

# Lessons from MTN-025/HOPE

## OLE of MTN-020/ASPIRE

Thesla Palanee-Phillips (MMed Sci, PhD, MSc)

Nyaradzo M. Mgodi (MBChB, MMed)

Protocol Co-Chairs for and on behalf of the HOPE Team

MTN Annual Meeting, Feb, 11 2019

MD, USA



UNIVERSITY OF THE  
WITWATERSRAND,  
JOHANNESBURG



# Background

Two phase III clinical trials showed that a monthly vaginal ring containing dapivirine was well tolerated and reduced HIV-1 incidence by approximately 30% compared to placebo.



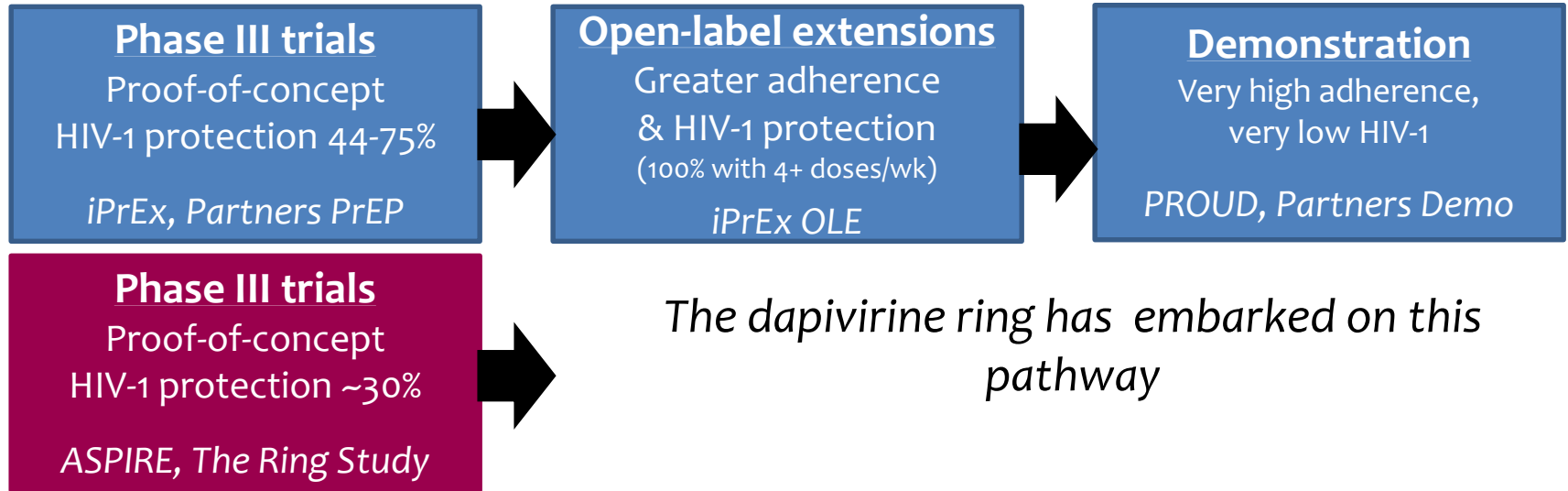
ASPIRE



Baeten et al., Nel et al., NEJM 2016

# Open-label HIV-1 prevention

For PrEP, open-label extensions provided key information beyond what was learned in phase III trials, moving the field towards demonstration and scale-up:

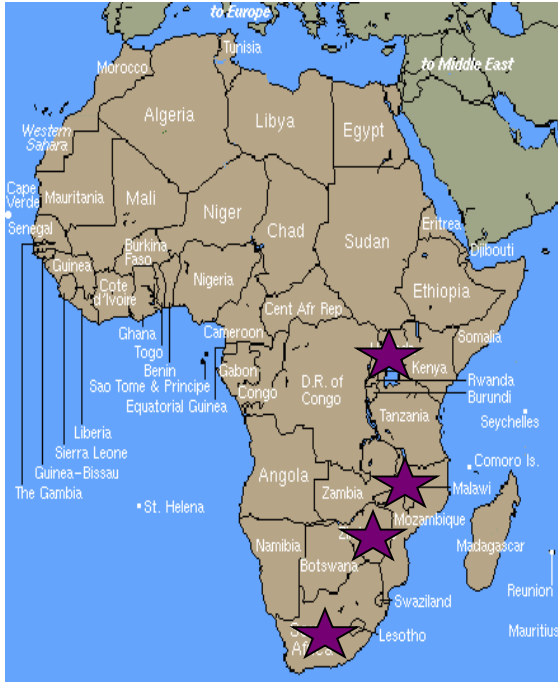


# MTN-025/HOPE

- Multi-center, open-label, phase IIIb trial of the dapivirine vaginal ring (25 mg, replaced monthly).
- **Population:** HIV-1 uninfected women who previously participated in MTN-020/ASPIRE.
  - Women chose to accept or not accept the ring at each follow-up visit.
- **Primary objectives:** assess adherence and safety in an open-label setting.



# Final Enrollment numbers



- Between August 2016 and May 2018, a total of 1456 women were enrolled
- Participants are from 14 sites in 4 countries:
  - Malawi (n=157, 11%)
  - South Africa (n=707, 49%)
  - Uganda (n=172, 12%)
  - Zimbabwe (n=420, 29%)

# Where we live

Johannesburg



Harare, Zimbabwe



Durban



Cape Town



Kampala,  
Uganda



Blantyre, Malawi



Lilongwe, Malawi



# The communities where we work

Johannesburg

Chitungwiza, Zim

Durban

Cape Town

Lilongwe, Malawi

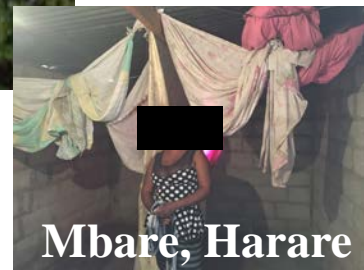
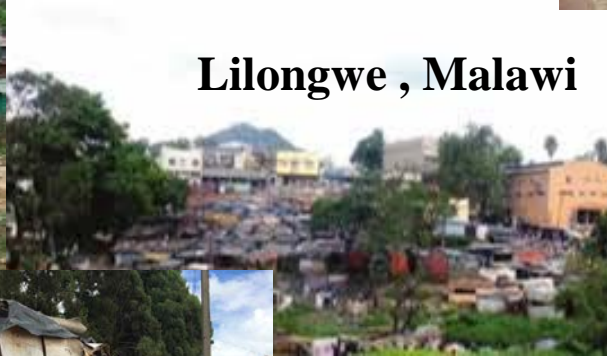
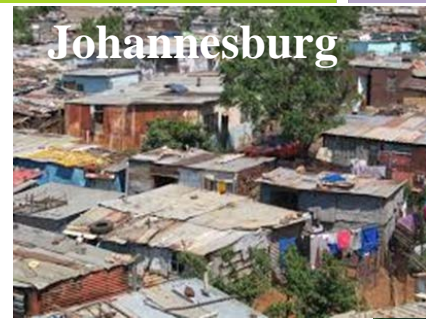
Hillbrow, Jhb

Blantyre, Malawi

Uganda

Mbare, Harare

Mbare, Harare



# Participant characteristics

Participant characteristics defined a population at risk for HIV-1 (n=1407)

*Although population characteristics had somewhat evolved since enrollment into MTN-020/ASPIRE*

<b>Characteristics at study entry</b>	<b>MTN-025 HOPE</b>	<b>MTN-020 ASPIRE</b>
<b>Age, median</b>	31 (IQR 27-37)	26 (IQR 22-31)
<b>Age, &lt;25 years</b>	13%	39%
<b>Married</b>	53%	41%
<b>Sexually transmitted infection (GC/CT/TV/TP)</b>	16%	21%
<b>Used a condom with last sex act</b>	44%	57%





# High uptake and reduced HIV-1 incidence in an open-label trial of the dapivirine ring

---

The MTN-025/HOPE Study Team  
CROI 2018, Boston, USA

# Ring Uptake and Adherence

- 92% accepted ring at Enrollment
- To date, **89% of returned rings** have residual drug levels  $<23.5$  mg, indicating at least some adherence
  - Compared to **77% of rings** in MTN-020/ASPIRE



The MTN-025/HOPE Study Team  
CROI 2018, Boston, USA

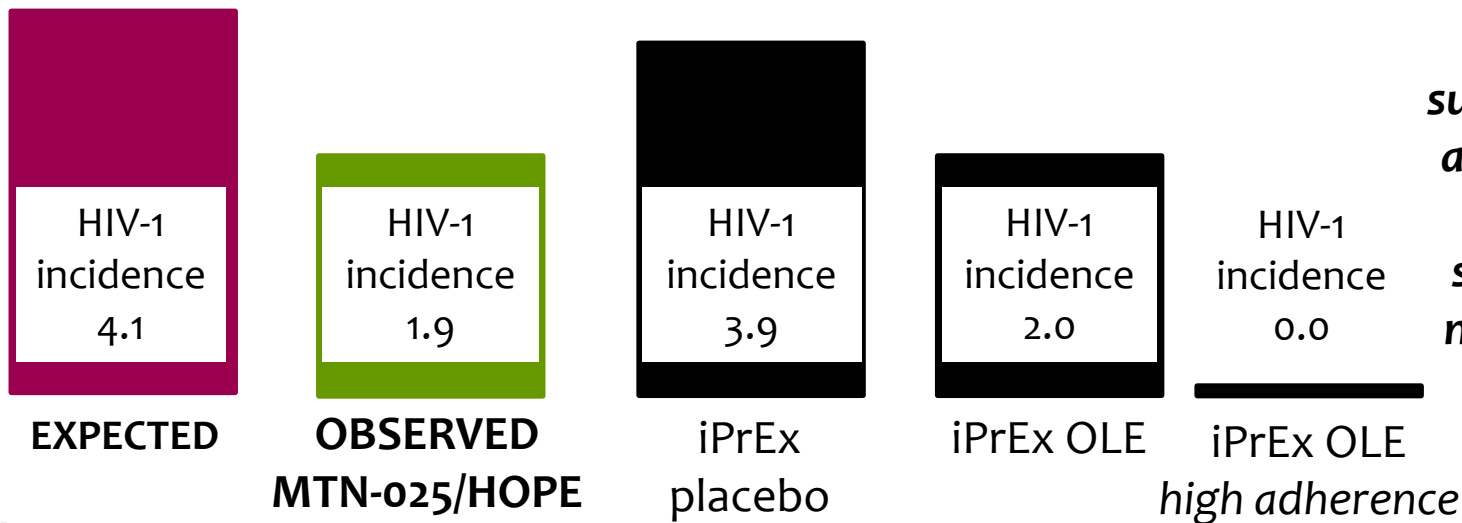
# HIV-1 incidence

**MTN-025/HOPE HIV-1 incidence:  
1.9 per 100 person-years (95% CI 1.0-3.4)**

**MTN-020/ASPIRE HIV-1 incidence in placebo arm:  
4.5 per 100 person-years (95% CI 3.7-5.5)**

# Comparison to other open-label data

- The HIV-1 incidence observed to date in MTN-025/HOPE compares favorably to that seen in prior open-label extension studies, for example iPrEx OLE:



***HIV incidence in iPrEx OLE among the subset with high PrEP adherence was zero. Similar adherent subset analyses are not yet available for MTN-025/HOPE.***

# What have we learned?

---

# Something imperfect can still be wanted, used, and impactful



- Knowing that an intervention works to reduce risk and having a choice to use it matters
- Adherence *is* higher in HOPE (CROI 2018 data) than in ASPIRE and incidence is lower
- We need to do better for young women (where adherence was low). What we will learn from MTN-034/REACH is critical.



# 2

## Women need choices

- Ring is not for everyone, and not for everyone all the time
- Need support of counsellors, of partners, of each other – *i.e. may accept a ring but still face challenges*
- Overall top reasons for decline are:
  - Prefers alternate HIV prevention method
  - Undecided /not ready
  - Participant not interested
  - Partner concerns/wants to inform partner before initiating use

Study Month	Ring Acceptors
Enrollment	92%
Month 1	90%
Month 2	89%
Month 3	87%
Month 6	83%
Month 9	79%



# Counselling to Optimize Adherence, Choice and Honest Reporting

- Counselling is hard!
- Desire to help often leads one to try and persuade participants to take certain actions.

## **COACH**

- Client-centered counselling skills.
- Facilitated individualized feedback for counsellors.
- Improvement in skills and fidelity monitoring.

Counselling for cause - improving fidelity – Ivan Balan



# 4

## Contraception and Pregnancy

- Women in SSA have relatively high fertility rates.



- Unmet need for contraception also high but we fulfilled this in ASPIRE and HOPE.
- **Low pregnancy rates – CAT team! Persistence of LARC method use between ASPIRE and HOPE.**
- At baseline, Screened out 43(29%) of 187 (11%) of ineligible participants due to Pregnancy or Pregnancy intentions and 26(17%) due to breastfeeding.
- Baseline contraceptive use among enrolled was high : OC (14%), Implants (23%), IUDs( 18.2%), DMPA (32%), NET-EN (7%), Sterilization (5%).

# 4a

# Safety in Pregnancy and Breastfeeding



- Most studies of investigational drugs intentionally exclude pregnant women and breastfeeding (BF) women.
- Most drugs are released onto the market without an indication for use in pregnancy and BF.
- Unmet need for safe HIV prevention interventions during pregnancy and BF.
- If a prevention method is proven safe/effective--timeline to pregnant/BF use is even longer!
- MTN- 041 : Learning how best to conduct studies in pregnant and BF women.

DELIVER – Katie Bunge

B-PROTECTED – Lisa Noguchi/Jen Balkus



# 5 Efficiency Impacts everything

- Streamline protocol requirements/visit procedures, shorten ICFs.
- Balance between desired/required questionnaires, CRFs, samples.
- Consider level of counseling needed, staffing requirements .



Maintain  
Quality



Maximise  
Efficiency

From retention to adherence to data quality; respect participant's time and value what they are giving.

It starts with protocol development and design, and we need to do better.

# 6 People, Products and Partnerships

- Impact people first and behaviour next!
- Desire for products that fit into peoples lives.
- Communities/Community Advisory Boards - important input on the concept, implementation, design, cultural sensitivity and acceptability.



# 7

## Taking care of the carer

### Compassionate Fatigue

- Staff working across multiple networks with high risk participants also need support.
- Along with participants and communities, our staff are critical to success and valuing their work and supporting their health is paramount.

### Burnout

### Vicarious Trauma



# 8 Celebrating a product that works

- Exciting to work on something that works to reduce HIV risk.
- Years of funding, multiple networks - MPT potential?
- A product that might one day get to women in need.
- Progress along the path towards licensure - people who are committed to people made this happen - we salute you!

*We Change Lives*



# Summary



- Something imperfect can still be wanted, used, and impactful
- Choices, choices, choices!

Case from Harare, IMPAACT - 27 year old *Stella*, para 2, planned 3<sup>rd</sup> pregnancy, preconception care, tested for HIV before conception - negative, booked for ANC at 8 weeks, regular HIV testing, tested in labour – negative. Delivered a healthy baby, *Tanaka*. Exclusive breast feeding for 6 months, Regular VCT post delivery – both mother and baby HIV negative but, partner promiscuity cited, inconsistent use of condoms, partner against use of oral PrEP. At 12 months post-delivery, **both *Stella* and baby *Tanaka* HIV infected.**

- It is all about **people** – **leave no woman behind**, be efficient - women are autonomous beings, respect their time and give them choices.
- It takes a village





# It Takes a Village !

## MTN-025/HOPE Study Team



- **Leadership:** Jared Baeten (protocol chair), Thesla Palanee-Phillips (protocol co-chair), Nyaradzo Mgodzi (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, Lameck Chinula
  - **South Africa: Cape Town site (University of Cape Town):** Lulu Nair, Linda-Gail Bekker
  - **South Africa: Durban eThekweni site (Centre for AIDS Programme of Research in South Africa):** 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, Simone Hendricks, Shaamilah Suleman, 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 College of Health Sciences Clinical Trials Unit):** Nyaradzo Mgodzi, 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):** Sharon Hillier, Ian McGowan, Ivan Balan, Katherine Bunge, Beth Galaska, Morgan Garcia, Cindy Jacobson, Judith Jones, Ashley Mayo, Barbara Mensch, Elizabeth Montgomery, Patrick Ndase, Kenneth Nguni, 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, Karen Patterson, Melissa Peda, Barbra Richardson, Daniel Szydio
- **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.



# Acknowledgements

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