

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

A Study to Prevent Infection  
with a Ring for Extended Use

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Jared Baeten MD, PhD

Thesla Palanee, PhD

*Implementation Update*

ASPIRE Protocol Team Meeting

October 2013



# MTN-020 / ASPIRE

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# Outline

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- Meeting overview

## **ASPIRE**

- Where we've been
- Where we are
- Where we are going



# Meeting overview

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- A packed day:
  - MORNING: focus on adherence – what we are *doing, learning, and changing* at the community, in-clinic, and individual levels
  - AFTERNOON: lively discussion of clinical safety, retention, and data quality
  - THROUGHOUT: remembering our Big 5 metrics, working together as a team
  - END OF THE DAY: Awards!



# Where we have been

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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**



# The Big Five

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**Accrual**

**Data Quality  
and Timeliness**

**Retention**



**Clinical and  
Laboratory  
Safety**

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**Adherence**

# ASPIRE calendar

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- January 2011 and ongoing
  - Multilevel consultations on the science and implementation, leading to protocol version 1.0 in September 2011
- August 2012 - present
  - Start and go! Enrollments, follow-up, highest-quality execution of all protocol aspects



# October 2012

(<100 enrolments)



# ASPIRE calendar

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- **November 2012, May 2013**
  - **DSMB**
- **May 2013**
  - **Malawi sites activated**
- **April, August & October 2013**
  - **SMC reviews**

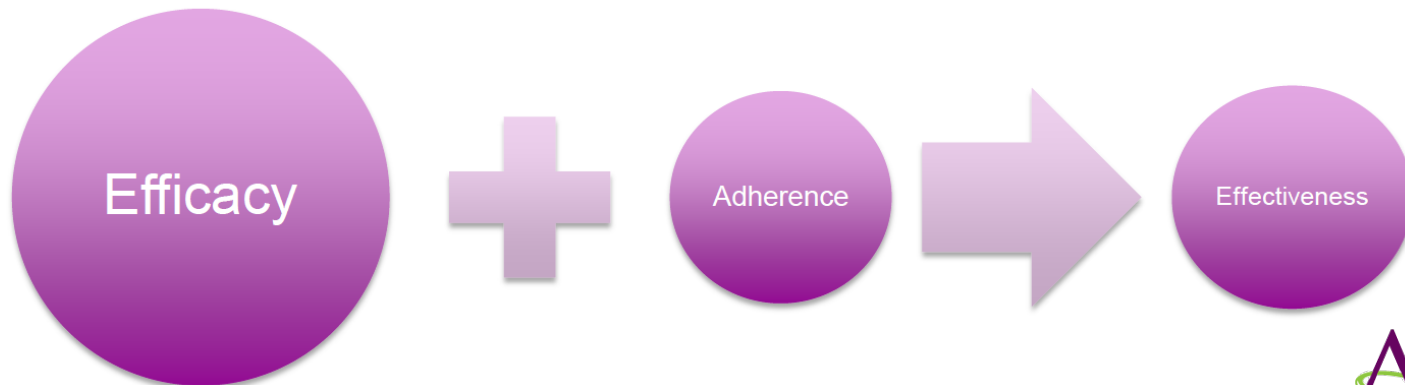
# March 2013: learning from PrEP trials

	<b>HIV protection for FTC/TDF versus placebo</b>	<b>% of blood samples with tenofovir detected</b>
<b>Partners PrEP</b>	75%	81%
<b>TDF2</b>	62%	79%
<b>iPrEx</b>	44%	51%
<b>FEM-PrEP</b>	<b>No HIV protection</b>	~30%
<b>VOICE</b>	<b>No HIV protection</b>	~30%

**No adherence = no HIV protection**

# Efficacy and effectiveness

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# Adherence is Everything

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Jared Baeten MD PhD  
Thesla Palanee PhD

**ASPIRE Adherence Meeting**  
**Durban, South Africa**  
**14 March 2013**

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# Adherence Action!

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

- Since March 2013:

  - Recognition of priority : scale-up across sites*

  - Participant and staff engagement activities*

  - IoR and SCs involved with difficult participants counselling*

  - Fun waiting room discussions and social events*

  - HIV ribbon and ring activities*

  - Male partner engagement efforts*

  - Visual inspection of the rings*

  - PK data reviewed, shared, and acted upon*

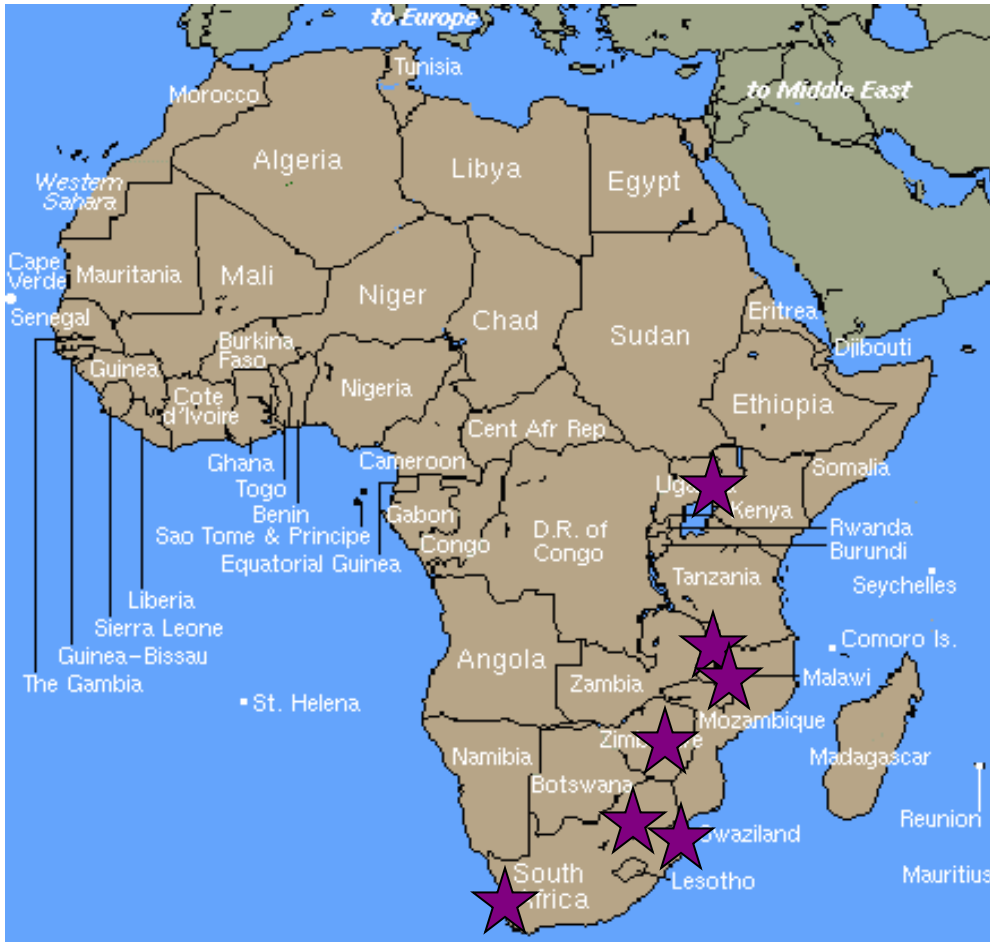
  - Learning from qualitative component of ASPIRE*



# Where we are

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# 15 Sites across 4 countries



Blantyre  
Lilongwe  
**Malawi**

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

Kampala  
**Uganda**

Harare/Chitungwiza (3 sites)  
**Zimbabwe**



# Accrual (23 Oct 2013)

Site	First enr	# enr	scr:enr ratio
MA – Blantyre	13 JUN 13	36	1.6
MA – Lilongwe	17 JUN 13	43	1.5
SA – Cape Town	19 SEP 2012	150	1.3
SA – CAPRISA eThekwini	10 OCT2012	150	3.2
SA – MRC/Botha's Hill	10 SEP 2012	120	2.5
SA – MRC/Chatsworth	11 SEP 2012	115	2.7
SA – MRC/Isipingo	19 SEP 2012	117	2.6
SA – MRC/Tongaat	17 SEP 2012	103	3.3
SA – MRC/Verulam	13 SEP 2012	114	2.4
SA – MRC/Umkomaas	14 SEP 2012	87	2.5
SA – WHRI/Hillbrow	30 OCT 2012	141	1.8
UG – Kampala	21 AUG 2012	205	1.6
ZI – Seke South	01 NOV 12	155	1.9
ZI – Spilhaus	30 OCT 12	150	1.8
ZI– Zengeza	13 NOV 12	146	1.8
<b>TOTAL</b>		<b>1832</b>	<b>2.1</b>

# Screen outs

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- As of 24 October 2013:
  - 3940 screened, 1840 enrolled (2.1 ratio)
  - 242 did not complete screening
  - 27 declined enrollment
  - 2100 ineligible
    - 718 (34.1%) HIV+
    - 71 (8.1%) pregnant, planning, or breastfeeding
    - 408 (19.4 %) clinical/laboratory exclusion
    - 507 (24.1%)“other” including investigator decision

# Who is enrolling?

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- Mean age: 27.1 years, Median: 26 years
  - 41% <25 years, 15% ≥35 years
- Unmarried: MA (33%), SA (92%), UG (37%), ZI (13%)
- Secondary schooling: MA (56%), SA (96%), UG (50%), ZI (85%)
- 100% had a primary partner in past 3 months
  - 19% had ≥1 other partner in past 3 months

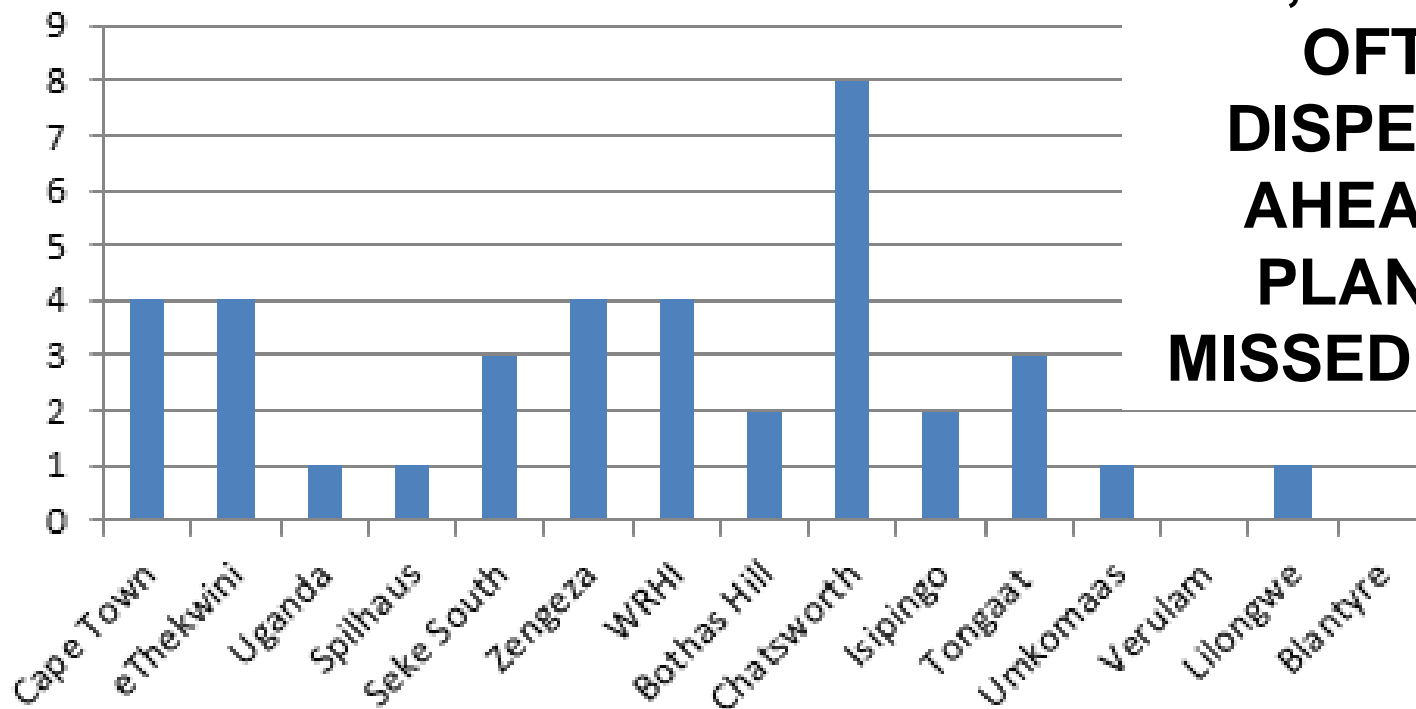
# Retention : As at 17 Oct 13

- 1667/1701 Month 1 visits (98%)
- 1562/1622 Month 2 visits (96%)
- 1485/1549 Month 3 visits (96%)
- 1392/1467 Month 4 visits (95%)
- 1273/1355 Month 5 visits (94%)
- 1183/1272 Month 6 visits (93%)
- 1096/1172 Month 7 visits (94%)
- 961/1038 Month 8 visits (93%)
- 813/870 Month 9 visits (93%)
- 704/768 Month 10 visits (92%)
- 576/626 Month 11 visits (92%)
- 324/351 Month 12 visits (92%)
- 111/119 Month 13 visits (93%)
- 23/23 Month 14 visits (100%)



# Retention : few missed visits!

Missed Visits - October



**AND, RINGS ARE  
OFTEN  
DISPENSED  
AHEAD OF  
PLANNED  
MISSED VISITS!**

# Adherence Measurements and Monitoring

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- We have learned much (and reacted to much) about non-use, non-interest?
  - Who returns without rings in place? Rings coming out?
  - Qualitative interviews, staff observations
  - Blood and swab samples

# Data Quality = unmatched!



## MTN-020 (ASPIRE) DATA MANAGEMENT QUALITY REPORT September 2013



Cumulative: Study Start through September 2013

Site	Total Records	Total QCs	QC Rate Per 100 Records	% QCs Resolved	% CRF Pages Received Within 7 Days	Mean Days to Fax in AE
Spilhaus/Zimbabwe	10294	103	1.0	98%	98%	3.5
Seke South/Zimbabwe	9883	163	1.6	99%	99%	11
Blantyre/Malawi	812	25	3.1	96%	89%	7.0
Lilongwe/Malawi	894	21	2.3	100%	98%	3.1
MRC - Chatsworth	11509	632	5.5	98%	93%	11.3
MRC - Botha's Hill	12038	697	5.8	100%	97%	7.8
MRC - Umkomaas	8691	400	4.6	100%	95%	3.6
MU-JHU/Kampala, Uganda	15239	390	2.6	97%	97%	11.1
Zengeza/Zimbabwe	9345	127	1.4	100%	99%	7.8
MRC - Isipingo	10616	271	2.6	94%	95%	3.6
MRC - Tongaat	10002	380	3.8	99%	99%	2.6
MRC - Verulam	11265	296	2.6	100%	98%	4.0
CAPRISA eThekweni	12089	422	3.5	98%	98%	2.3
WRHI/Johannesburg	9179	509	5.5	98%	96%	4.8
Emavundleni/Cape Town	11226	418	3.7	100%	99%	2.1
<b>TOTAL</b>	<b>143082</b>	<b>4854</b>	<b>3.4</b>	<b>99%</b>	<b>97%</b>	<b>5.8</b>

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# 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
  - Regulatory authorities will scrutinize safety data and careful attention to safety documentation is critical



# Laboratory

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- Laboratory results and archived samples are central to this study
  - THANK YOU TO ALL THE WORK!



# Contraceptive Action Team

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- Incredibly motivated and innovative approaches to broaden contraceptive mix, counsel on highly-effective and safe methods, and provide methods on site
- Mix is diverse: 20% IUDs, ~15% implants currently!

# Team communications

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- Monthly team calls
  - Tremendously valuable, site-driven, sharing experiences
  
- Weekly priority emails from FHI360 to sites
  - Collating protocol team priorities
  
- Listservs
  - Cross-site communications/sharing



# Where we are going

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# End of enrollment

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- ASPIRE protocol planned to enroll approximately 3476 women, anticipating a background HIV incidence of 3.9% per year
  - With at least 120 HIV seroconversions required to assess HIV protection with confidence
  - Goal to have 12 months of safety data per participant to assess safety, with early participants contributing longer
  
- Recent data (VOICE, FEM-PrEP) have demonstrated that HIV incidence is, unfortunately, higher than 3.9% per year in several settings
  - Fewer than 3476 enrollees may be necessary.
  - Considerations ongoing. End enrollment = Q1/Q2 2014.

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- May 2013
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- August & October 2013
  - SMC reviews
- **19 November 2013**
  - **DSMB review**

# Timeline

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2011

- Initiate site IRB and regulatory approval process

2012

- IRB/regulatory approvals, trainings, start

2013

- Enrollments, follow-up

2014

- End of enrollment, continue follow-up

2015

- Completion of follow-up, results

# Retention from day 1 to day X

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- Every enrolment should be considered
  - ASPIRE is a many-month, multi-hour commitment
  - Trust your instincts, trust team instincts, keep your enthusiasm
  
- How can we continue to create cultures that make sites places where participants want to spend several hours each month? (and staff each day of each month)

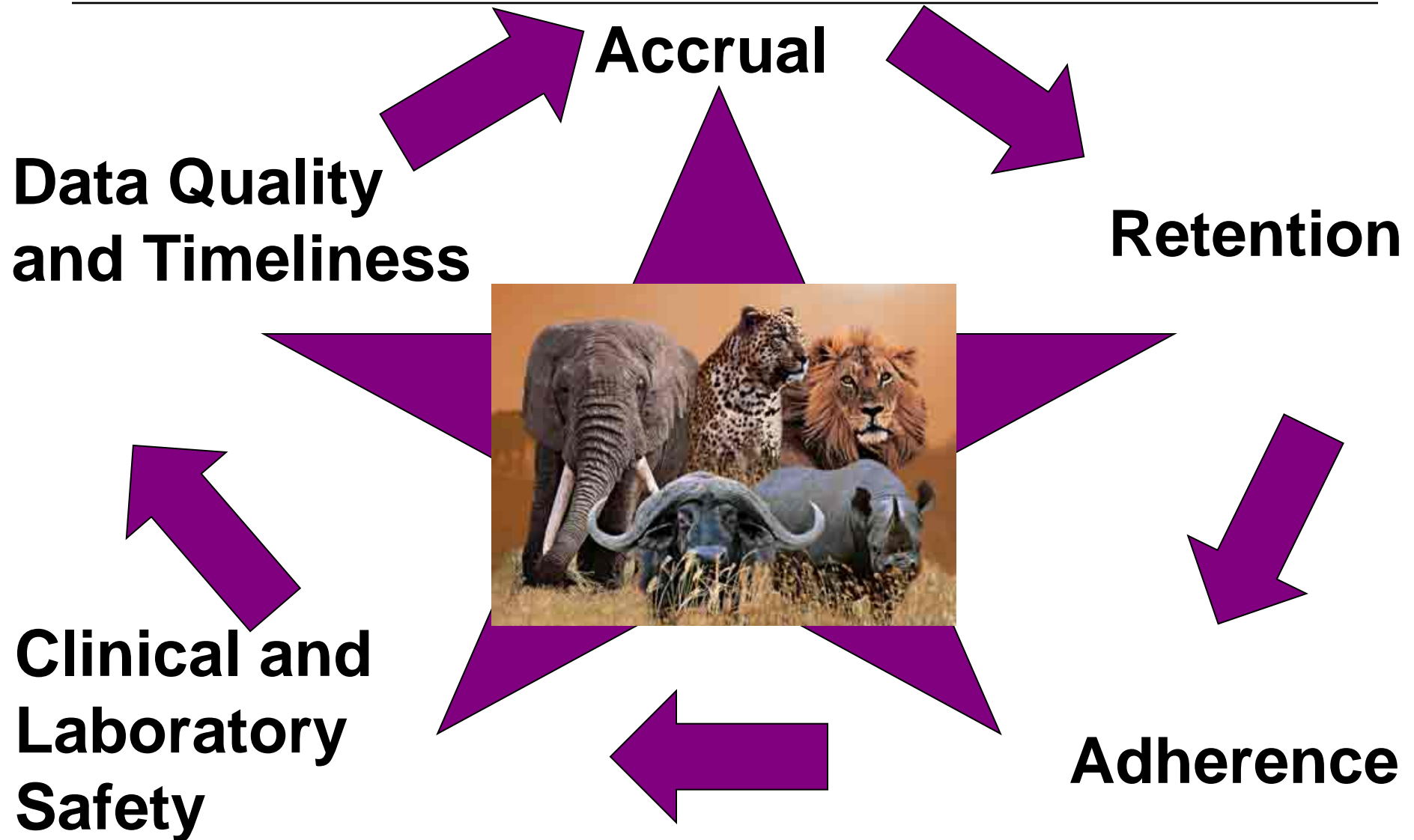


# Adherence Success (?!)

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- Creative ideas from all members of the team are leading to adherence success in ASPIRE
  - Counseling
  - Engagement
  - Analysis
- We truly have the opportunity to demonstrate a potentially revolutionary HIV prevention intervention

# The Big Five



# Accrual→Retention→Adherence→Safety→ Quality

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- Smart accrual
- High retention
- Motivated adherence (engagement)
- 100% attention to data quality & participant 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



ASPIRE ...

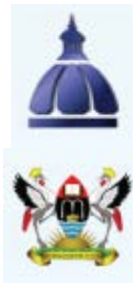
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OPPORTUNITY

# IT TAKES A TEAM



Malawi College of  
Medicine – JHU  
Research Project



UNC Project -  
Malawi



INTERNATIONAL  
PARTNERSHIP FOR  
MICROBICIDES



University of Zimbabwe,  
School of Medicine



DESMOND TUTU  
HIV FOUNDATION