

# **ASPIRE:**

## **Implementation Update**

*a quantitative and qualitative view*

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ASPIRE Protocol Team Meeting  
10 February 2013



# MTN-020 / ASPIRE

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# Quantitative

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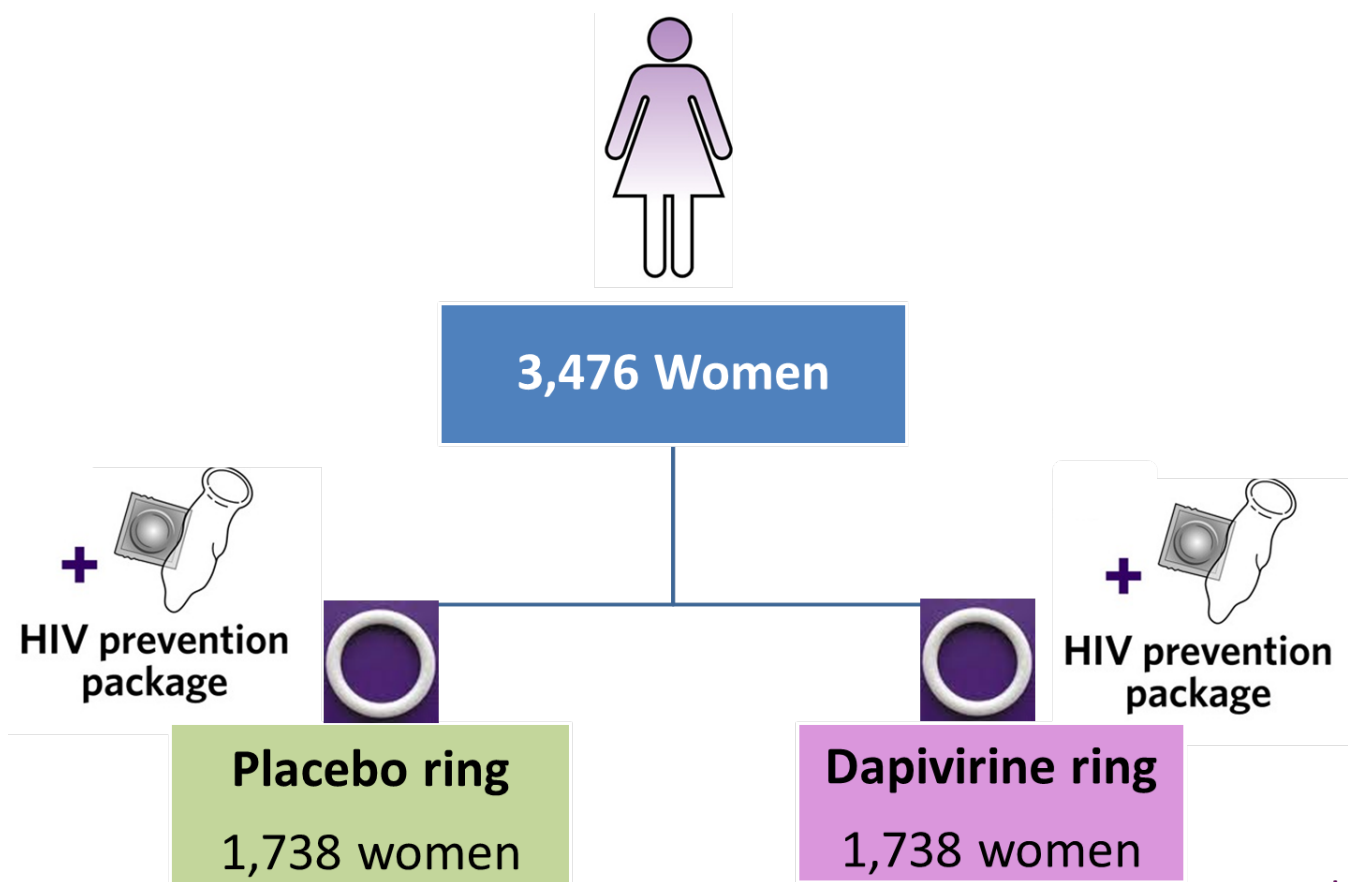
# MTN-020 / ASPIRE

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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**



# ASPIRE Overview



# ASPIRE to date

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- January - October 2011
  - Network, NIAID SWG, PSRC review
  - Protocol Team & Community Consultations
- January 2012
  - DSMB protocol review
- 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
- February 2013
  - First qualitative interview

# Site activations



A Study to Prevent Infection  
with a Ring for Extended Use

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

# The Big Five

**Accrual**

**Data Quality  
and Timeliness**

**Retention**



**Clinical and  
Laboratory  
Safety**

**ASPIRE**  
A Study to Prevent Infection  
with a Ring for Extended Use

**Adherence**



# Accrual (6 Feb 2013)

Site	First enr	# enr	scr:enr ratio
SA – Cape Town	19 SEP 2012	62	1.3
SA – CAPRISA eThekwini	10 OCT2012	67	2.2
SA – MRC/Botha's Hill	10 SEP 2012	93	2.0
SA – MRC/Chatsworth	11 SEP 2012	86	2.3
SA – MRC/Isipingo	19 SEP 2012	74	2.5
SA – MRC/Tongaat	17 SEP 2012	70	3.0
SA – MRC/Verulam	13 SEP 2012	81	2.5
SA – MRC/Umkomaas	14 SEP 2012	72	2.1
SA- WHRI/Hillbrow	30 OCT 2012	51	1.7
UG – Kampala	21 AUG 2012	93	1.5
Zim – Seke South	01 NOV 12	54	2.0
Zim – Spilhaus	30 OCT 12	58	1.6
Zim – Zengeza	13 NOV 12	47	1.9
<b>TOTAL</b>		<b>875</b>	<b>2.1</b>

# Screen outs

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- As of 6 February 2013:
  - 1891 screened, 908 enrolled (2.1:1 ratio)
  - 47 did not complete screening
  - 15 declined enrollment
  - 921 ineligible
    - 403 (44%) HIV+
    - 86 (9%) pregnant/breastfeeding
    - 196 (21%) clinical/laboratory exclusion klm
    - 212 (23%) “other” including investigator decision

# Who is enrolling?

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- Median age = 25 years
  - 44% <25 years, 15% ≥35 years
  
- 28% are married
  - 9% SA, 61% Ug, 86% Zim
  
- 99% had a primary partner in past 3 months
  - 23% had ≥1 other partner in past 3 months

# Retention

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- As of 6 February 2013:
  - 751/768 Month 1 visits (98%)
  - 554/578 Month 2 visits (96%)
  - 270/278 Month 3 visits (97%)
  - 107/110 Month 4 visits (97%)
  - 18/18 Month 5 visits (100%)

# Retention

## Month 1 Visit

	Malawi - Blantyre	Malawi - Lilongwe	SA - Cape Town	SA - CAPRISA eThekweni	SA - MRC Botha's Hill	SA - MRC Chatsworth	SA - MRC Isipingo	SA - MRC Tongaat	SA - MRC Verulam
Participants Enrolled	0	0	61	67	92	86	74	69	80
Month 1 visit									
Expected <sup>2</sup>	0	0	53	62	84	80	63	60	78
Completed <sup>3</sup>	0/0 (-%)	0/0 (-%)	52/53 (98%)	60/62 (97%)	84/84 (100%)	78/80 (98%)	61/63 (97%)	56/60 (93%)	77/78 (99%)
Not Completed	0/0 (-%)	0/0 (-%)	1/53 (2%)	2/62 (3%)	0/84 (0%)	2/80 (3%)	2/63 (3%)	4/60 (7%)	1/78 (1%)
Missed	0/0 (-%)	0/0 (-%)	1/1 (100%)	2/2 (100%)	0/0 (-%)	2/2 (100%)	2/2 (100%)	4/4 (100%)	1/1 (100%)
Product Available <sup>4</sup>	0/0 (-%)	0/0 (-%)	0/1 (0%)	0/2 (0%)	0/0 (-%)	0/2 (0%)	0/2 (0%)	0/4 (0%)	0/1 (0%)
Terminated Early	0/0 (-%)	0/0 (-%)	0/1 (0%)	0/2 (0%)	0/0 (-%)	0/2 (0%)	0/2 (0%)	0/4 (0%)	0/1 (0%)
Not Expected	0	0	8	5	8	6	11	9	2

	SA - MRC Umkomaas	SA - WRHI	Uganda - Kampala	Zambia - Lusaka	Zimbabwe - Seke South	Zimbabwe - Spilhaus	Zimbabwe - Zengeza	All Sites
Participants Enrolled	70	50	91	0	54	54	46	894
Month 1 visit								
Expected <sup>2</sup>	66	29	81	0	36	39	35	766
Completed <sup>3</sup>	63/66 (95%)	29/29 (100%)	81/81 (100%)	0/0 (-%)	36/36 (100%)	39/39 (100%)	33/35 (94%)	749/766 (98%)
Not Completed	3/66 (5%)	0/29 (0%)	0/81 (0%)	0/0 (-%)	0/36 (0%)	0/39 (0%)	2/35 (6%)	17/766 (2%)
Missed	3/3 (100%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	2/2 (100%)	17/17 (100%)
Product Available <sup>4</sup>	0/3 (0%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/2 (0%)	0/17 (0%)
Terminated Early	0/3 (0%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/2 (0%)	0/17 (0%)
Not Expected	4	21	10	0	18	15	11	128

# Adherence

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- We cannot test whether this product prevents HIV if it isn't used
  
- Adherence has multiple components:
  - Showing up for the visit to receive the product
  - Wearing the ring, without interruption, each month
  - Reporting accurately when a ring is not used

# Data Quality

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- Follow the metrics –
  - Enrollments
  - Retention
  - Contraceptive use
  - Procedure completion
  - QCs
  - Etc.

# Data Quality

## MTN 020 - A Study to Prevent Infection with a Ring for Extended Use (ASPIRE) Data as of February 6, 2013

### Visit Adherence: Completion of Procedures During Follow-up<sup>1</sup> - First 8 Sites

	All Sites	Malawi - Blantyre	Malawi - Lilongwe	SA - Cape Town	SA - CAPRISA eThekwinl	SA - MRC/ Botha's Hill	SA - MRC/ Chatsworth	SA - MRC/ Isipingo	SA - MRC/ Tongaat
Participants Enrolled	908	0	0	62	67	93	86	74	70
1. Behavioral Assessment Required and Expected	270	0	0	22	10	48	37	20	18
Completed	270 (100%)	- (-%)	- (-%)	22 (100%)	10 (100%)	48 (100%)	37 (100%)	20 (100%)	18 (100%)
2. Adherence Assessment Required and Expected	1700	0	0	120	109	223	201	132	122
Completed	1700 (100%)	- (-%)	- (-%)	120 (100%)	109 (100%)	223 (100%)	201 (100%)	132 (100%)	122 (100%)
3. Acceptability Assessment Required and Expected	270	0	0	22	10	48	37	20	18
Completed	270 (100%)	- (-%)	- (-%)	22 (100%)	10 (100%)	48 (100%)	37 (100%)	20 (100%)	18 (100%)
4. Social Harms Assessment Required and Expected	270	0	0	22	10	48	37	20	18
Completed	270 (100%)	- (-%)	- (-%)	22 (100%)	10 (100%)	48 (100%)	37 (100%)	20 (100%)	18 (100%)
5. Pelvic Exams Required and Expected	0	0	0	0	0	0	0	0	0
6. Pregnancy Tests Required and Expected	1691	0	0	120	109	222	197	132	119
Completed	1691 (100%)	- (-%)	- (-%)	120 (100%)	109 (100%)	222 (100%)	197 (100%)	132 (100%)	119 (100%)



# 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



# Pay attention to the participants

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- Participants give much to be in this study
  - Time
  - Blood
  - Privacy
  - Effort

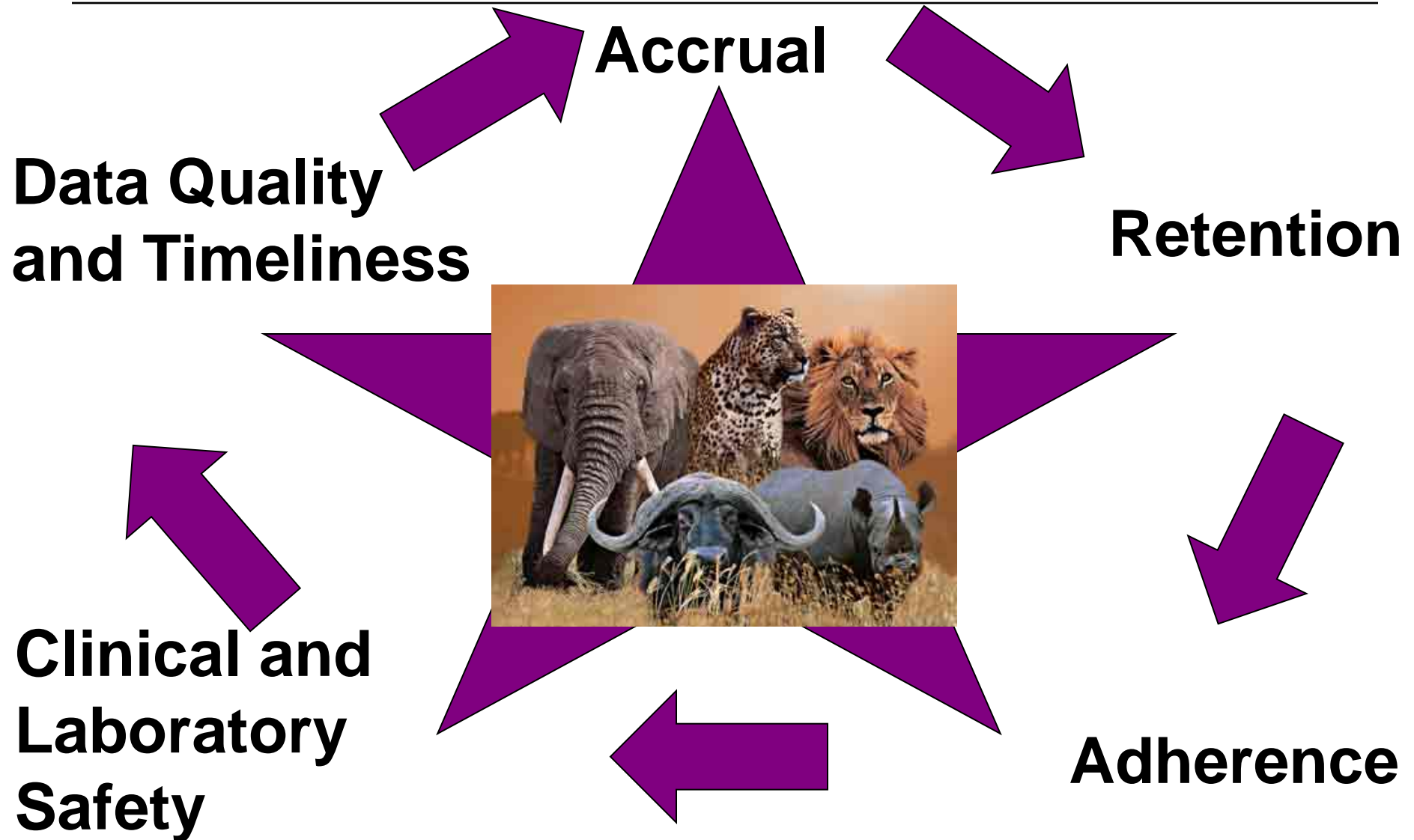
*We have much to learn from them.*



# Qualitative

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# The Big Five



# Accrual is Retention

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- Every enrolment should be considered
  - ASPIRE is a monthly, multi-hour commitment until sometime in 2014....
  - Trust your instincts, trust team instincts
  
- How can we continue to create cultures that make sites places where participants want to spend several hours each month?
  - How do we remind ourselves and participants about their important volunteerism?

# Screen outs

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- Who is not enrolling:
  - “unable to commit to study”
  - “participant not reliable in adhering to scheduled visits”
  - “participant likely to have adherence and retention problems”
  - “IoR discretion”

# Timeline and quality

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- Estimated that accrual will require **approximately** 12-16 months, with total study duration approximately 24 months
  - We only get one chance at this study – sole goal is quality
    - Attention to enrolling those committed to this study for as long as 2 years
    - Continuous involvement of our teams and communities
  - *We are in this as a team*



# Retention is Adherence

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



# Retention

## Month 2 Visit

	Malawi - Blantyre	Malawi - Lilongwe	SA - Cape Town	SA - CAPRISA eThekwinini	SA - MRC Botha's Hill	SA - MRC Chatsworth	SA - MRC Isipingo	SA - MRC Tongaat	SA - MRC Verulam
Participants Enrolled	0	0	61	67	92	86	74	69	80
Month 2 visit									
Expected <sup>2</sup>	0	0	44	39	78	69	48	48	58
Completed <sup>3</sup>	0/0 (-%)	0/0 (-%)	41/44 (93%)	38/39 (97%)	77/78 (99%)	67/69 (97%)	45/48 (94%)	43/48 (90%)	53/58 (91%)
Not Completed	0/0 (-%)	0/0 (-%)	3/44 (7%)	1/39 (3%)	1/78 (1%)	2/69 (3%)	3/48 (6%)	5/48 (10%)	5/58 (9%)
Missed	0/0 (-%)	0/0 (-%)	3/3 (100%)	1/1 (100%)	1/1 (100%)	2/2 (100%)	3/3 (100%)	5/5 (100%)	5/5 (100%)
Product Available <sup>4</sup>	0/0 (-%)	0/0 (-%)	0/3 (0%)	0/1 (0%)	1/1 (100%)	0/2 (0%)	1/3 (33%)	2/5 (40%)	0/5 (0%)
Terminated Early	0/0 (-%)	0/0 (-%)	0/3 (0%)	0/1 (0%)	0/1 (0%)	0/2 (0%)	0/3 (0%)	0/5 (0%)	0/5 (0%)
Not Expected	0	0	17	28	14	17	26	21	22

	SA - MRC Umkomaas	SA - WRHI	Uganda - Kampala	Zambia - Lusaka	Zimbabwe - Seke South	Zimbabwe - Spilhaus	Zimbabwe - Zengeza	All Sites
Participants Enrolled	70	50	91	0	54	54	46	894
Month 2 visit								
Expected <sup>2</sup>	59	16	57	0	17	21	12	566
Completed <sup>3</sup>	57/59 (97%)	16/16 (100%)	56/57 (98%)	0/0 (-%)	17/17 (100%)	21/21 (100%)	11/12 (92%)	542/566 (96%)
Not Completed	2/59 (3%)	0/16 (0%)	1/57 (2%)	0/0 (-%)	0/17 (0%)	0/21 (0%)	1/12 (8%)	24/566 (4%)
Missed	2/2 (100%)	0/0 (-%)	1/1 (100%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	1/1 (100%)	24/24 (100%)
Product Available <sup>4</sup>	0/2 (0%)	0/0 (-%)	0/1 (0%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/1 (0%)	4/24 (17%)
Terminated Early	0/2 (0%)	0/0 (-%)	0/1 (0%)	0/0 (-%)	0/0 (-%)	0/0 (-%)	0/1 (0%)	8/24 (33%)
Not Expected	11	34	34	0	37	33	34	328

# Adherence is Everything

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- Products don't work if they aren't used
- How can we set up a culture in ASPIRE so that women want to come, want to use, feel important and part of something?
- Adherence is closely linked to *who* we accrue and that participants are retained

# 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

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- What can we learn from every study we have collectively done before to maximize product use in this trial?
- What can we learn (and react to) about non-use, non-interest?
  - Who returns without rings in place? Rings coming out?
  - Qualitative interviews, staff observations
  - Blood and swab samples

# Accural→Retention→Adherence→Safety→ Quality

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- 3476 = total number of women enrolled
- >95% = retention, adherence
- 100% = attention to data quality, safety

*Everything else flows from these*

# Contraceptive action

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- Ongoing efforts at every site to diversify contraceptive mix is working
  - 45 IUDs (6% of participants)
  - 73 implants (10%)
  - Mix of DMPA, NET-EN, OCPs, other methods
  - With no individual method currently >50%

# 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

# 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

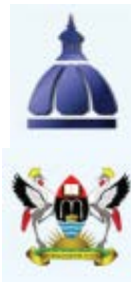
Monitoring follow-up



# IT TAKES A TEAM



Malawi College of  
Medicine – JHU  
Research Project



UNC Project -  
Malawi



INTERNATIONAL  
PARTNERSHIP FOR  
MICROBICIDES



University of Zimbabwe,  
School of Medicine