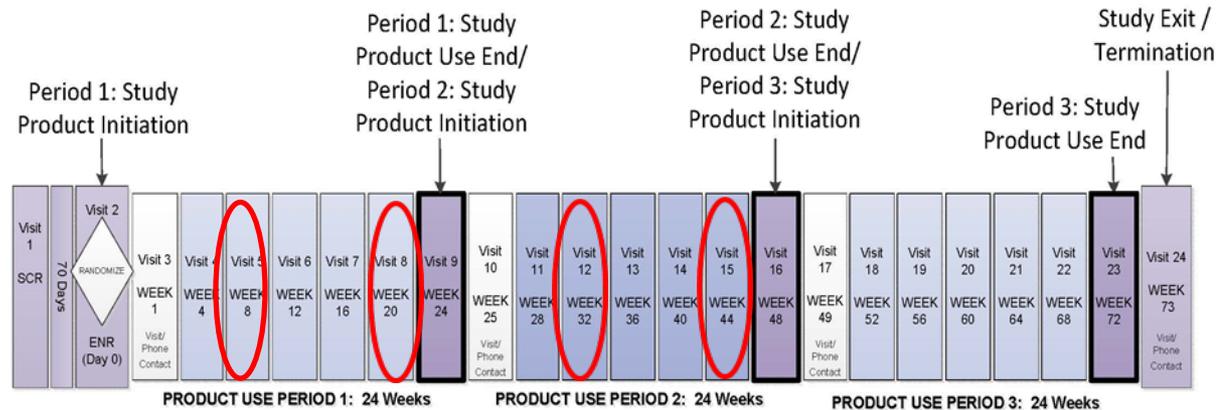
- Participants will be counseled at each monthly visit
- They will also be able to choose from a “menu” of adherence support measures -  
- text messages, phone calls, peer support groups
- With the ring, more support will be needed in the beginning, until confident inserting and removing and using during sex and periods.
- With PrEP, sustained support will be needed
  - A daily regimen is difficult and can get in the way
  - The size of the pills, side effects and stigma of ARVs will be challenges





# DBS/Residual ring Drug Levels

- Product use disclosure counselling to occur at month 2 and month 5 follow up visits



Previous months product use results will be used to tailor adherence counselling messages

“I would have taken my pills if I had known that drug levels were being checked” –VOICE

# How will MTN 034 meet its objectives?

Adolescent  
**Friendly**  
Services:  
Easy  
Quick  
Immediate  
Private  
Directed  
relevant



## Flexibility:

Opening times that suit them, is close to them & adapts around their school obligations



- Non judgmental
- Staff know-how
- Staff continuity
- Peer involvement
- Relaxed
- Psychosocial support
- Other services available



# Behavioral evaluations:

- Both quantitative and qualitative to assess:
  - Acceptability: during sex and menstruation
  - Preference:
    - Preference at beginning of study
    - Change in preference after each phase
    - factors that influenced product preference
    - Preferences for future use at end of study after experience with each product
  - Adherence: correlates/ barriers/facilitators
  - User experiences: sexual activity/condom use
- Assessments: Baseline, Monthly/Quarterly and exit

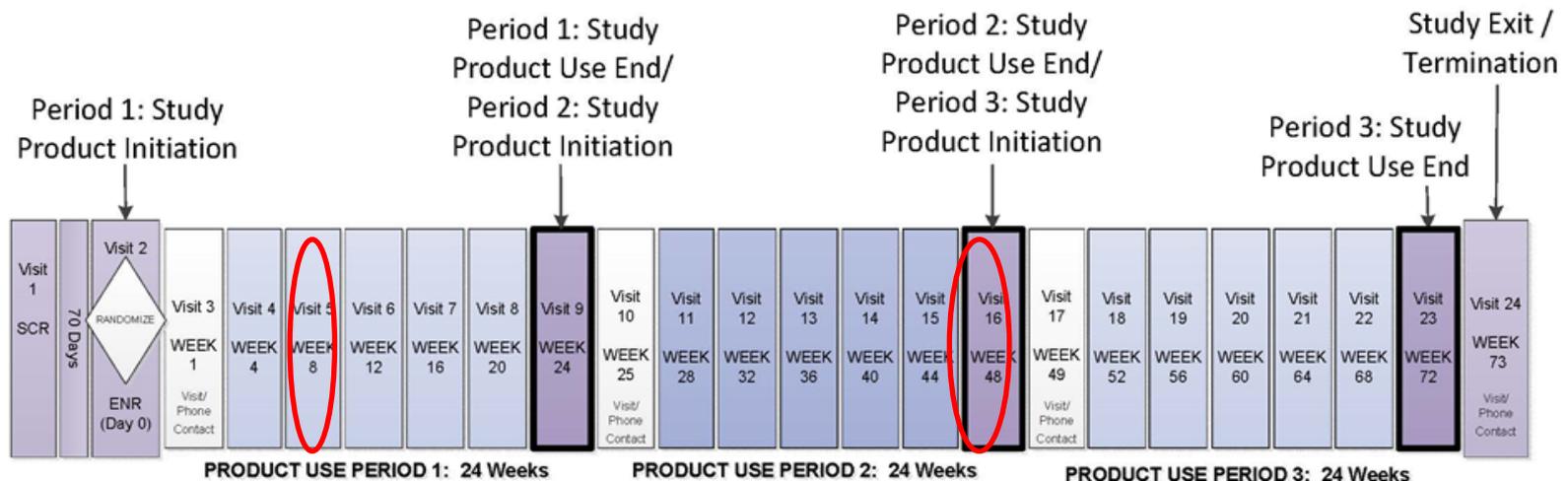


# Behavioural evaluations:

IDs: visits 5/16 (120 IDs in total)

- Serial IDs: during each product use phase
- Single IDs: interesting cases

FGDs: during 3<sup>rd</sup> product use period





# Timeline

**DAIDS  
approval  
Feb 2017**



**IRB and  
regulatory  
approvals  
Sep 2017**



**Site Activation  
Nov 2017**

**Accrual  
Dec 2017-  
1<sup>st</sup> quarter 2019**



**Follow up  
Feb 2017-  
3<sup>rd</sup> quarter  
2020**



# Summary



- Young women in Africa are hardest hit by HIV infection
- So far have been poorly adherent to biomedical prevention interventions
- REACH will provide valuable information on safety, adherence, acceptability and preference in this group
- REACH will provide the required data for licensure of PrEP and the VR in an African adolescent population

# Acknowledgments

- Protocol and site teams
- Drs Sharon Hillier, Linda – Gail Bekker, Connie Celum
- Ms Lisa Rossi
- Young women involved in stakeholder consultations
- The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068633, UM1AI068615, 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.