

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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Implementation Update

ASPIRE Protocol Team Meeting

October 2014





Meeting overview

- A great afternoon:
 - Where we are now: update from ASPIRE, The Ring Study, Laboratory Center, and qualitative component
 - Site presentations: Maximizing adherence and retention, community perspectives, contraceptive counseling as women leave ASPIRE
 - Preparing for closeout: coming soon...!



Outline

ASPIRE

- Looking back
- Looking ahead



ASPIRE

Looking Back

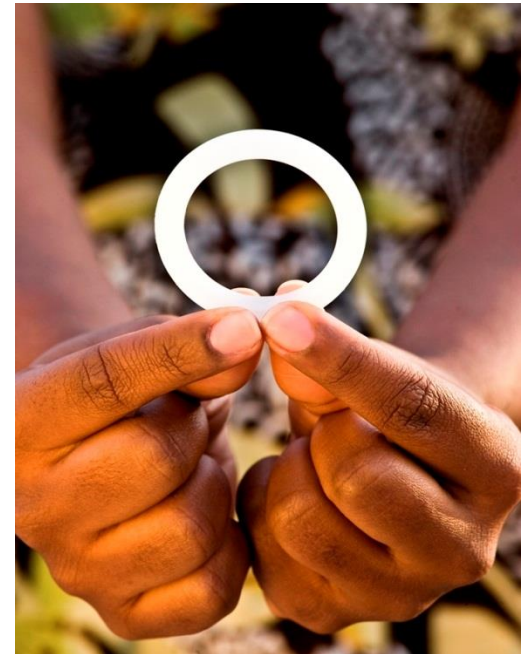
MTN-020 / ASPIRE

- **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**

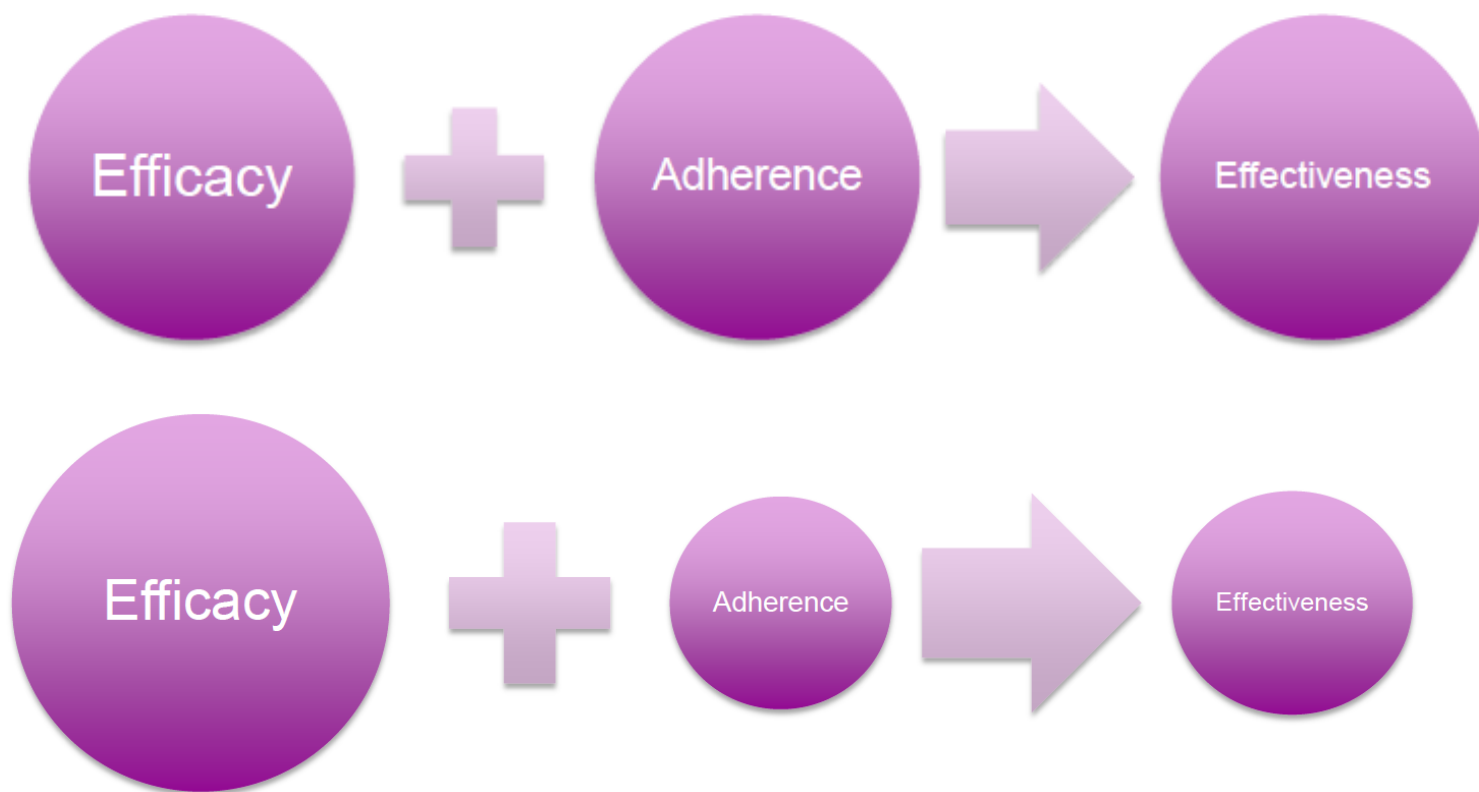


Developing dapivirine ring for HIV prevention

- Dapivirine is a non-nucleoside reverse transcriptase inhibitor of HIV
- Formulated into a flexible silicone ring, it could provide a reliable, long-lasting, woman-initiated method to protect against HIV acquisition
- MTN-020 was designed as a pivotal clinical trial to provide the strength of evidence to support licensure of dapivirine ring for HIV prevention, along with complementary studies:
 - IPM 027 (efficacy & safety)
 - >25 completed phase I/II studies
 - ongoing/planned work in adolescents/post-menopausal women, drug-drug interactions

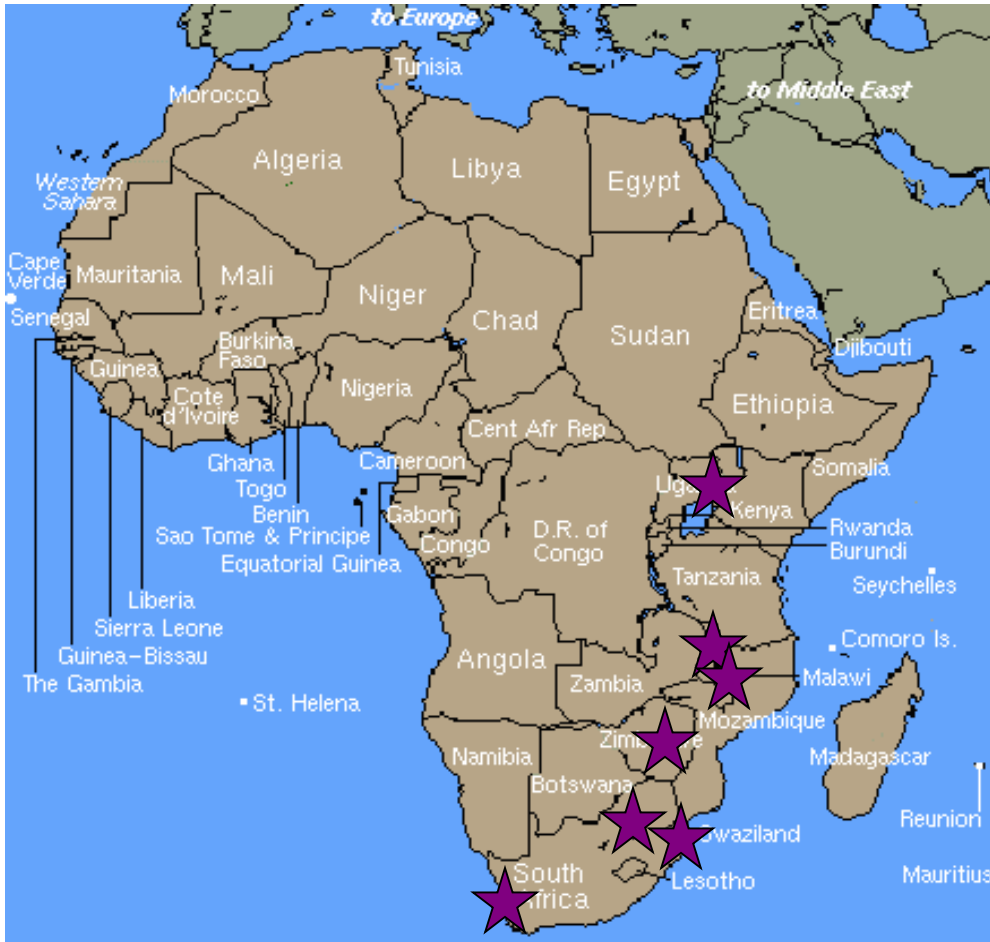


Challenges of the past: adherence and learning from PrEP trials



No adherence = no HIV protection

15 Sites across 4 countries



Blantyre
Lilongwe
Malawi

Cape Town
Durban (7 sites)
Johannesburg
South Africa

Kampala
Uganda

Harare/Chitungwiza (3 sites)
Zimbabwe

Timeline

2011

- Initiate site IRB and regulatory approval process

2012

- IRB/regulatory approvals, trainings, START!

2013

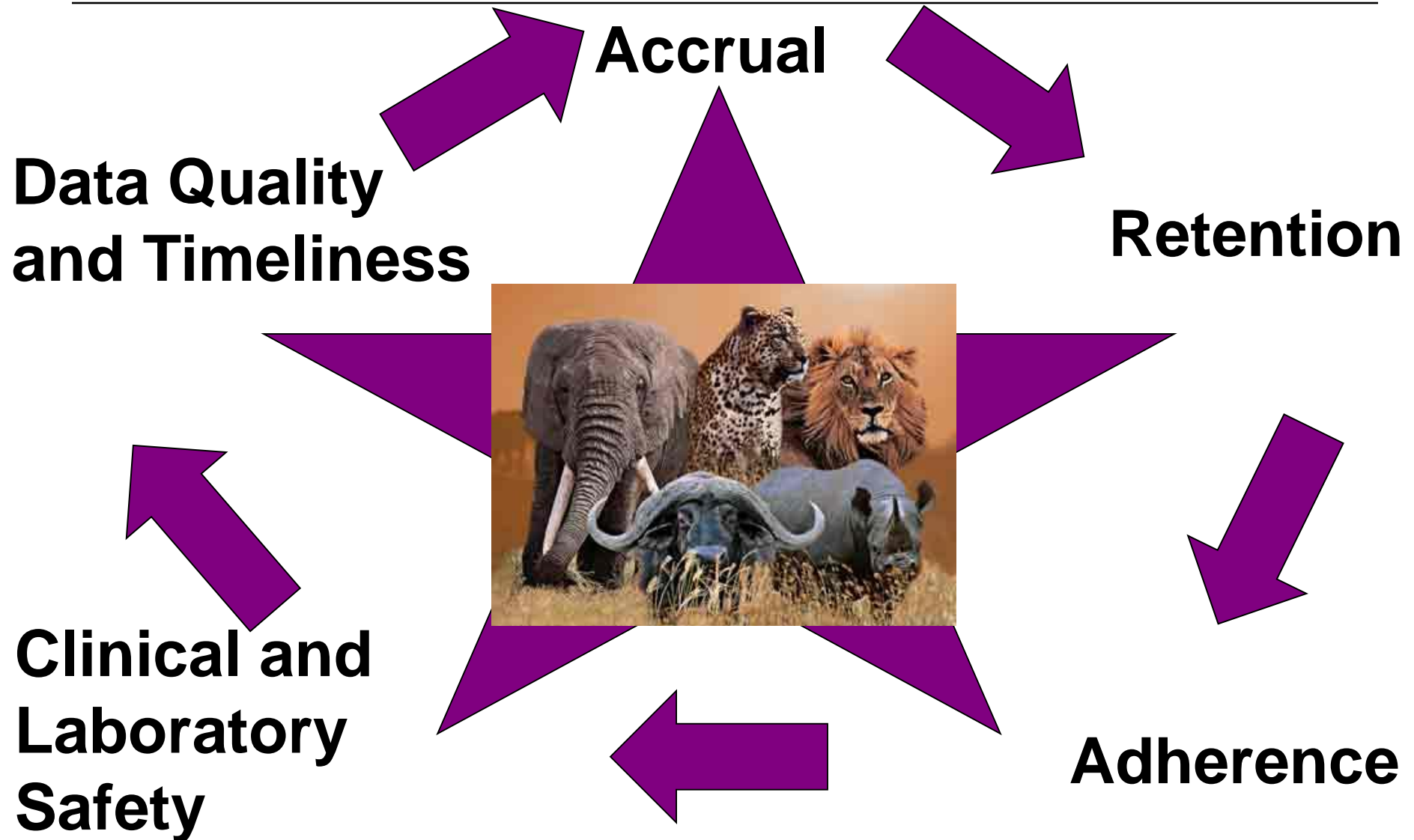
- Enrollments, follow-up

2014

- Completion of enrollment, follow-up

2015

The Big Five



Accrual on target & on schedule

Site	First enr	# enr
MA – Blantyre	13 JUN 13	130
MA – Lilongwe	17 JUN 13	142
SA – Cape Town	19 SEP 2012	166
SA – CAPRISA eThekwini	10 OCT 2012	244
SA – MRC/Botha's Hill	10 SEP 2012	180
SA – MRC/Chatsworth	11 SEP 2012	150
SA – MRC/Isipingo	19 SEP 2012	117
SA – MRC/Tongaat	17 SEP 2012	103
SA – MRC/Verulam	13 SEP 2012	150
SA – MRC/Umkomaas	14 SEP 2012	103
SA – WRHI	30 OCT 2012	213
UG – Kampala	21 AUG 2012	253
ZI – Seke South	01 NOV 12	224
ZI – Spilhaus	30 OCT 12	230
ZI – Zengeza	13 NOV 12	224
TOTAL		2629

Screen outs

- Final numbers:
 - 5446 screened, 2629 enrolled (2.1 ratio)
 - 356 (7%) did not complete screening
 - 50 (1%) declined enrollment
 - 2411 (44%) ineligible
 - 847 (35%) HIV+
 - 198 (8%) pregnant; 31 (1%) breastfeeding
 - 488 (20%) clinical/laboratory exclusion
 - 735 (30%) “other” including investigator decision

Who enrolled?

- Median age: 26 years
 - 39% <25 years, 14% ≥35 years
- Unmarried: 41% overall, 92% in SA
- 100% had a primary partner in past 3 months
 - 17% had ≥1 other partner in past 3 months
- STIs common at screening: 12% CT, 4% GC, 7% TV, 1% syphilis

A population at risk for HIV and in need of new prevention strategies

Retention

□ Current #s:

- Month 1: 98%
- Month 3: 96% (97% when accounting for early terminations)
- Month 6: 94% (96%)
- Month 12: 90% (97%)
- Month 18: 88% (98%)

RETENTION SUMMARY:

OVERALL = 92.1% of all expected visits
EXCLUDING TERMINATIONS = 97.1%
LAST 3 MONTHS = 97.7%

Adherence Action!

□ What we've done together:

Recognition of adherence a priority across all ASPIRE sites

Participant and staff engagement activities

Careful counselling for challenging cases

Fun waiting room discussions and social events

HIV ribbon and ring activities

Male partner engagement efforts

Learning from qualitative component of ASPIRE

Visual inspection of rings and collection of used rings

Testing of plasma and rings, with real-time action, tailored to each site's needs

Data Quality and Timeliness

DATA MANAGEMENT QUALITY REPORT Previous Month: August 2014

Site	Total Records	Total QCs	QC Rate Per 100 Records (Goal < 5)	%CRF Records Faxed within 7 days (Goal ≥ 95%)	Mean Days to Fax in AE
1. Blantyre/Malawi	1274	18	1.4	98%	33.5
2. Lilongwe/Malawi	1229	28	2.3	90%	5.8
3. Emavundleni/Cape Town	1411	33	2.3	99%	2.9
4. CAPRISA eThekweni	2462	93	3.8	97%	11.0
5. MRC - Botha's Hill	1711	48	2.8	91%	7.4
6. MRC - Chatsworth	1153	21	1.8	96%	0.7
7. MRC - Isipingo	996	17	1.7	98%	10.5
8. MRC - Tongaat	765	23	3.0	100%	2.9
9. MRC - Verulam	1180	14	1.2	100%	0.2
10. MRC - Umkomaas	933	16	1.7	99%	1.3
11. WRHI/Johannesburg	1665	75	4.5	99%	8.9
12. MY-JHU/Kampala, Uganda	2329	36	1.5	99%	3.3
13. Seke South/Zimbabwe	1832	16	0.9	97%	2.1
14. Spilhaus/Zimbabwe	1890	13	0.7	97%	2.9
15. Zengeza/Zimbabwe	1726	21	1.2	98%	1.3
TOTAL	22556	472	2.1	97%	6.7

Safety

- Safety monitoring
 - Evaluating whether the product is safe is just as important as whether the product is effective for HIV prevention
 - Excellent safety monitoring

Laboratory

- Laboratory results and archived samples are central to this study
- Real-time shipping and testing of plasma and residual drug levels in ASPIRE is revolutionary
- THANK YOU FOR ALL THE HARD WORK

Team communications

- Monthly Protocol team calls
 - Tremendously valuable, site-driven, sharing experiences
- IoR calls regards the PK data
- Qualitative calls
- Weekly priority emails from FHI360 to sites
 - Collating protocol team priorities
- Listservs
 - Cross-site communications/sharing
- FHI360 Site assessment visits
- Patrick Ndase, MTN Regional Physicians site visits



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Looking Ahead

Accrual→Retention→Adherence→Safety→ Quality

- Smart accrual
- High retention
- Motivated adherence (engagement)
- 100% attention to data quality & participant safety, including reproductive health choices

Everything else flows from these

End of follow-up

- ASPIRE protocol planned to continue until at least 120 HIV seroconversions were accrued, to provide the required statistical power to assess HIV protection with confidence
- We anticipate that the required number of HIV seroconversions will be accrued in the first half of 2015, permitting us to initiate study close-out.
- The plan for close-out (more this afternoon) will focus on an orderly exit of study participants between March and June 2014, followed by rapid data cleaning and database closure.

Retention and adherence

Retention and adherence have been priorities since Day 1. How can we keep them as priorities until the last day of data collection?

- ASPIRE is a many-month, multi-hour commitment
 - We have amazing retention now
 - Let's maintain this all the way to the end

- How can we keep up the enthusiasm and commitment all the way until the last participant exit?

MTN-015 and 016

- The only controlled data on periconception safety and early HIV disease related to dapivirine exposure will come from these studies.
 - A few more months to get this valuable information

ASPIRE calendar

- 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
- November 2012, May 2013, November 2013, May 2014
 - DSMB reviews
- **November 2014**
 - **DSMB review**
- **March-June 2015, then Q3 2015**
 - **Participant exits, final data cleaning**
- **By the end of 2015**
 - **Results**



What we have learned

- Adherence
- Importance of prevention options
- Involving men
- Contraceptive action

Adherence monitoring in MTN-020

- Monthly shipping, testing, and review of plasma and residual ring dapivirine data, according to a pre-defined plan
- Information is reviewed by-site, rather than by-subject, preserving blinding.
- Results? *We are optimistic!*

Prevention options

- Quotes from the qualitative component of ASPIRE:
- Self-efficacy: *The ring is different from the condom ‘because’ you can wear it and your man will not feel it ‘but’ you will know that “I am protecting myself”.*

Prevention options

- Quotes from the qualitative component of ASPIRE:
- Study clinics as important spaces: *I am not talking about other people but I am talking about myself, that I know I have used the ring, I insert it in the clinic and I remove it here, in the clinic. Nobody forced me to come here, I came on my own and I like being here.*

Prevention options

- Quotes from the qualitative component of ASPIRE:
- Looking ahead: *If we find something that helps us it will not just help me alone but it will also help future ‘generations’. This is something which is good.*

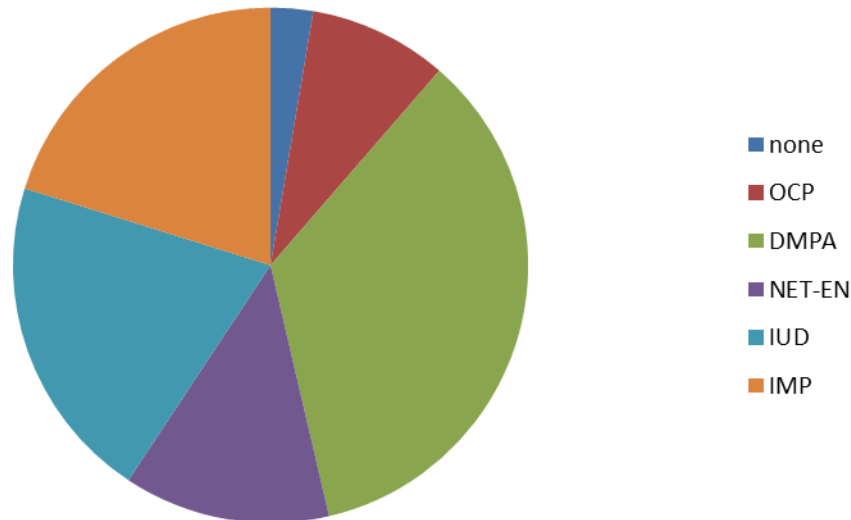
Male involvement

- Two-thirds of participants at baseline reported having told their primary partners about their plans to use the ring in the trial
- However, some participants in the trial face social risks because of participating in an HIV prevention trial / using an HIV prevention option
- We have learned much (and can teach much) about male involvement in prevention work

Contraceptive Action Team

- Incredible motivation, amazing change, and true leadership for women's health

Jun-14



- In addition, an unbelievably low rate of pregnancies (~3% per year), vs. >10% per year in prior studies

We are all in this together

- 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

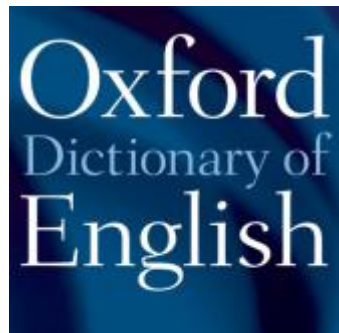
Study drug/pharmacy

Contraception

Lab-clinic interface

Monitoring follow-up

What does ASPIRE mean?



aspire(as·pire)

Pronunciation: /ə'spɪ(ə)r/

verb

[*no object*]

direct one's hopes or ambitions toward achieving something:

*we never thought that we might **aspire to** those heights*

[*with infinitive*] :

*other people will **aspire to** be like you*

ASPIRE

\ə-'spɪ(-ə)r\

noun:

1. A Phase III study that seeks to determine whether a woman's use of a vaginal ring containing dapivirine is a safe and effective method for protecting against HIV infection.
2. **A Study to Prevent Infection with a Ring for Extended Use**

verb:

1. **To seek to end the HIV epidemic** < *We **aspire to** prevent HIV*>





ASPIRE ...

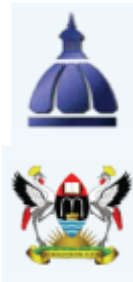
ONE CHANCE

OUR CHANCE

Thank you



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