

The REACH Study (MTN-034)

Filling the Gaps for HIV Prevention in
Adolescent Girls and Young Women in Africa

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Young Women Need Prevention

- Adolescent girls and young women (AGYW) are especially at high risk of HIV and need methods for protection
- Young women 15-24 years account for 30% of new adult infections in SSA
- Twice as likely to acquire HIV infection as young men
- 25% of maternal mortality related to HIV/AIDS
- Women who experience IPV and sexual assault 1.5 times more at risk for HIV infection

Prevention Options For Women

- Negotiate male condom use- can incite violence
- Female condoms: unpopular, indiscreet and difficult to access
- TasP: Rely on partner to test, disclose status, seek treatment and adhere to treatment
- Oral PrEP

Current HIV Prevention Landscape

“Available” Now



Oral PrEP

Available 2020?



Vaginal ring

**Results 2023?
(Approval 2026?)**



Injectable

**Results 2021-22?
(Approvals 2024?)**



Vaccine

- Current strategies have not significantly impacted the vulnerability of adolescent girls and young women to HIV
- Adherence remains a challenge: No product can protect against HIV if it is not used
- Women need prevention modalities that meet their individual needs and fit their lifestyle
- Choice is important for effective use: uptake, persistence and adherence



What we know about the ring and PrEP



- Monthly dapivirine ring
 - Developed by the International Partnership for Microbicides, which is seeking its regulatory approval – for women ages 18 and older
- Regulatory approvals are based mainly on results of Phase III placebo-controlled trials (in 18+)
- Both PrEP and ring are user-controlled, discreet methods and only effective if used as indicated
- PrEP and ring trials had similar results
 - Both approaches were safe and effective with consistent use
 - Not effective in younger women – ages 18-25 – due to poor adherence

What we know about PrEP and ring adherence

- Both topical and oral PrEP effectiveness increase with higher adherence
- In phase III trials, product adherence among AGYW has been sub-optimal and is related to the following:
 - Healthy participants may not perceive themselves to be at risk
 - Motivation to participate in order to access high quality, confidential services from non judgmental and supportive staff
 - Unknown safety and efficacy profile of product
 - Possible randomization to placebo

What do we know about the ring in *adolescent girls*?



- In MTN-023/IPM 030, 96 girls in the U.S. ages 15-17 were randomized to use a placebo ring or the dapivirine ring monthly for 6 months
 - The dapivirine ring was safe and acceptable; adherence was very high
 - **What about girls in Africa?**

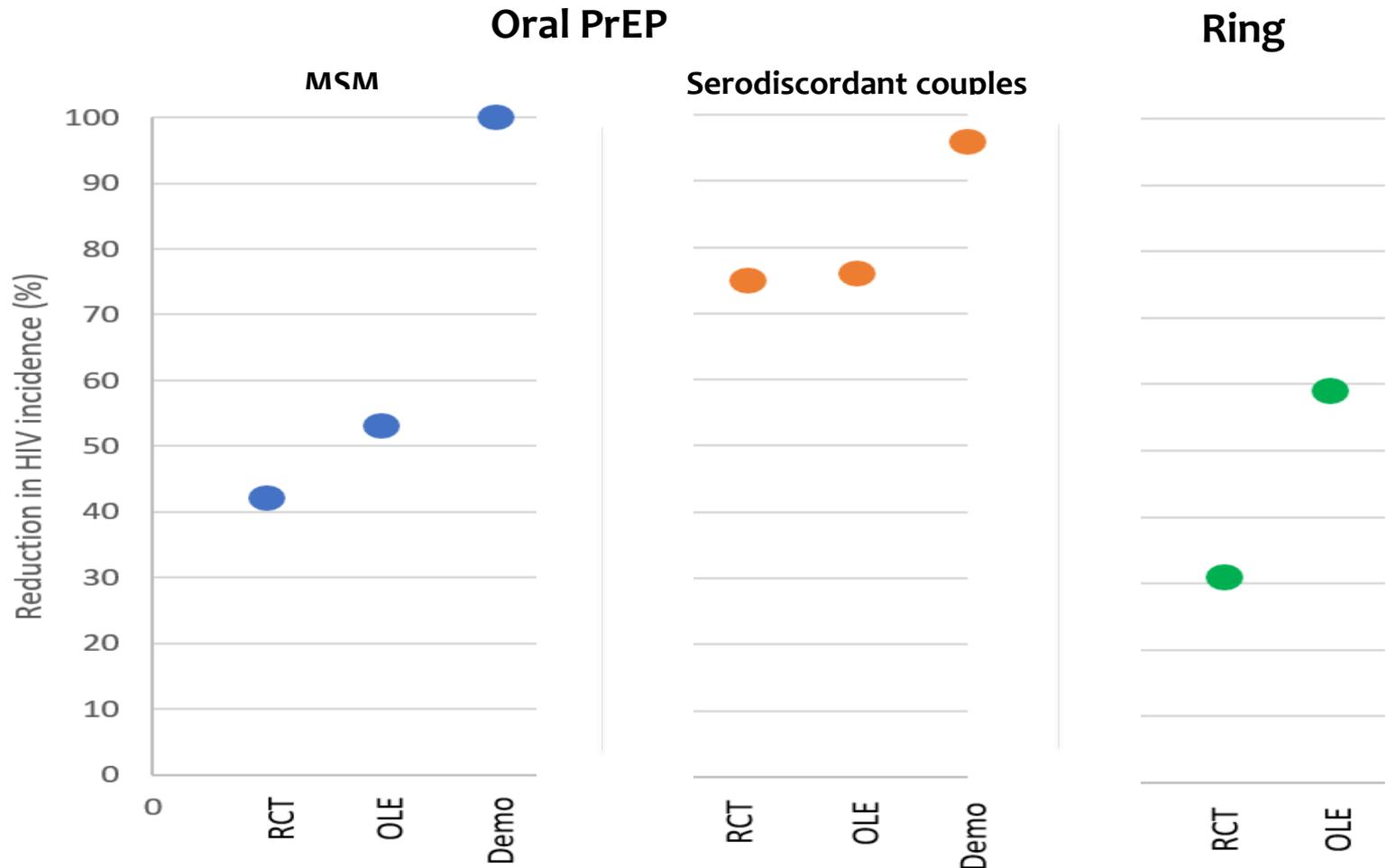


What do we know about PrEP in *adolescent girls*?

- POWER study: Study of PrEP delivery among women ages 16-24 in South Africa and Kenya
 - About half do not return at 1 month; 20% restart within 3 months
 - Discontinuations due to AEs (13%) and challenges with adhering to a daily pill regimen (13%) were common during first month of use
- PlusPills: Open-label study with 150 adolescents ages 15-19 from South Africa:
 - Adherence did not differ between sexes
 - Adherence decreased as visit frequency decreased from monthly to quarterly

Increased Effectiveness

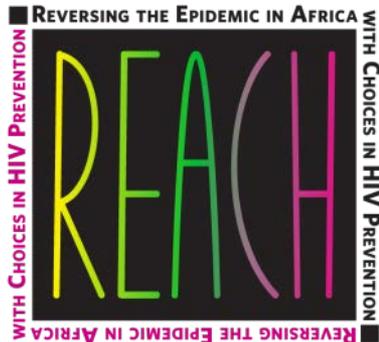
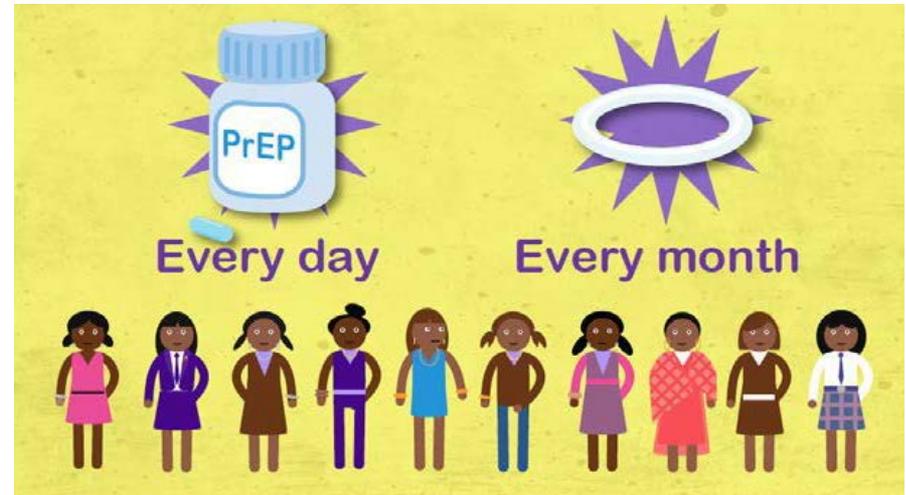
RCTs → Open label extensions → Demo projects



Sources: **MSM**: Grant, 2011; Grant, 2014; Molina, 2018; Vuylsteke, 2018;
SDC: Baeten, 2012; Baeten, 2014; Baeten, 2016; **Ring**: Nel, 2016; Nel, 2018

Why REACH?

We need to see that PrEP and the ring can work for and be made available to adolescent girls and young women ... How?

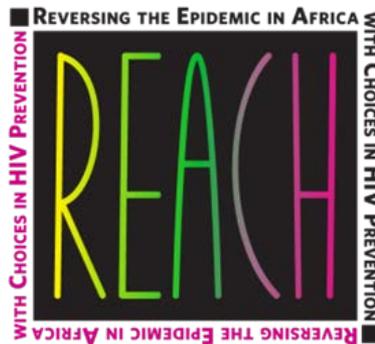


REACH aims to:

- Learn how to help young women use these methods better so they have the benefit of protection
- Collect more information about the safety of PrEP and the ring – including in girls under age 18 – so drug regulatory authorities can consider expanding approval

REACH (MTN-034) at a Glance

Reversing the Epidemic in Africa with Choices in HIV Prevention



- Randomized, open-label safety and adherence study of the dapivirine vaginal ring and oral PrEP
- Will enroll 300 girls and young women at 5 trial sites in Kenya, Uganda, South Africa and Zimbabwe
 - 100 girls ages 16-17
 - 200 young women ages 18-21
- Crossover design -- All participants will use PrEP and the ring – each for 6 months – and choose which to use for another 6 months

The REACH Study: Try each, then choose

6 months
once a month



6 months
once a day



6 months



or



6 months



once a day
6 months



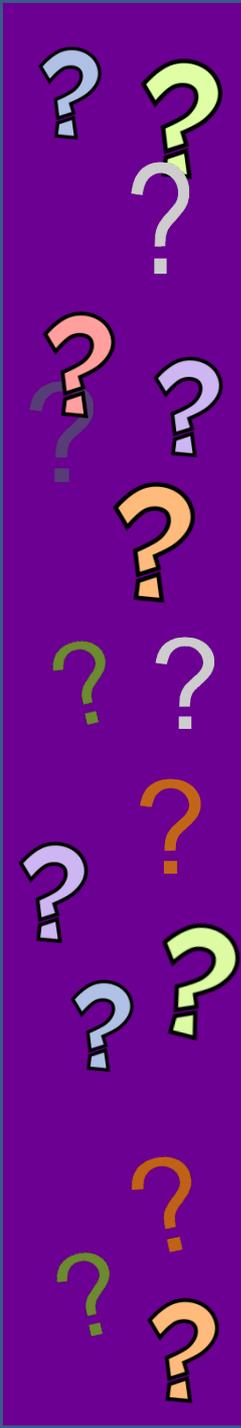
once a month
6 months





Questions being asked in REACH

- Will young women be more inclined to use these products...
 - In a study with no placebo?
 - Knowing that previous studies found them safe?
 - Knowing they can only work with consistent use?
- Is one easier to use than the other?
- Do they like one more than the other?
Or do they not like either?
- How might life circumstances influence choice?
- What can we do to help them to use these products?
- What about 16-17 year old girls? They are at risk for HIV & need access to effective products



Questions being asked about REACH

- Is it ethical to study dapivirine ring in AGYW, given no efficacy in ASPIRE and RING study in 18-21 year olds, and given that oral PrEP has known efficacy?
 - *Reminiscent of critiques of oral PrEP in AGYW*
 - *Open label studies showing higher adherence than in VOICE & FEM-PrEP*
 - *Learning from PrEP demonstration projects that people self-sort into users or non-users*
- What will we learn in MTN 034?
 - *Safety in 16-17 year old women – key for product licensure*
 - *Patterns of adherence*
 - *Product Preference: will AGYW who cannot use a pill a day be able and willing to use a monthly vaginal ring?*

REACH Stakeholders Meetings 2016-2018



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
- Included also young women experienced with using PrEP and ring (former ASPIRE participants)
- Pre-meeting workshops convened by AVAC and partners helped build confidence prior to the larger meetings

What we have heard young women say

- Neither the ring nor PrEP (or other methods) will be right for everyone
- Having choice is empowering; gives us control of our health and lives
- The products in REACH are themselves empowering
- It's time we placed our own health above our partner's desires

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.

If he says 'don't use it,' I won't. So, I think we should first deal with women – empower each other.

Study Timeline and Update



- First participant enrolled at the Uganda Site on 6 February .
- Screening ongoing at the Ugandan and Zimbabwean sites
- Remaining sites to be activated during Q1 2019
- Accrual completed by early-mid 2020
- Follow-up completed by mid-late 2021
- Results 2022



Early Lessons Learnt

- Community engagement to include male partners and significant others
- AGYW have little/no knowledge of contraception – critical that this be addressed during community engagement and pre-screening
- Bottle necks identified and visit flow to be streamlined
- Choosing participants with team analysis of potential participant profiles
- Menu of adherence support options, including adherence clubs.





Why do we need REACH?

- REACH will answer key questions about adherence and safety of PrEP and the ring in young women, including under age 18
- With PrEP being made available and the possibility that the ring will be approved...
 - We want to ensure these products can work for and be made available to **all girls and young women – regardless of age**
- The time is now – we can't afford to wait for a vaccine or something that may be better
- Ultimately, REACH is about empowering young women...
 - By putting HIV prevention in their hands, and ensuring they have different options from which to choose

Reverse the Epidemic in Africa with Choices in HIV Prevention



Acknowledgments



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- Young women involved in stakeholder consultations

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