# Overview of PrEP studies:

## *UZCHS-CTRC experience*

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Saving Lives Through Innovative Research Strategies

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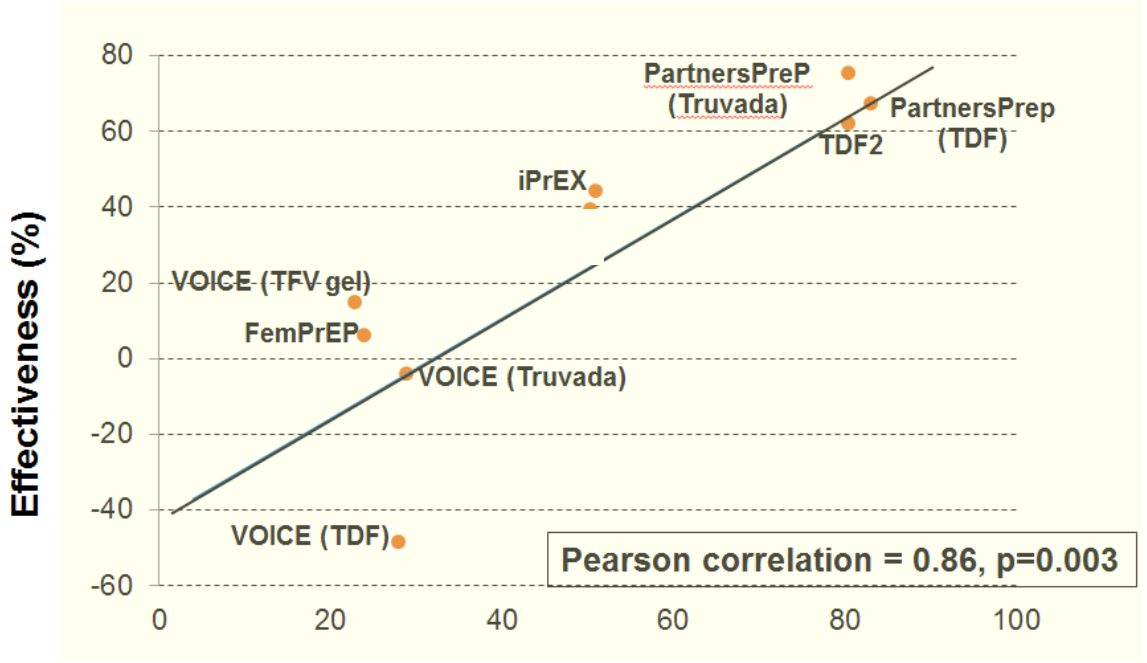
# Outline

- Introduction
- Studies conducted by UZCHS-CTRC involving :
  - Oral PrEP
  - Vaginal rings
  - Long acting Injectable PrEP
- Conclusion

# Introduction

- Oral Truvada (FTC/TDF) was FDA Approved for use for prevention on July 16,2012.
- However, effectiveness is largely dependent on adherence .
- Newer, safer products that do not need to be taken every day are needed for people who may not want to take a daily pill or who may find it difficult to take a pill every day




**Adherence (%) adjudicated by drug levels**

Abdool Karim, SS IAS 2014

# Understanding HIV Prevention in adolescents & young African women


- Women in sub-Saharan Africa are at risk for HIV and new effective methods of HIV prevention are needed
- HIV prevalence up to 8 times more in young women than men*
- Given lower adherence & efficacy with Truvada (FTC/TDF) & dapivirine (DPV) ring among young women in clinical trials there is :
- Need to understand acceptability and adherence to oral PrEP & vaginal rings in adolescents & young women

**Abdool Karim, TUSS0602, AIDS2016*

# HPTN Q82 HERS


- **Purpose** - to assess acceptability and adherence of oral PrEP among HIV-uninfected young women (16-25yrs) in Southern Africa.
- **Study size** - 400 young women who accept PrEP at enrollment and up to 200 young women who decline PrEP at enrollment.
- **Study sites** – Spilhaus - Harare, Emavundhleni – Cape Town, Wits – Johannesburg
- **Status**- study follow-up complete

**Results –**

- 94% of young women who enrolled in HPTN 082 initiated PrEP
- Two-thirds of women attended at least one PrEP adherence support club in the first 3 months
- The majority used PrEP at 3 months; 84% had detectable intracellular TFV –DP levels in DBS
- Adherence in HPTN 082 was significantly higher than in VOICE and FEM-PrEP, which assessed PrEP use by plasma TFV levels

*2019 CROI Conference*

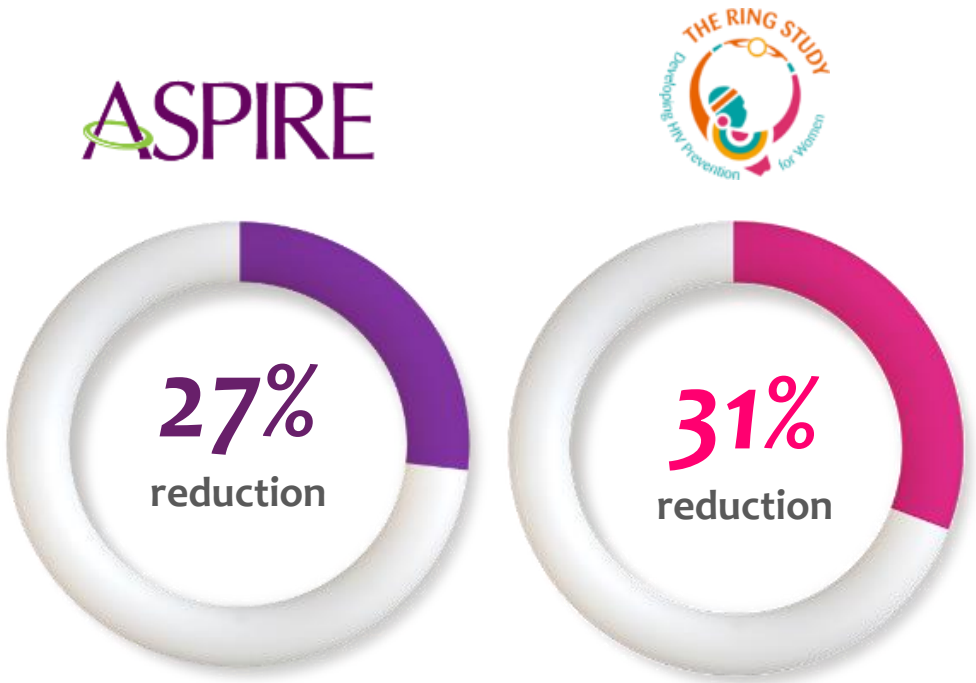
INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

# The Dapivirine Vaginal Ring

- The dapivirine ring was developed by the International Partnership for Microbicides (IPM)
- The ring contains an ARV -- dapivirine -- to offer women potentially longer-acting protection against HIV
- It is the first vaginal ring being tested for HIV prevention
- The ring is designed to be worn for a month at a time
  - The ring slowly releases dapivirine into the cervix and vagina over the month it is worn
- 20 early phase (Phase I/II) studies have shown dapivirine is safe as both a gel and ring

# ASPIRE and The Ring Study

- Two phase III clinical trials – MTN-020/ASPIRE and IPM 027/The Ring Study – showed that the monthly dapivirine vaginal ring was **safe** and **reduced HIV risk**
- Higher levels of protection were seen in women who used the ring most regularly




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

MTN microbicide trials network

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

# Phase III Trial Locations

**The Ring Study: 7 Research Centres n = 1959**

- **South Africa (n=1762):**
  - Kwa-Zulu Natal (3 sites)
  - North-West
  - Western Cape
  - Limpopo
- **Uganda:**
  - Masaka

**ASPIRE: 15 NIH Clinical Research Sites n= 2629**

- **South Africa (n=1426):**
  - Western Cape
  - Kwa-Zulu Natal (7 sites)
  - Gauteng
- **Uganda:**
  - Kampala
- **Zimbabwe: (n=678)**
  - Harare (3 sites)
- **Malawi:**
  - Blantyre
  - Lilongwe


**The Ring Study**

| Enrolment | Total Number Screened | Total Number Enrolled |
|---|---|---|
| South Africa: Kwa-Zulu Natal | 2038 | 1064 |
| South Africa: North West | 795 | 482 |
| South Africa: Western Cape | 116 | 97 |
| South Africa: Limpopo | 150 | 119 |
| Uganda: Masaka | 325 | 197 |

**ASPIRE**

| Enrolment | Total Number Screened | Total Number Enrolled |
|---|---|---|
| Malawi: Blantyre | 199 | 130 |
| Malawi: Lilongwe | 200 | 142 |
| South Africa: Western Cape | 217 | 166 |
| South Africa: Kwa-Zulu Natal | 2853 | 1047 |
| South Africa: Gauteng | 401 | 213 |
| Uganda: Kampala | 408 | 253 |
| Zimbabwe: Chitungwiza | 835 | 448 |
| Zimbabwe: Harare – Spilhaus | 403 | 230 |

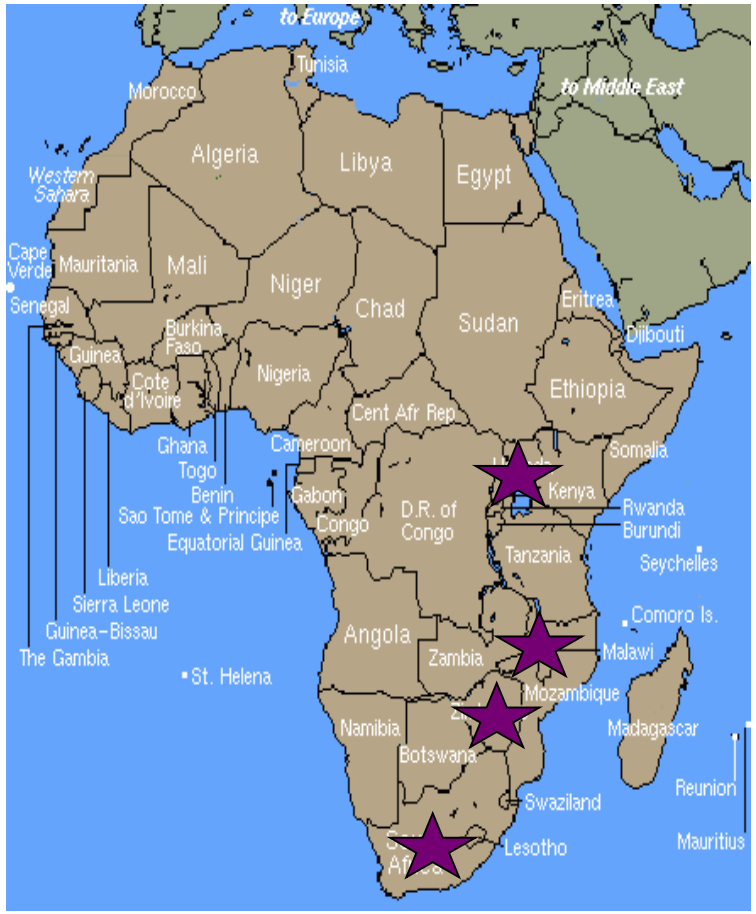
# MTN-025/HOPE

- MTN-025/HOPE was a **multi-center open-label extension study** (a phase IIIb trial) of the dapivirine vaginal ring (25 mg, replaced monthly).
- The **population** was HIV-1 uninfected women who had previously participated in MTN-020/ASPIRE.
- The **primary objectives** of MTN-025/HOPE were to assess **adherence** and **safety** in an open-label setting.
- **Secondary objectives** included assessing **HIV-1 incidence** and **HIV-1 antiretroviral resistance.**

MTN
microbicide trials network

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

# Enrollment




- For MTN-025/HOPE, 1643 women were screened and 1456 women were enrolled, 59% of those HIV-1 uninfected at the completion of MTN-020/ASPIRE.
  - Most common reasons for not enrolling were having acquired HIV-1 (30%) & wanting to become pregnant (29%)
- Participants were from 14 sites in 4 countries:
  - Malawi (n=157, 11%)
  - South Africa (n=707, 49%)
  - Uganda (n=172, 12%)
  - Zimbabwe (n=420, 29%)

MTN microbicide trials network

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

# MTN-025/HOPEHOPE Results Summary

- Most women who enrolled **chose to accept the ring (92% at enrollment)**, and used it with **higher adherence** than in ASPIRE
- The ring is **very safe**
- The ring **reduced HIV risk by 39%**

MTN
microbicide trials network



# HOPE and its "Sister Study"

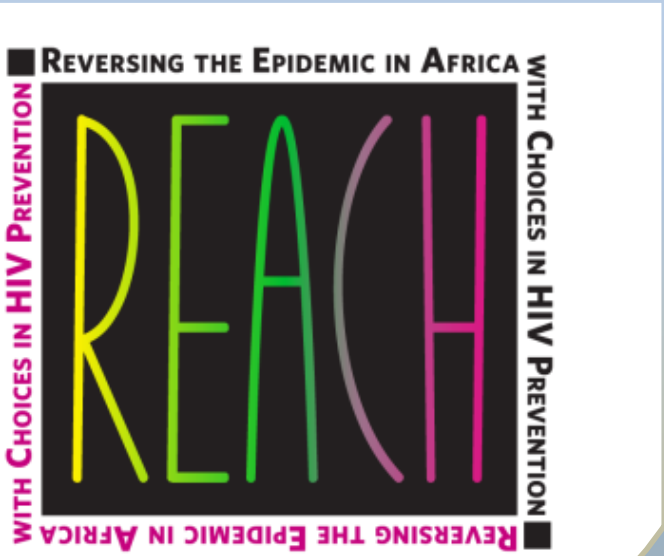
- Both studies suggest **interest in, adherence to**, and **HIV-1 risk reduction effectiveness of** the dapivirine vaginal ring when used in an open-label setting, making the dapivirine vaginal ring a potential HIV-1 prevention option for women.

# What's next for the ring?

- The dapivirine ring is currently under regulatory review by the European Medicines Agency (EMA) through the Article 58 procedure, which allows the EMA, in cooperation with the World Health Organization (WHO), to provide a scientific opinion on the ring's use in low- and middle-income countries.
- Separately, IPM plans to submit applications to the South African Health Products Regulatory Authority (SAHPRA) and to the U.S. Food and Drug Administration (FDA).
- If approved, the dapivirine ring would be the first biomedical HIV prevention product exclusively for women – and the first long-acting product.

# Additional Research with the Ring

- Studies to better understand HIV prevention needs of younger women and adolescent girls are ongoing (MTN-034/REACH).
- Safety studies of ring use during pregnancy (MTN-042/DELIVER) and breastfeeding (MTN-043/B-PROTECTED) are also being planned.
- Other studies looking at a 3-month ring and a ring that includes both a contraceptive and dapivirine are underway.





deliver


# Long acting Injectable PrEP

- To evaluate the relative safety and efficacy of injectable PrEP Cabotegravir (CAB) vs. daily oral Truvada (TDF/FTC) for HIV prevention.
- Phase 3 superiority trial
- Randomized, Double Blind,
  Double Dummy
- All study volunteers receive one active and one inactive product
- 20 sites in 7 countries in SSA
- 5 sites in Zimbabwe, 3 in Chitungwiza and 2 in Harare .
- 3,200 women

HPTN 084

Long-acting Injectable For the Epidemic

# Study update

- Study opened November 07, 2017
- All Sites activated
- 2 048 women enrolled (64%)  as of 20 August 2019
- Zimbabwe  currently has 614 women enrolled across 5 sites
- Retention – high, >92% for all visit types
- Study ongoing, results expected 2023

# In conclusion,

- Women need choices and their preferences are not all the same.
- Even the most effective product cannot protect against HIV if it is not used. Higher adherence results in higher protection.
- Long acting PrEP may remedy adherence issues.
- If approved, the dapivirine ring would be the first biomedical HIV prevention product exclusively for women – and the first long-acting product.
- Involving young women and adolescents in HIV prevention study is necessary to ending the HIV epidemic.

# Acknowledgements


- UZ-CHS-CTRC
- Clinic staff, recruiters and investigators
- Study participants and Community
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