



# What We Will Learn From the REACH Study

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On behalf of protocol team

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# Overview

- Importance / Value of REACH (MTN 034/ IPM 045)
- Key challenges and possible solutions
- Feedback from stakeholders
- Summary and conclusions

# Adolescent Girls in Africa

- Established that AGYW :
  - bear a huge burden of HIV
    - AIDS is the #1 cause of adolescent deaths in Africa
    - account for 22% of new infections
  - Are disproportionately affected in comparison to male peers
    - 8x higher risk of HIV
    - Get HIV 5-7 years earlier
  - Are especially vulnerable due to cultural, social and economic factors
- If any impact is to be made on the general epidemic, HIV in this age group must be addressed

# What Do We Know About Product Use in Adolescents?

- Younger women are less adherent to contraception, ARVs for treatment, and prevention products
- Younger women in VOICE had lower adherence to oral PrEP and tenofovir gel...and higher incidence of HIV
- The same trend was seen in the two dapivirine ring studies
  - Efficacy 56% in women 22 and older who used the ring more regularly
  - not effective in 18-21 year age group in whom adherence was poor

# Why REACH?

**Available Now**



**Oral PrEP**

**Available 2019-20?**



**Vaginal ring**

**Results 2021?**



**Injectable**

**Results 2020?**



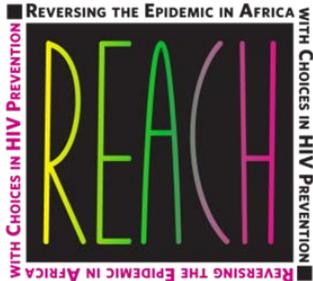
**Vaccine**

- Availability of a vaccine/injectable dependent on clinical trials to be completed in 2020
- Current products with proven efficacy are PrEP and the dapivirine ring
- Through REACH we hope to understand how to :
  - Make these products work for young women – support adherence
  - Increase accessibility – by providing additional safety data that will support licensure in young women 18 and younger

# What do we know about safety of PrEP and the ring in adolescent girls?

- What do we know about the dapivirine ring so far?
  - MTN 023: US adolescents (15-17 years) liked the ring, were comfortable with use, reported consistent use which was supported by PK adherence measures and there was no difference in safety.
  - **Still need data in African girls**
- What do we know about oral PrEP so far?
  - Results of PlusPills conducted among 150 boys and girls in 15-19 year age group in SA to be presented
  - tailored adherence support and more frequent visits required to support PrEP use.
  - **Data limited to South African girls**

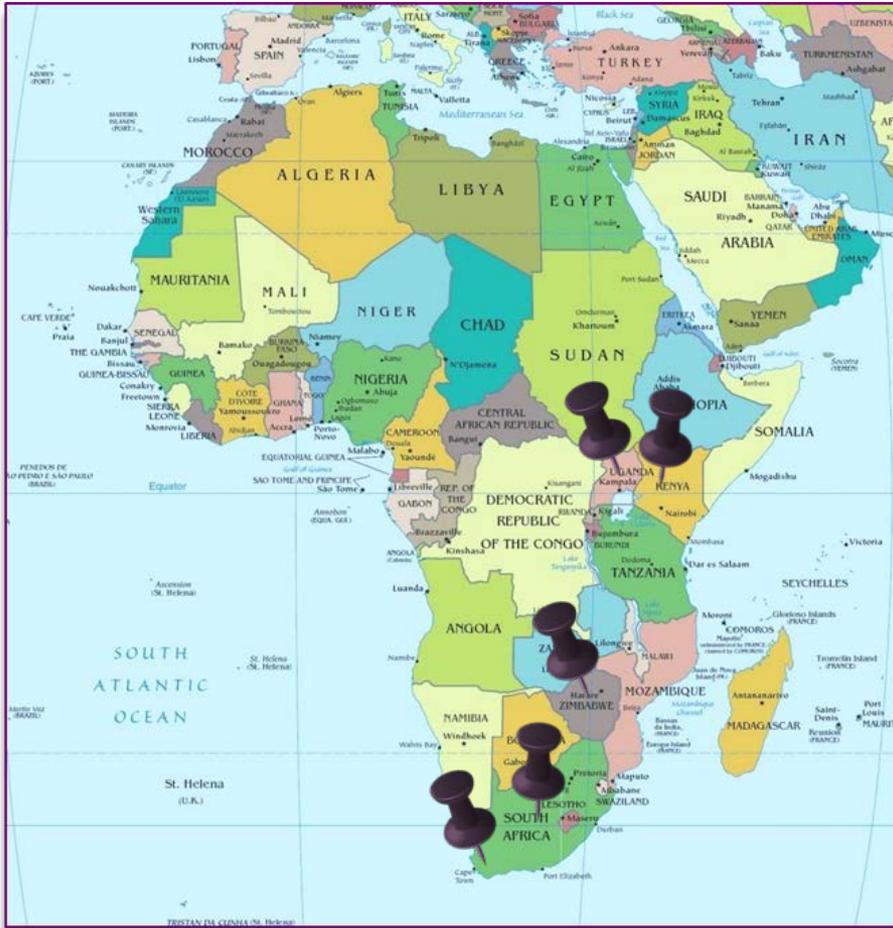
# MTN 034/IPM 045 - REACH



- Open-label Safety and Adherence Study of the DPV (25 mg) VR and TDF/FTC Tablet in a Young African Female Population
- Sample Size: 300 participants
- Study Population: Healthy, HIV-uninfected, adolescent females (16 - 17 years old/ n= 100) and young women (18-21 years old/ n =200) on effective contraception



# REACH Study Sites



## Kenya

- CDC/KEMRI CRS- Kisumu

## South Africa

- Desmond Tutu HIV Foundation (DTHV) Emavundleni clinical research site - Cape Town
- Wits Reproductive Health and HIV Institute – Johannesburg

## Uganda

- Makerere University-JHU Research Collaboration - Kampala

## Zimbabwe

- University of Zimbabwe-University of California San Francisco (UZ- UCSF) Clinical Trials Unit Spilhaus Site - Harare

# Study Design: Two-Sequence, Crossover, Randomized Trial



Assigned Study  
Product Period 1  
(24 Weeks)

Assigned Study  
Product Period 2  
(24 Weeks)

Choice of product  
period 3  
(24 Weeks)

Sequence A



Sequence B





# Key Challenges

- Cross-over study design where all women use two products
  - Will it be harder to enroll and retain participants?
  - Will study's rationale be understood by and accepted in communities where PrEP access may be feasible?
- Sex, parents and consent
  - Girls must have had sex, and if under 18, must also have a parent's permission to enrol – how to enrol the 100 16-17 year-olds?
- Contraception requirement
  - Overcoming community and provider biases and misinformation, especially regarding Long Acting Reversible Contraceptives (LARCs)
- Achieving adherence in a population that is rarely adherent
  - Study to encourage and support adherence while understanding why participants can't or don't want to use products
- Keeping young people engaged over 18 months



# REACH Stakeholders Meetings

- Regional Consultation Sept. 29-30, 2016 in Johannesburg
  - Stakeholders from Kenya, South Africa and Zimbabwe
- Follow-up in-country meetings
  - South Africa (28 February 2017 – at Wits RHI)
  - Zimbabwe (24 February 2017)
  - Uganda (23-24 August 2017)
  - Kenya meeting delayed but still being planned
- All meetings co-hosted by MTN and AVAC- with in-country partners



# Young Women Took Center Stage

- At least one-third of stakeholders at each meeting were young women under age 25 – some as young as 16 and 17



*“... what I appreciated most was the fact that young women were invited and given the opportunity to freely speak their minds regarding the REACH Study .... ”*

- Paul Ndebele, PhD, Medical Research Council of Zimbabwe



*“I’m getting more excited. It’s not just for me. There is a young generation that is behind us – kids, daughters who’ll grow up. They will say my great-granny was part of this and now we’re living in an AIDS-free generation!”*

- Lucy, 24, former ASPIRE Study participant, Johannesburg





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# Study design and concept of choice

- Young women said that choice is important and empowering
  - Neither the ring nor PrEP (or other methods) will be right for everyone
  - Places their own needs above their partner's desires – it's time they took control
  - PrEP and the ring are themselves empowering
- We need to enroll young girls who see the value in this kind of study and are willing to make a commitment – REACH will not be for everyone

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.

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.



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# Sex, parents and consent

- Most girls will not be able to admit they are having sex, especially where cultural and societal beliefs are non-accepting of premarital sex
- Parental waiver is not possible because the dapivirine ring is an investigational product
- Need to consider best sources of referrals to meet our target enrollment of 16-17 year-olds -- and that we also enroll the “right participants”

# Community Engagement

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- Focus on identifying and engaging with NGOs/ public health facilities who work with adolescents
- Engagement with DOE officials/local community leaders
- Interaction with youth CAB
- Engagement with young women focused on providing information on current prevention methods, informal assessment of preference and willingness to involve parents.

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# Contraception Requirement

- Must be on contraceptives for at least two months prior to enrolment - Long screen : enrolment window (70 days)
  - To allow for resolution of contraceptive related side effects prior to enrolment
  - We will start them on a method if they are not already on one
- Site staff will counsel participants on the different options
  - All options will be available directly at the site
- Participants will choose the method they want
  - But we will encourage LARCs - IUDs and implants



# Community biases against young women seeking contraception....

We are privileged because we are able to go to centres where we get things easy but other young people have to go to public health centres. It will be like why do you want contraceptives, is it because you wanna sleep around? So you just get up and leave

I am not comfortable going to the clinics because the staff are old and they discourage contraceptives

**We must ensure study staff are neither biased nor judgmental – contraception counseling will be the first impression of REACH**

The experience must be welcoming and positive!



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# Adherence support and counseling

- Tailor made adherence support:
  - Not a “one size fits all” approach
  - Participants will be able to choose from a “menu” of adherence support measures
- Product use feedback to occur at month 2 and month 5 follow-up visits
  - PrEP: based on tenofovir levels in dried blood sample taken the previous month
  - Ring: residual dapivirine levels in ring returned the month before



# Product Adherence and Counseling: Feedback from Young Women

*I had side effects ... the first few days – stomach aches, headaches, sleeping – and had to stop taking it [PrEP] because I had to study.*

*The pill is too big and you must take it every day like a person who's HIV-positive.*

*When I first saw it [the ring], it was like, WOW!*

- With the ring, more support will be needed in the beginning, until confident inserting/removing, and using during sex and menses
- With PrEP, sustained support needed – a daily regimen is difficult, size of pills and stigma are issues
- Adherence menu and individual adherence feedback are good ideas – provided counselors are supportive and nonjudgmental

Participants should be willing to use the products as directed, but if they are unable to we also want them to be open and honest with staff

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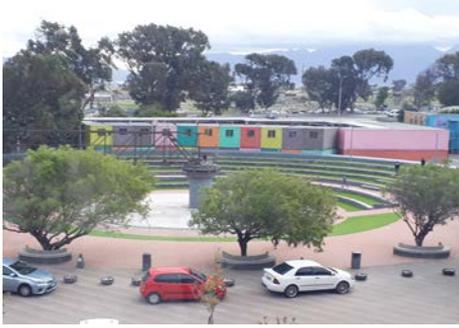
# Keeping Young People Engaged

## Visit Length:

- As short as possible- procedures and questionnaires included only if there to answer research question
- Dedicated adolescent clinic/staff
- Flexibility with scheduling of visits: afternoon/ Saturday clinics
- Flow through the clinic: “participant flow” vs “staff flow”
- Review of lengthy procedures (IC procedure)
- M&E tools to monitor visit flow

# Keeping Young People Engaged

Clinic space: youth friendly with a dedicated area for adolescent studies



# Keeping Young People Engaged

Research staff – approachable / non-judgmental/ well informed/manageable work load/ willing to build relationship with participants – to encourage openness and build trust

**We really need those 50 year old doctors to be young at heart, because it may not be possible to get a 19 year old doctor. But it is wonderful to interact with a service provider who adapts to our needs and language as young people**

# REACH Summary

- We need to ensure that PrEP and the ring can work for and be made available to adolescent girls and young women
  - By understanding how to help young women use these products better - we know that young women *can* be adherent
  - By collecting more safety data on PrEP and the ring so that regulators can consider expanding approval for girls under 18
- The REACH study aims to fill important gaps in information about adherence and safety of oral PrEP and the dapivirine ring in this population by allowing direct comparison.
- REACH is about empowering young women with choices in HIV prevention
- Activation: first quarter 2018

**S** STAY TUNED...

# Acknowledgments

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- MTN director of communications: Ms Lisa Rossi
- Young women involved in stakeholder consultations

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