REACH: Overview and Rationale

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Meeting the HIV Prevention Needs of Adolescent Girls and Young Women South Africa Stakeholders Meeting on REACH

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Women need options

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
- No product can protect against HIV if it is not used
- 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

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What you need to know

- Oral PrEP and the dapivirine ring are safe and effective – *with consistent use*
  - But in clinical trials, young women had difficulty with adherence, and little or no HIV protection
- Unanswered questions about teen girls and young women:
  - Will adherence be better in “open-label” context (closer to real world)?
  - 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
- Answers are needed for regulatory approvals and to ensure access for this population

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Overview

- What we know about PrEP
- What we know about the dapivirine ring
- Why REACH? Unanswered questions in adolescent girls and young women
- REACH study design and primary questions

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Pre-exposure Prophylaxis (PrEP)

What is PrEP?

- PrEP is an HIV prevention method that involves daily use of an ARV tablet - Truvada
- Truvada contains two ARV drugs – tenofovir (TDF) & emtricitabine (FTC)
  - Was already approved for treatment of HIV in combination with other ARVs as part of ART

Many trials tested Truvada for prevention:

- **iPrEx** - in men who have sex with men - (44% effective)
- **Partners PrEP**- in couples with an HIV-infected partner - (75% effective)
- **TDF-2** - in men and women - (62% effective)
- **FEM-PrEP** - in women - (not effective)
- **VOICE** - in women - (not effective)

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PrEP works when taken

- Partners PrEP Study of “serodiscordant” couples - efficacy about 70% in women
  - High adherence (drug detected in 82% of blood samples)
  - No difference in efficacy between women younger than 25 and older than 25
- VOICE and FEM-PrEP studies – PrEP was not effective
  - Enrolled mostly single and younger women
  - Most study participants did not take the tablets (drug detected in less than 30% of blood samples)

FEM-PrEP

VOICE
VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC

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Why didn't more women use PrEP in VOICE and FEM-PrEP?

- These were "blinded" randomized trials
  - Participants (and researchers) didn't know if they were using placebo or active product - or whether products were safe and effective
- Women had concerns:
  - About stigma, side effects and partner's reaction if they found out they were using ARVs
  - That they would not be able to stay in the study - and have access to the services - if they told staff they were not using the products
- Were influenced by what other women said
- Didn't perceive themselves at risk of HIV

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Where are we now?

- The World Health Organization (WHO) recommends oral PrEP for all persons at substantial HIV risk
- Several countries, including South Africa, have approved Truvada as PrEP for adults **18 and older**, and implementing in different populations.
  - People with ability to pay can access PrEP in the private sector
- Approvals expected in Zimbabwe and other countries very soon
- Several ongoing or planned demonstration projects are geared for adolescent girls and young women.

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Dapivirine Vaginal Ring

What is the dapivirine ring?

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

- Flexible silicone vaginal ring developed by the International Partnership for Microbicides (IPM) - a nonprofit group
- Intended to be used for a month at a time
  - Women can insert and remove the ring themselves
  - Discreet
- Slowly releases ARV drug dapivirine inside the vagina
- First HIV prevention product **developed specifically for women** found to be safe and protect against HIV in two independently conducted large-scale trials

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ASPIRE and The Ring Study

ASPIRE

- Conducted by the Microbicide Trials Network (MTN)
- Funded by the US National Institutes of Health (NIH)
- **Conducted at 15 sites in Malawi, Uganda, South Africa and Zimbabwe**
- **Enrolled 2,629 women age 18-45**

4,588 women in four countries

THE RING STUDY
Developing HIV Prevention for Women

- Conducted by the International Partnership for Microbicides (IPM)
- Support from governments, multilateral organizations, foundations
- **Conducted at 7 sites in South Africa and Uganda**
- **Enrolled 1,959 women age 18-45**

Study Questions

What were the results?

- The dapivirine ring was very safe and reduced risk of HIV by approximately 30% across both studies (CROI 2016, NEJM)
  - Results account for ALL study participants – including nonadherant
- Protection was higher in women 22 and older in ASPIRE, who used more consistently
  - Risk reduced by 56% – there were 56% fewer women ages 22-45 who acquired HIV in the dapivirine ring group vs. placebo group.
- Age 18-21 – no protection (and lowest adherence)
- More analysis – **As high as 75% protection with most consistent use** (Brown, IAS 2016)
  - Women under age 25 who used the ring most consistently, HIV risk was reduced by about 84%.

Where are we now?

The dapivirine ring could be right around the corner

- IPM plans to seek regulatory approval for use by women ages 18-45, based on results of The Ring Study and ASPIRE, and several smaller studies.
  - Submission by July 2017(?) and potential approval by late 2018(?) or early 2019 (?)

- In parallel former participants have access to the ring through open-label extension studies (OLE)
- HOPE for former ASPIRE participants
- DREAM for former Ring Study participants
  - Will adherence – and efficacy – be higher knowing they are using the active ring and that it is safe and can protect against HIV?

HOPE
HIV Open-label Prevention Extension
Out of ASPIRE, there is HOPE

DREAM
Dapivirine Ring Extended Access and Monitoring

Why REACH?

Unanswered questions in adolescent girls and young women

The promise and challenges

- PrEP and the dapivirine ring (if approved) could help curtail rate of new infections in young women
- But neither can be effective if not used with sufficient adherence
  - Adherence has been challenging for younger women.
- We need to understand the challenges young women face in using these products so strategies can be identified that may help

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No safety data in younger women

- Specific data on the ring's safety and use among women younger than 18 will be required for the ring to be approved for and made available to this population.
  - A safety study of the ring has been completed in 96 US girls ages 15-17 (MTN-023)
  - Additional safety data of the ring will be needed in young African women
- There is no safety data on oral PrEP in women under age 18
  - National programs and regulators may be reluctant to rollout to this population - despite the very high risk of HIV

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Why REACH?

- REACH (MTN-034) aims to fill important gaps in understanding about daily oral PrEP and the monthly vaginal ring in adolescent girls and young women
  - Are these approaches safe and acceptable to young women?
  - Are they willing to use these products?
  - Which one do they prefer?
- Answers to these questions are especially important for regulatory bodies and national programs to have

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Why REACH?

REACH - Reversing the Epidemic in Africa with Choices in HIV Prevention

Adolescent girls and young women are among those at highest risk - they both need and deserve to have HIV prevention options

Women need options

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REACH at a glance

- Will evaluate the **safety** and **adherence** of the monthly dapivirine ring and daily oral PrEP and ***preferences*** for each
- Will enroll 300 girls and young women ages 16-21 at 4 trial sites in Kenya, South Africa and Zimbabwe
  - 100 girls ages 16-17
  - 200 young women ages 18-21
- Conducted by the Microbicide Trials Network (MTN) and funded by the US National Institutes of Health
  - Gilead and IPM providing products for the study
- Expected to start August-December, pending approvals

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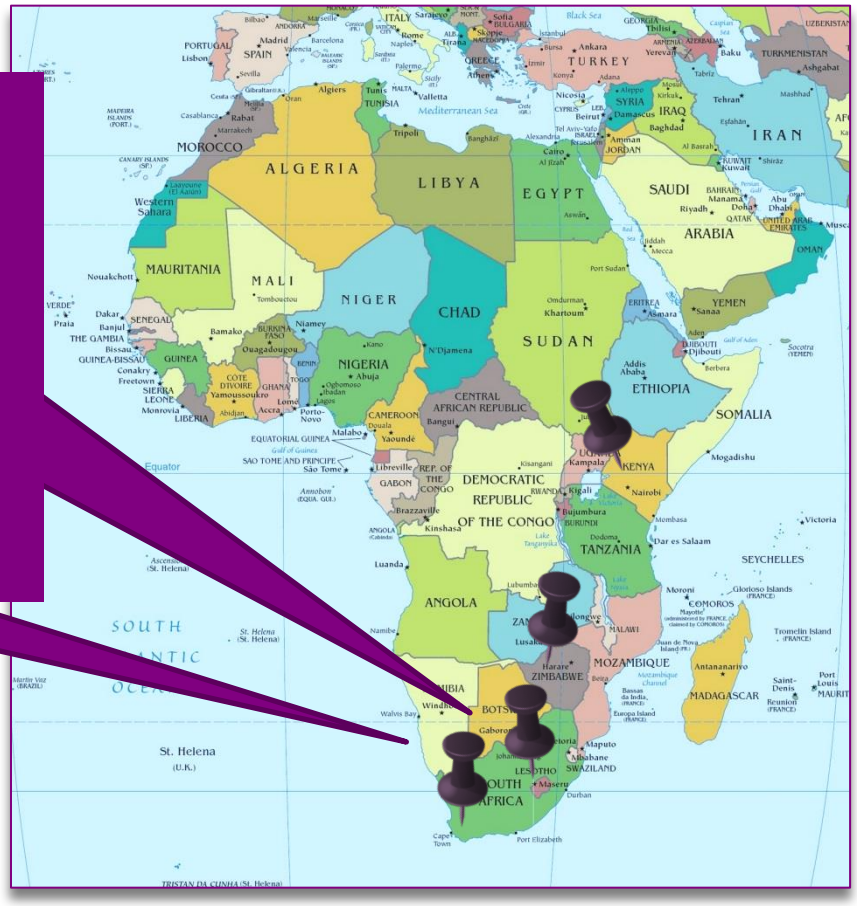
REACH in South Africa

REACH will be conducted at two sites in South Africa:

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



How REACH is designed

- Participants are in the study for about 18 months
- The study is divided into three 6-month periods
- **All** participants use the ring and PrEP for 6 months each
  - Half will use the ring the first 6 months and then switch to PrEP
  - Half will use PrEP first and then ring
  - Order will be determined by random assignment
- Participants will ***choose*** which product they would like to use for the final six months - or they may choose not to use either

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Three 6-month periods

Participants get a new ring or 30-day supply of Truvada every month

A
6 months

B
6 months

C
6 months

?

6 months
A

6 months
B

6 months
C

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How will we assess safety?

Site staff will:

- Monitor any symptoms or side effects
- Conduct medical exams and do laboratory tests of blood, urine and vaginal fluid
- Some tests can detect changes, even if there are no symptoms
  - Changes in the good and bad bacteria living in the vagina
  - Changes in immune cells (“soldier cells”) in the vagina
  - Evidence of HIV infection
  - Evidence of sexually transmitted infections (0ther than HIV)
  - Markers of good health

How will we learn whether young women are able to use the products?

- Participants will answer questions every time they come to the clinic, including with a private computer
  - How do they like the products?
  - Did they use them?
  - Did they have sex?
  - Did they use condoms?
- To assess adherence to PrEP, researchers will also measure drug levels in small blood samples taken at monthly visits
- For the ring, researchers will look at the amount of drug leftover in rings that participants return each month after use

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What about acceptability and preference?

- There will be longer face-to-face conversations with some young women, and some will take part in group discussions
- Will help us better understand
  - What motivates or is challenging about using each?
  - Acceptability - including during sex and menstrual periods
  - Whether they experience stigma - is there more with PrEP because the pills are the same for treating HIV?
  - How relationships with family, friends and male partners may impact product use
  - Preferences for either or both PrEP and the ring

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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
- At some visits, individual adherence results will be shared to let them know if they are using the product in a way that will provide HIV protection
  - For a participants using PrEP, will from the blood sample taken the previous month
  - For the ring, will be of the used ring they returned the month before

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Questions and Discussion