What will HOPE teach us?

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From ASPIRE to HOPE

- What have we learned
- What will we learn

What have we learned

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The dapivirine ring was effective

ASPIRE

THE RING STUDY
Developing HIV Prevention for Women

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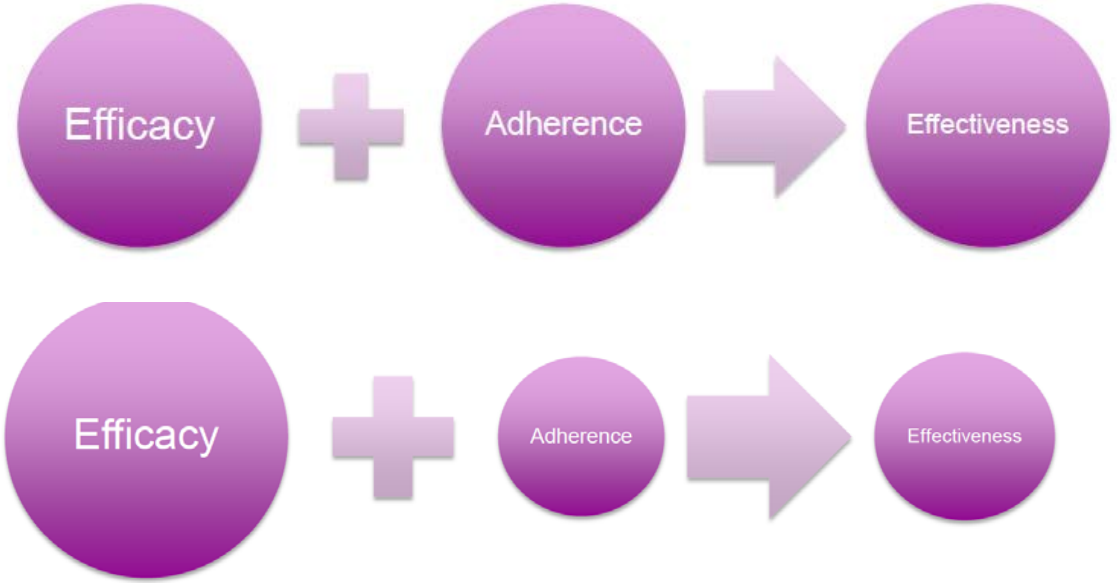
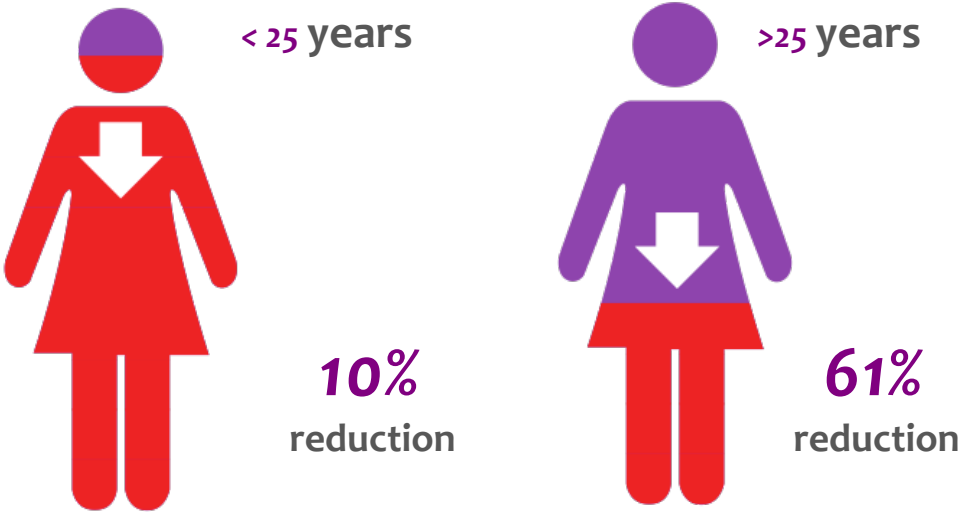
Of course, adherence was important



HIV protection differed by age

Women age ***25 or older*** had ***substantial HIV protection*** while those ***younger than age 25*** had ***no significant reduction*** in HIV incidence



This difference in HIV protection was associated with differences in adherence

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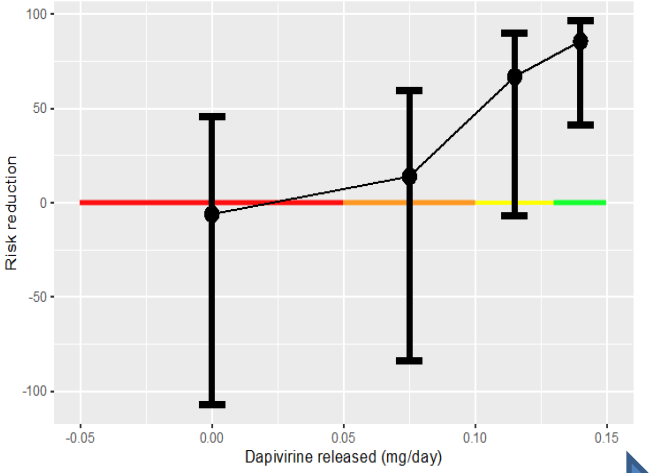
HIV protection appears to be high with high adherence

When taking into account residual levels of dapivirine in the ring – HIV protection was 55%, 59%, 75%, 92% across several analyses.



More dapivirine released = more use = more protection

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The dapivirine ring was safe

- No safety risk seen in ASPIRE and The Ring Study:
  - SAEs, genital AEs
  - HIV resistance in seroconverters
- Emerging data (MTN-015 and MTN-016) showing safety in women who became pregnant or acquired HIV and started ART

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The dapivirine ring was appealing, wanted, and owned

"I like that the ring stays inside you and nobody can see it…. you don't have to disclose ring use to others if you want. My family doesn't know that I am using the ring. … And the partner can't feel it as well."

"No, I told him to take the ring as the condom. I said: 'Because you do not want the condom, this is now our condom, just ignore it, it's inside my body and it's mine.' We never had problems about it and we never spoke about it again."

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Challenges to ring use

- Factors that negatively impacted ring use:
  - Friends, other study participants and former ASPIRE participants comments about ring use, especially rumors about the ring causing cervical cancer or infertility
  - Woman removed the ring before having sex and then forget to re-insert it or removed the ring during menses
  - Partner concerns
  - Younger women had more partners - needed to explain the ring to more people
  - Mistrust of the study – unproven, unclear, frightening

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What we will learn

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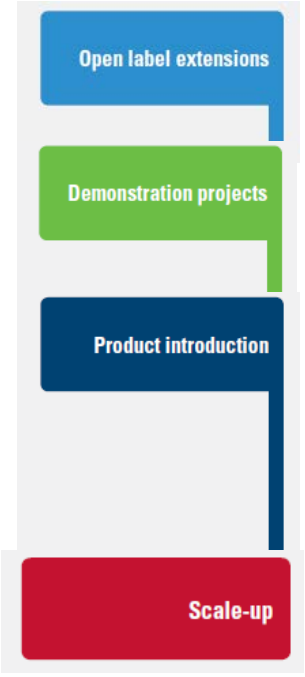
Why do HOPE?

- Because there are unanswered questions.
- Because showing that a product is effective and safe is only the beginning of achieving impact.
- Because we have a long way to go.

- *We are now where oral PrEP was 5 years ago:*
  - Imperfect efficacy (iPrEx = 44% overall, not significant <25 years) and just beginning open-label studies – i.e., where participants know it is safe and know it is not placebo.



Graphic: AVAC

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MTN-025/HOPE: What We Will Learn

- Now that we know the ring works and is safe, do women want it, use it, and achieve HIV protection.
  - In open-label projects of oral PrEP for HIV prevention, those who chose to use PrEP had **higher** adherence and **better** HIV protection than in blinded, placebo-controlled trials. *This strongly suggests that adherence and HIV protection will be higher in MTN-025/HOPE than in MTN-020/ASPIRE.*

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MTN-025/HOPE

- **Study Population:** Former MTN-020 participants who are HIV-uninfected and not pregnant
  - *Decliner Population: Former MTN-020 participants who decline participation in the main MTN-025 study and meet eligibility criteria for decliner group*
- **Sites**: Former ASPIRE sites
- **Study Design**: Phase 3B, open-label, multi-site trial
- **Study Duration**: Approximately 13 months of follow-up per participant with a projected accrual period of approximately 6 months at each site.
- **Study Product**: Dapivirine Vaginal Ring, 25 mg, replaced monthly
- **Objectives:** adherence, safety, HIV-1 incidence, HIV-1 resistance, acceptability and feasibility, decline of ring and study

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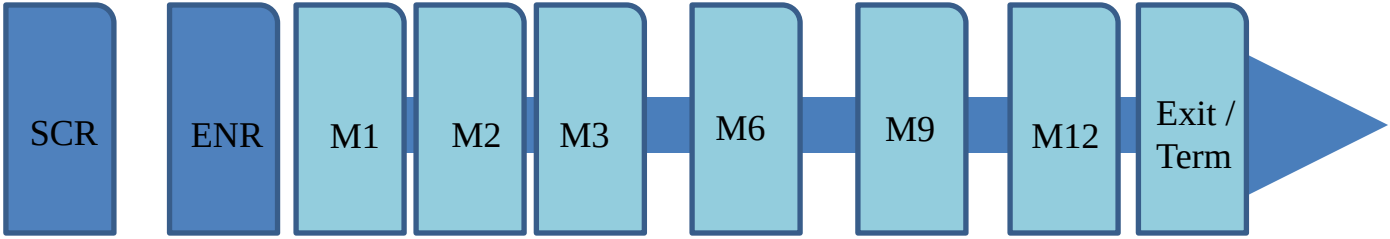
MTN-025/HOPE Design



- **Visit Schedule**: Monthly for the first three months, then quarterly thereafter (non-randomized)
  - A goal to assess a more "real world" frequency for clinic follow-up and distribution of rings
- **Study Procedures:** HIV testing, risk-reduction counseling, pregnancy testing, contraceptive counseling/provision, safety monitoring, product counseling/provision

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HOPE is different than ASPIRE

- ASPIRE & HOPE are different studies and we must think of them differently:

	ASPIRE	HOPE
Design	Randomized, blinded phase III trial	Open-label phase IIIB trial w/ no randomization or blinding
Placebo	Yes	No
Product	Unproven efficacy, may be placebo, unproven safety	Proven to prevent HIV, proven safe
Goal	Determine whether the ring was effective and safe	Show whether women will use the ring, when given the opportunity

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Key Concepts in HOPE

CHOICE

ADHERENCE

ACCURATE REPORTING

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Counseling in HOPE

Counselling to Optimize Adherence, Choice, and Honest Reporting

COACH

- A new approach to counseling in HOPE
  - Training videos and counselor mock audio sessions to approve initiation
  - Recording of all counseling sessions and review for fidelity
  - Emphasis on choice to accept/not accept the ring, use with high adherence, and honest reporting of use

Counselling to Optimize Adherence, Choice, and Honest Reporting

CHOICE: Helping you choose the best HIV prevention for you

OPEN CONVERSATION: About decisions regarding using the Ring or any other HIV prevention method

In our sessions, we will…

- **Discuss the Ring & other HIV prevention methods you choose**
- **Help you decide on the best HIV prevention plan for you**
- **Help you adjust your plan**

Key messages:

- ✓ **The Ring can greatly reduce a woman's chance of HIV infection**
- ✓ **Protection is highest when the Ring is used all the time**
- ✓ **The Ring is not protective when it is not used**
- ✓ **The Ring is very safe to use**

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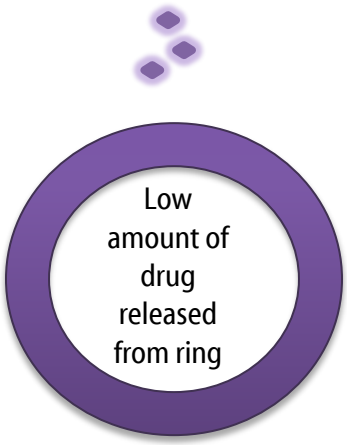
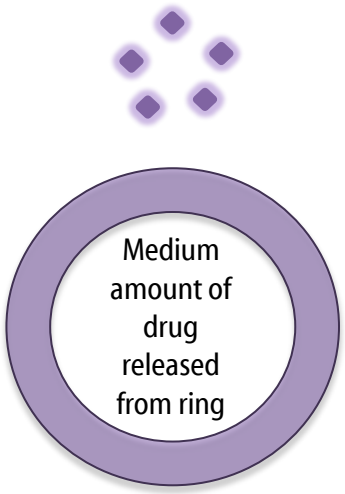
HOPE counseling: ring data feedback

Low level of drug in body



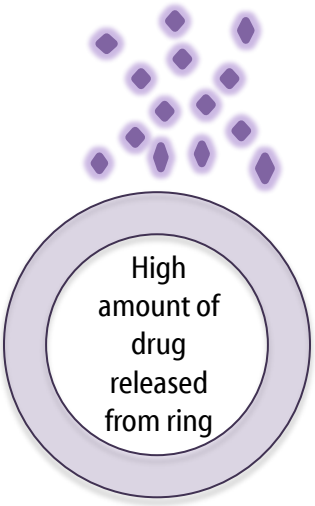
Low or No Protection

Uncertain level of drug in body



Uncertain Protection

High level of drug in body



High Protection

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Women are ready for an open-label study

"I now know that the ring works, so of course I want to use it so I can be protected."

"My partner said the ring enhanced our sexual life, so I can't wait for HOPE to start."

"My body, my choice, my ring."

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Where we are : activation update

- First site (Verulam) activated: 16 July 2016
- First enrollment: 15 August 2016
  - 16 screened, 6 enrolled and accepted ring, 1 enrolled but declined the ring, 2 declined enrollment but completed the decliner interview on why they did not want to be in 025
- 4 more sites activated: eThekwini, Botha's Hill, Chatsworth, Blantyre & 9 sites poised to activate between now and November: Cape Town, Isipingo, Johannesburg, Kampala, Lilongwe, Seke South, Spilhaus, Tongaat, Zengeza
- Qualitative site trainings done

Summary

- We have learned much, we have much to learn

What will adherence and HIV protection be in an open-label study, where women are given the choice to use an active, proven, and safe product?

The HOPE study will provide important answers to this question and many others.

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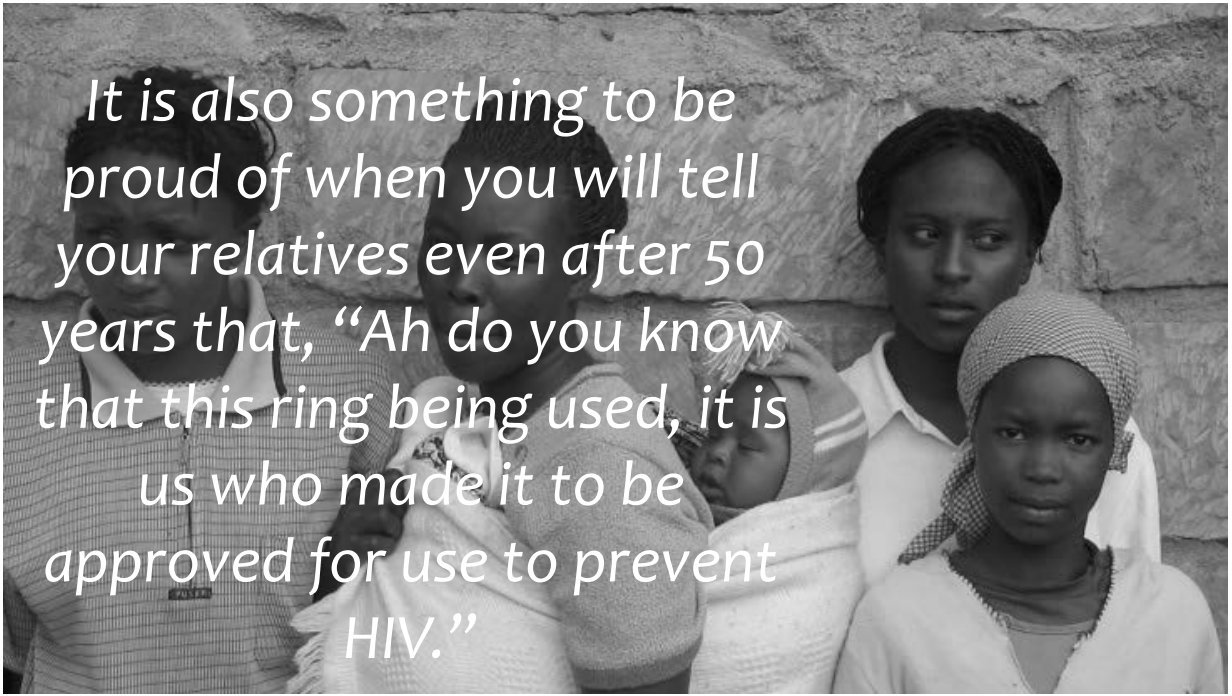
Looking ahead



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MTN-020/ASPIRE & MTN-025/HOPE Study Team

- **MTN-020/ASPIRE & MTN-025/HOPE leadership:** Jared Baeten (protocol chair), Thesla Palanee-Phillips (protocol co-chair), Nyaradzo Mgodi (protocol co-chair), Elizabeth Brown (protocol statistician), Katie Schwartz & Ashley Mayo (FHI 360), Lydia Soto-Torres (DAIDS medical officer)
- **Study sites:**
  - **Malawi: Blantyre site (Malawi College of Medicine-John Hopkins University Research Project):** Bonus Makanani, Taha Taha
  - **Malawi: Lilongwe site (University of North Carolina Project):** Francis Martinson
  - **South Africa: Cape Town site (University of Cape Town):** Lulu Nair, Linda-Gail Bekker
  - **South Africa: Durban eThekwini site (Centre for AIDS Programme of Research in South Africa):** Gonasagrie Nair, Leila Mansour
  - **South Africa: Durban – Botha's Hill, Chatsworth, Isipingo, Tongaat, Umkomaas, Verulam sites (South African Medical Research Council):** Anamika Premrajh, Arendevi Pather, Logashvari Naidoo, Nishanta Singh, Nitesha Jeenarain, Samantha Siva, Vaneshree Govender, Vimla Naicker, Zakir Gaffoor, Gita Ramjee
  - **South Africa: Johannesburg site (Wits Reproductive Health and HIV Institute):** Thesla Palanee-Phillips
  - **Uganda: Kampala site (Makerere University-Johns Hopkins University Research Collaboration):** Flavia Matovu Kiweewa, Brenda Gati, Clemensia Nakabiito
  - **Zimbabwe: Chitungwiza-Seke South, Chitungwiza-Zengeza, Harare-Spilhaus sites (University of Zimbabwe-University of California San Francisco Collaborative Research Program):** Nyaradzo Mgodi, Felix Mhlanga, Portia Hunidzarira, Zvavahera Chirenje
- **Microbicides Trials Network Leadership and Operations Center (University of Pittsburgh, Magee-Womens Research Institute, University of Washington, FHI 360, New York State Psychiatry Institute, Population Council, RTI International, Jomo Kenyatta University of Agriculture and Technology):** Sharon Hillier, Ian McGowan, Ivan Balan, Katherine Bunge, Beth Galaska, Morgan Garcia, Cindy Jacobson, Judith Jones, Ariana Katz, Barbara Mensch, Elizabeth Montgomery, Patrick Ndase, Kenneth Ngure, Rachel Scheckter, Devika Singh, Kristine Torjesen, Ariane van der Straten, Rhonda White
- **Microbicides Trials Network Laboratory Center (Magee-Womens Research Institute, University of Pittsburgh, Johns Hopkins University):** Craig Hendrix, Edward Livant, Mark Marzinke, John Mellors, Urvi Parikh
- **Microbicides Trials Network Statistical and Data Management Center (Fred Hutchinson Cancer Research Center):** Elizabeth Brown, Jennifer Berthiaume, Marla Husnik, Jason Pan, Karen Patterson, Melissa Peda, Barbra Richardson, Daniel Szydlo
- **US National Institutes of Health:** Nahida Chakhtoura, Donna Germuga, Cynthia Grossman, Diane Rausch, Lydia Soto-Torres
- **International Partnership for Microbicides:** Zeda Rosenberg, Annalene Nel
- **ASPIRE & HOPE participants and their communities and Community Working Group**
- The International Partnership for Microbicides provided the study rings.
- 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.