

The logo for ASPIRE features the word "ASPIRE" in a bold, purple, sans-serif font. A green ring is positioned around the letter "A".

# ASPIRE

A Study to Prevent Infection  
with a Ring for Extended Use

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On behalf of the ASPIRE team

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# MTN-020 / ASPIRE

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# Overview

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- Background and rationale
- Design and objectives
- Progress
- Optimizing implementation



# **Background and Rationale**

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# Antiretrovirals work for HIV prevention: successes

- Clinical trials of oral and topical tenofovir-based PrEP demonstrated efficacy for HIV protection:

Trial	PrEP regimen	Population	Reduction in HIV risk
CAPRISA 004	Peri-coital tenofovir gel	Women	39%
iPrEx	Daily oral FTC/TDF	Men who have sex with men	44%
TDF2	Daily oral FTC/TDF	Young heterosexuals	62%
Partners PrEP	Daily oral TDF and FTC/TDF	HIV serodiscordant couples	67% (TDF) 75% (FTC/TDF)

# Antiretrovirals for HIV prevention: challenges

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- However, not all trials of tenofovir-based PrEP found HIV protection:
  - No efficacy for daily oral FTC/TDF in FEM-PrEP trial and for daily tenofovir gel and daily TDF in VOICE study, both studies of women at high risk for HIV
- In the FEM-PrEP study, low adherence explains the failure of that trial to show HIV protection

# Antiretrovirals for HIV protection

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✓ Right drug

(safe, effective, potent)

✓ Right place

(sufficient concentrations at site of exposure)

✓ Right time

(present when exposed)

✓ Right use

(adherence, easy to use, acceptable)

# Developing a range of options for antiretroviral-based HIV prevention



Pill



Gel



Vaginal film



Vaginal ring



Injectable

- ✓ Truvada PrEP is critical first proof that we have powerful pathways to prevent HIV.
- ✓ But the trials of Truvada also illustrate that we need more strategies than pills alone, particularly strategies that might be easier to use.



# **Study Design and Objectives**

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# MTN-020 / ASPIRE

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- **A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase III Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women**

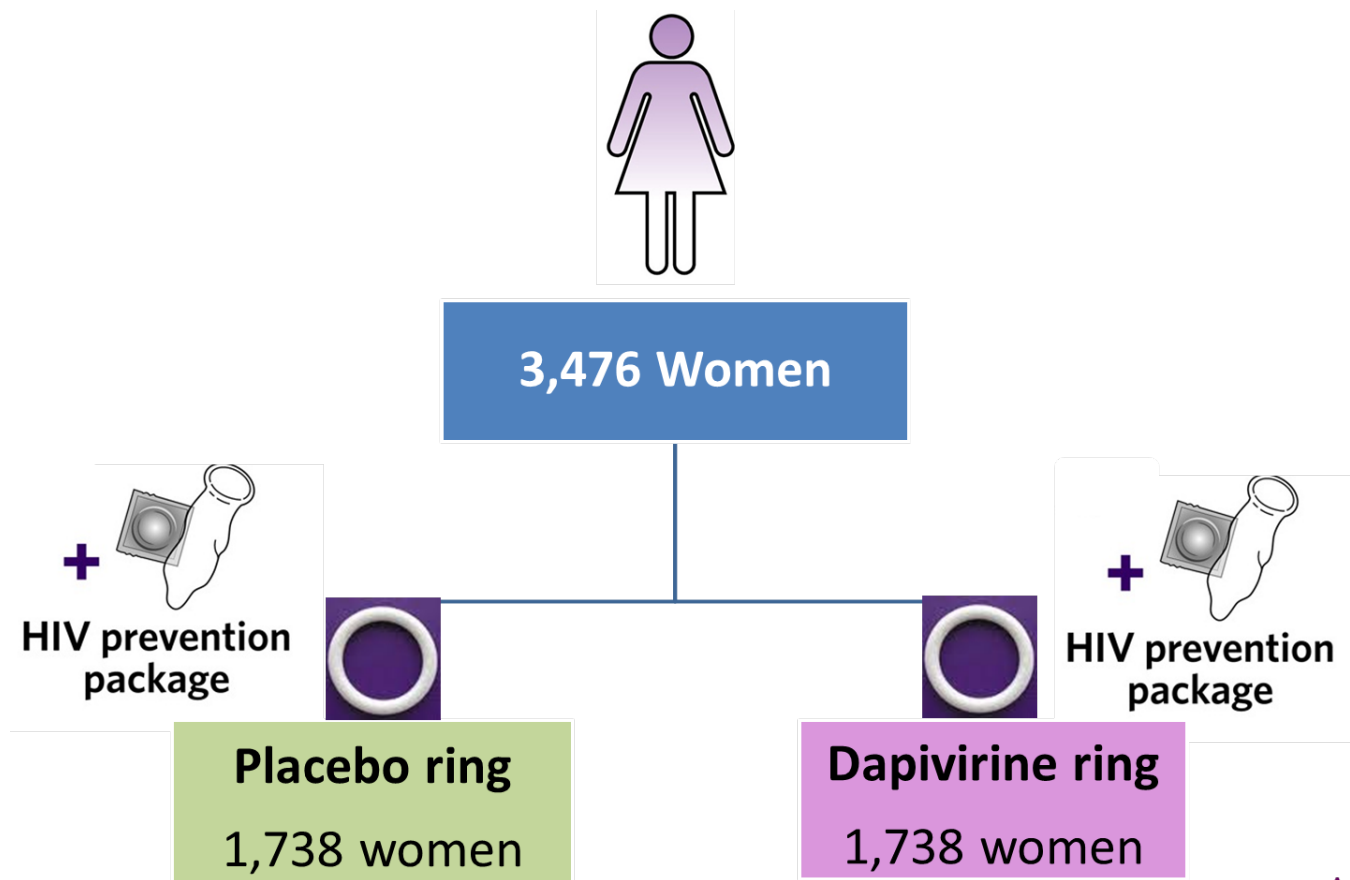
# Dapivirine ring for HIV prevention

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- Dapivirine is a non-nucleoside reverse transcriptase inhibitor
- Flexible ring made of an elastic silicone material, by the International Partnership for Microbicides (IPM)
- MTN-020, in concert with the entire dapivirine package, will provide strength of evidence to support potential licensure



# ASPIRE Study Design



# Objectives

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## PRIMARY

- Safety and effectiveness for HIV-1 prevention

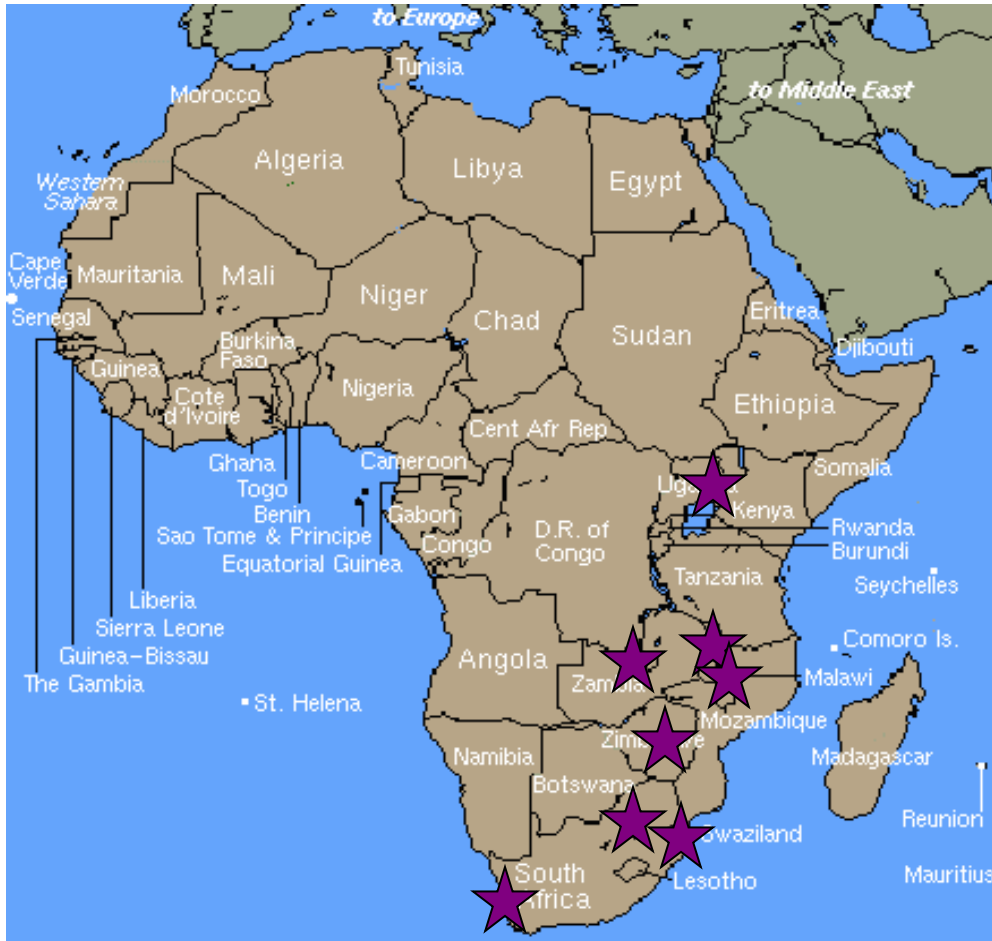
## SECONDARY

- Acceptability, adherence, resistance, PK/PD

## EXPLORATORY

- Genital microenvironment, adherence vs. PK, delayed seroconversion

# Proposed sites



Blantyre  
Lilongwe  
**Malawi**

Cape Town  
Durban (7 sites)  
Johannesburg  
**South Africa**

Kampala  
**Uganda**

Lusaka  
**Zambia**

Harare (3 sites)  
**Zimbabwe**

# Progress

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# ASPIRE to date

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- January - October 2011
  - Network, NIAID SWG, PSRC review
  - Protocol Team & Community Consultations
- June, July 2012
  - First site training (Cape Town), first activation (Kampala)
- August 21, 2012
  - First enrollment (Kampala)
- August 2012 - present
  - Ongoing site activations, enrollments, execution
- November 2012
  - DSMB review



# Site activations



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Site	Date of activation	Site	Date of activation
MA – Blantyre	Site preparations underway	SA – MRC/Verulam	28 AUG 2012
MA - Lilongwe	Site preparations underway	SA – MRC/Umkomaas	28 AUG 2012
SA – Cape Town	4 SEP 2012	SA – WRHI	16 OCT 2012
SA – CAPRISA eThekwini	13 SEP 2012	UG – Kampala	19 JUL 2012
SA – MRC/Botha’s Hill	28 AUG 2012	ZA – Lusaka	APPROVALS PENDING
SA – MRC/Chatsworth	28 AUG 2012	ZI – Seke South	22 OCT 2012
SA – MRC/Isipingo	28 AUG 2012	ZI – Spilhaus	22 OCT 2012
SA – MRC/Tongaat	28 AUG 2012	ZI – Zengeza	23 OCT 2012

# Enrollments (6 Feb 2013)

Site	First enr	# enr
SA – Cape Town	19 SEP 2012	62
SA – CAPRISA eThekwini	10 OCT2012	67
SA – MRC/Botha's Hill	10 SEP 2012	93
SA – MRC/Chatsworth	11 SEP 2012	86
SA – MRC/Isipingo	19 SEP 2012	74
SA – MRC/Tongaat	17 SEP 2012	70
SA – MRC/Verulam	13 SEP 2012	81
SA – MRC/Umkomaas	14 SEP 2012	72
SA- WHRI/Hillbrow	30 OCT 2012	51
UG – Kampala	21 AUG 2012	93
Zim – Seke South	01 NOV 12	54
Zim – Spilhaus	30 OCT 12	58
Zim – Zengeza	13 NOV 12	47
<b>TOTAL</b>		<b>875</b>

# Timeline

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2011

- Initiate site IRB and regulatory approval process

2012

- IRB/regulatory approvals, trainings, start

2013

- Enrollments, follow-up

2014

- Follow-up

2015

- Results

# Clinical development program for dapivirine for HIV prevention

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- To date, 25 phase I/II trials of dapivirine (in oral, gel, and ring form) have been conducted
- Trials have demonstrated high safety for topical dapivirine
- Agency reviews (FDA/EMA) have permitted move to efficacy evaluation
- In parallel to MTN-020, IPM is conducting IPM 027 (The Ring Study) – focus on extended safety plus efficacy

# MTN-020 and IPM 027

	<u>MTN-020</u>	<u>IPM 027</u>
<b>Design</b>	endpoint driven	fixed time
<b>No. of participants</b>	3,476	1,650
<b>Randomization</b>	1:1	2:1
<b>Age</b>	18-45 yrs	18-45 yrs
<b>Product use period</b>	Until end of study (12-24 months)	24 months fixed
<b>Person-years follow-up (all / Dapivirine Vaginal Ring)</b>	4,396 / 2,198	3,150 / 2,100
<b>HIV-1 seroconversions</b>	120	80

**ASPIRE**  
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# Optimizing ASPIRE

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# The Big Five

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**Accrual**

**Data Quality  
and Timeliness**

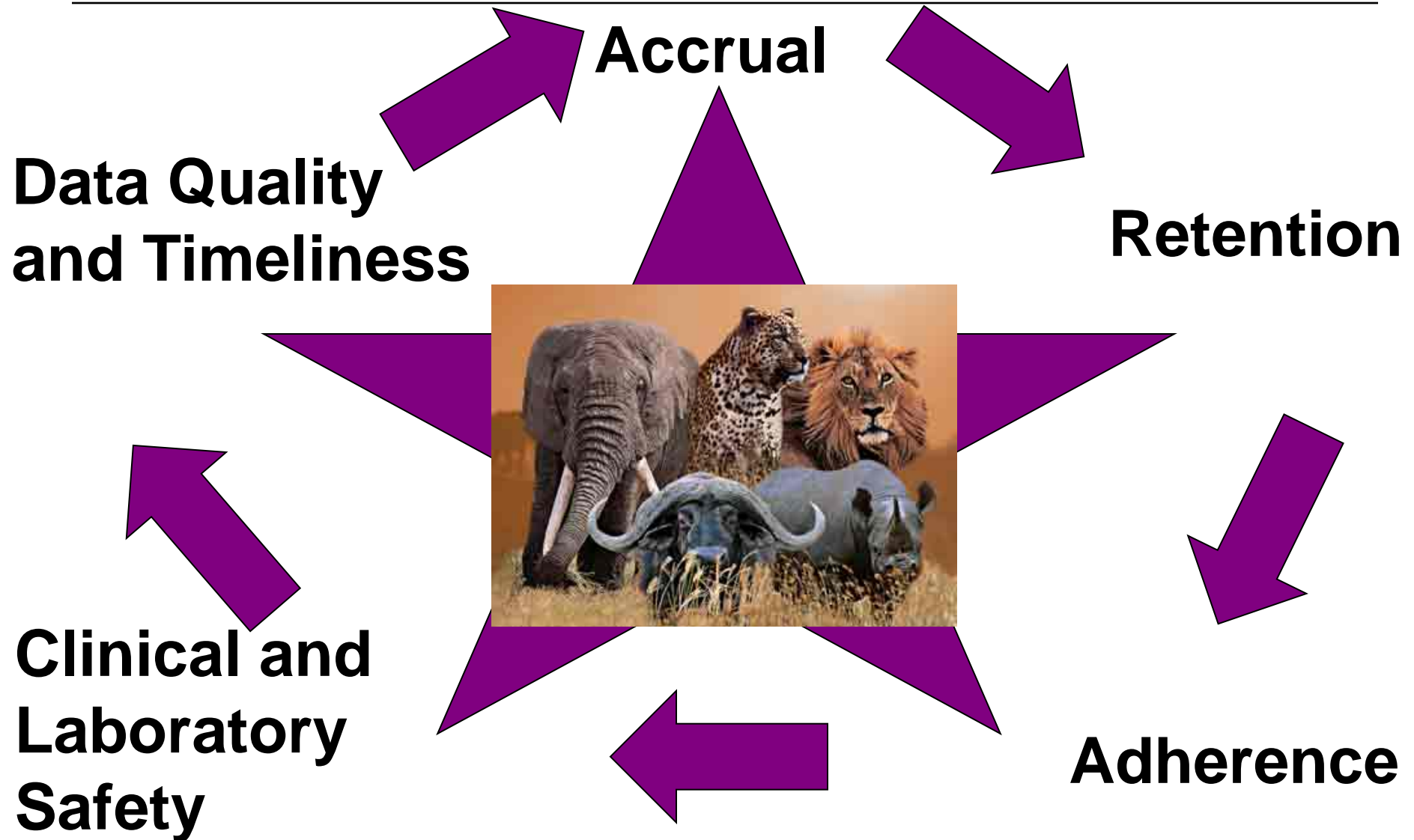
**Retention**



**Clinical and  
Laboratory  
Safety**

**Adherence**

# The Big Five





# Accrual is Retention

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- Enrollment into a trial like ASPIRE is an important commitment
  - To monthly visits
  - To questionnaires and blood/genital samples
  - To volunteerism and HIV prevention

*We are partnering with every participant to maximize the success of this study.*



# Retention is Adherence

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- Every missed visit is a month of **zero** adherence



# Adherence is Everything

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- Products don't work if they aren't used

# Learning from PrEP trials

	HIV protection <u>efficacy</u> for FTC/TDF versus placebo in randomized comparison	% of blood samples with tenofovir detected
Partners PrEP	75%	81%
TDF2	62%	79%
iPrEx	44%	51%
FEM-PrEP	6%	26%

**Clear dose-response between evidence of use & HIV protection**

# Adherence and prevention

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- How can we learn (and react to) ring non-use and challenges with participating in a multi-month study?
  - Qualitative interviews
  - Staff observations
  - Biologic assays to evaluate product adherence

# Safety

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- Safety is the co-primary endpoint of the study
  - Evaluating whether the product is safe is just as important as whether the product is effective for HIV prevention

# Accural → Retention → Adherence → Safety → Quality → Success

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- >95% = retention, product distribution, adherence
- 100% = attention to data quality, safety

*Everything else flows from these*

# We are all in this together

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- We all work together – all parts of the study are all our business

Recruitment

Retention

Adherence

Sample collection

Staff morale

Community/outreach

Communications

Lab quality

QC/QA

Regulatory

Safety Monitoring

Space/facilities

Study drug/pharmacy

Contraception

Lab-clinic interface

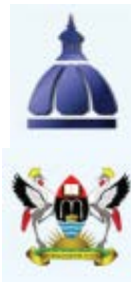
Monitoring follow-up



# IT TAKES A TEAM



Malawi College of  
Medicine – JHU  
Research Project



UNC Project -  
Malawi



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School of Medicine



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