

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

March 2015





Meeting overview

- An exciting day!
 - Updates on ASPIRE & The Ring Study and from SCHARP, Laboratory Center, Safety Docs, Communications, CWG and Qualitative Team
 - Site presentations: PUEV updates and participants responses, maintaining participant contact, and plans for results dissemination
 - General focus on preparations for closeout and beyond!



Outline

ASPIRE

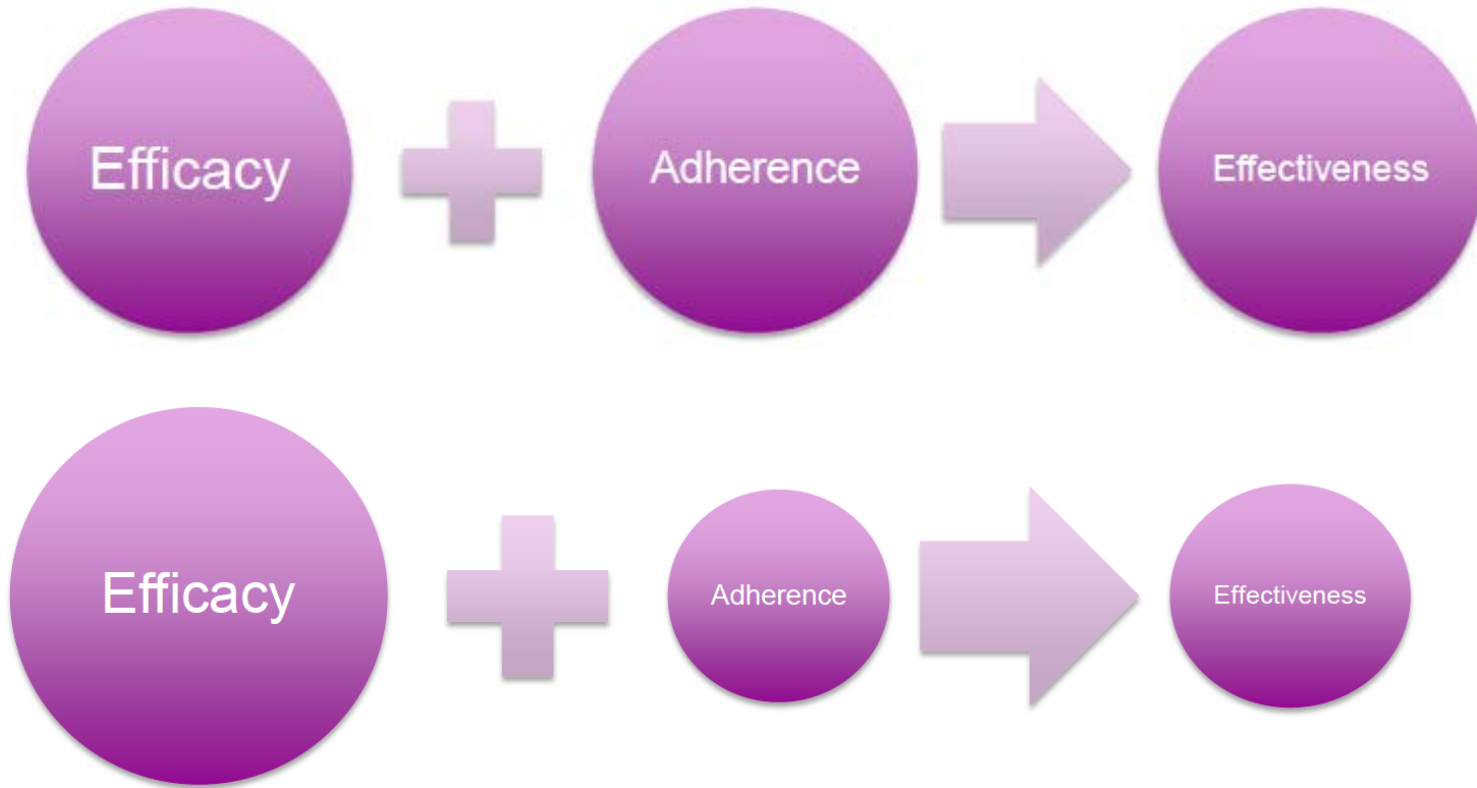
- *Looking back*
- *Looking forward*



ASPIRE

Looking Back

Challenges of the past: learning from tenofovir trials



No adherence = no HIV protection

Challenges of the past: learning from PrEP trials

	HIV protection: PrEP vs. placebo (when PrEP taken)	% of samples with tenofovir detected
Partners PrEP	75% (90+% when taken)	81%
TDF2	62%	79%
BTS	49%	67%
iPrEx	44% (90-100% when taken)	51%
FEM-PrEP	No HIV protection	<40%
VOICE	No HIV protection	<30%
FACTS 001	No HIV protection	<50%

***Women need strategies that make
adherence workable.***

FACTS 001



- Overall HIV incidence was no different for those randomized to tenofovir gel compared to placebo. There was evidence that HIV rates were lower in women with tenofovir detected in a genital sample.
- Many women seemed to have used the gel at some point in FACTS 001, but *not enough women used the gel enough of the time* to provide *enough HIV protection* to see an overall trial effect.
- Better products are needed in order for women to be able to achieve drug levels sufficient for HIV protection.

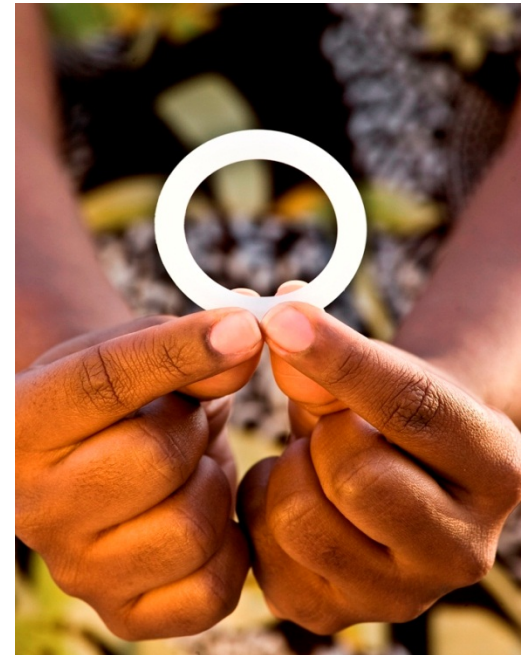
MTN-020 / ASPIRE

- **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**

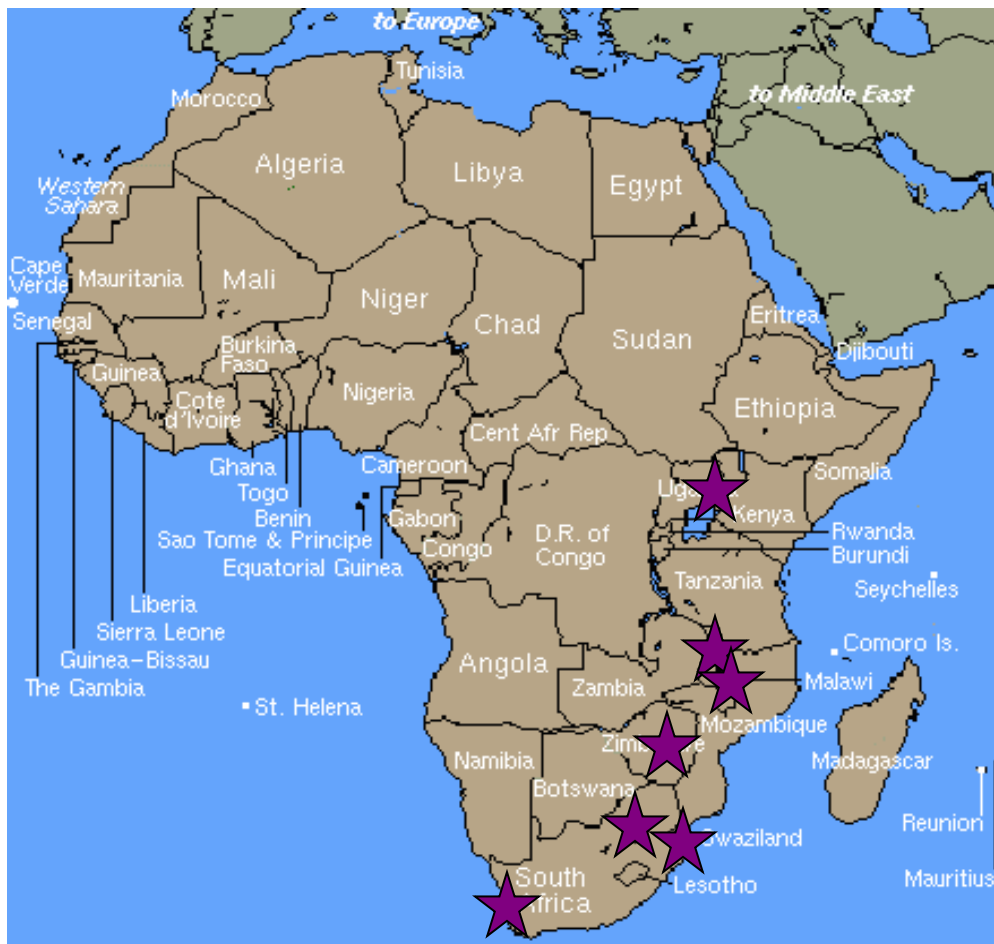


Developing dapivirine ring for HIV prevention

- 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



15 Sites across 4 countries



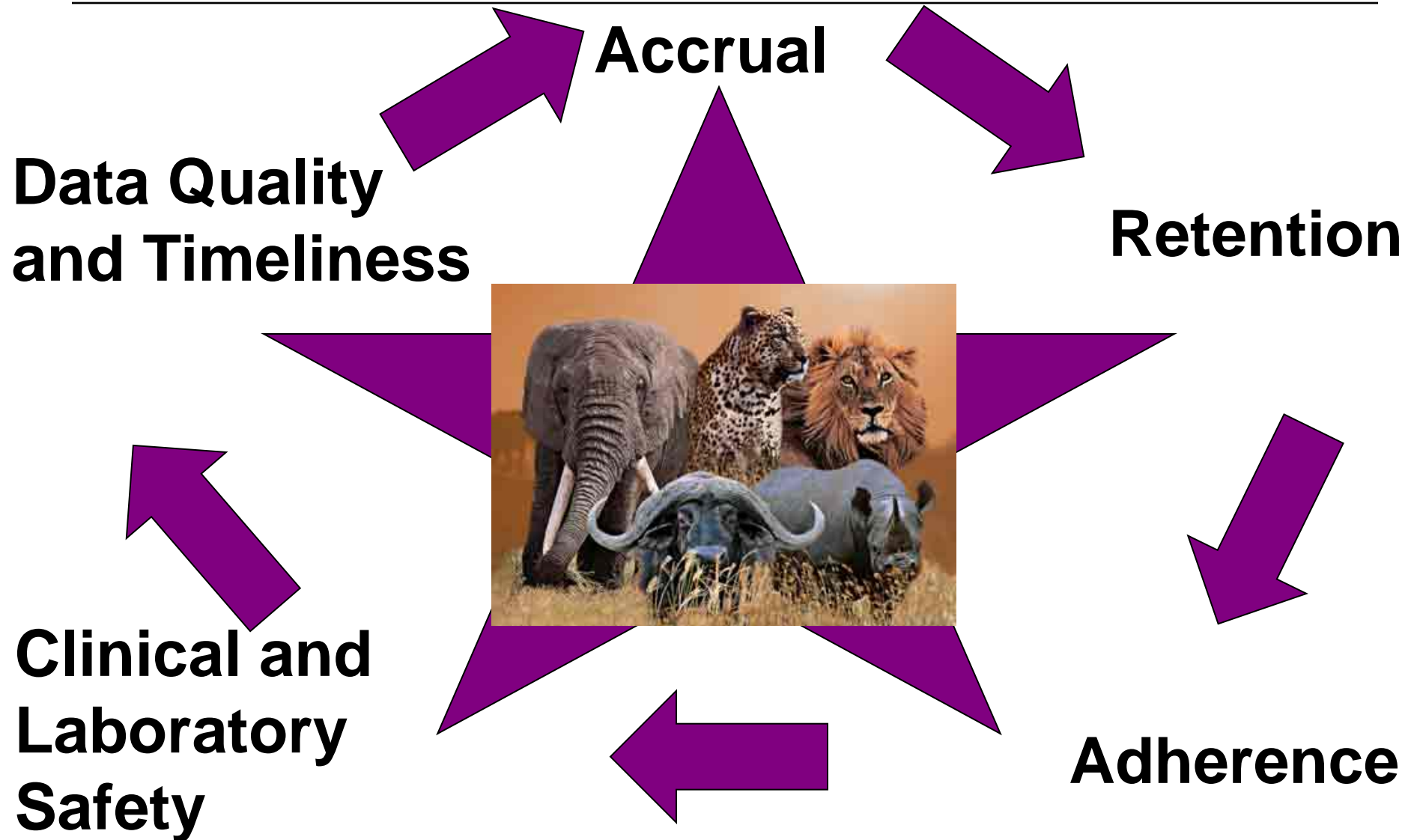
Blantyre
Lilongwe
Malawi

Cape Town
Durban (7 sites)
Johannesburg
South Africa

Kampala
Uganda

Harare/Chitungwiza (3 sites)
Zimbabwe

The Big Five



Accrual completed June 2014

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

Who enrolled?

- Median age: 26 years, with 39% <25 years
- Unmarried: 59% overall, 92% in SA
- 100% had a primary partner in past 3 months
 - 17% had ≥ 1 other partner in past 3 months
 - *64% had informed their primary partner about the ring at baseline*
- STIs were common: 12% CT, 4% GC, 7% TV

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

Retention

□ Current #s:

- Month 1: 98%
- Month 3: 96%
- Month 6: 94%
- Month 12: 91%
- Month 18: 89%
- Month 24 : 87%
- Month 32 : 100%

RETENTION SUMMARY:

OVERALL = 91.45% of all expected visits

EXCLUDING TERMINATIONS = 97.14%
LAST 3 MONTHS = 96.68%!

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

Male partner engagement efforts

Learning from the 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

MTN-020 A Study to Prevent Infection with a Ring for Extended Use (ASPIRE)

DATA MANAGEMENT QUALITY REPORT
Cumulative: Study Start through February 2015

Site	Total Records	Total QCs	QC Rate Per 100 Records (Goal < 5)	% QCs Resolved	%CRF Records Faxed within 7 days (Goal ≥ 95%)	Mean Days to Fax in AE
1. Blantyre/Malawi	18324	495	2.7	96%	91%	26.0
2. Lilongwe/Malawi	20460	646	3.2	96%	90%	10.5
3. Emavundleni/Cape Town	34986	1111	3.2	97%	99%	7.5
4. CAPRISA eThekwini	49237	1873	3.8	97%	96%	8.3
5. MRC - Botha's Hill	36677	1462	4.0	98%	95%	10.7
6. MRC - Chatsworth	31527	1107	3.5	95%	93%	12.9
7. MRC - Isipingo	27721	784	2.8	94%	97%	9.6
8. MRC - Tongaat	24486	885	3.6	98%	98%	5.8
9. MRC - Verulam	31086	623	2.0	96%	99%	3.0
10. MRC - Umkomaas	22282	743	3.3	99%	98%	6.0
11. WRHI/Johannesburg	39943	2039	5.1	97%	94%	12.3
12. MU-JHU/Kampala, Uganda	53022	1188	2.2	99%	98%	8.5
13. Seke South/Zimbabwe	41816	395	0.9	99%	98%	5.3
14. Spilhaus/Zimbabwe	44329	395	0.9	99%	98%	4.5
15. Zengeza/Zimbabwe	39367	431	1.1	89%	99%	7.6
TOTAL	515263	14177	2.8	97%	97%	8.7

ASPIRE

A Study to Prevent Infection
with a Ring for Extended Use

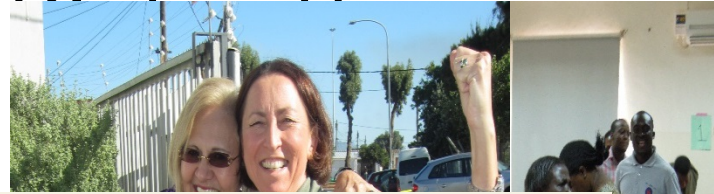
Clinical & Laboratory Safety

- **Thank you** for so much work in the safety management & monitoring and laboratory collaboration and oversight:
 - Tremendous efforts on clinical safety documentation and follow-through.
 - Huge efforts to do real-time shipping and testing of plasma and residual drug levels.
This has been a revolution for this study and the results will be a revelation for the field.



Timeline

2011-2012: Rapid



Phase III Trial of Dapivirine Ring Begins in Africa: ASPIRE testing new HIV prevention approach for women

WASHINGTON, D.C., July 24, 2012 – A large clinical trial testing the long-term safety and effectiveness of a new approach for preventing HIV in women – a vaginal ring used once a month – is now underway in Africa, researchers announced today at the XIX International AIDS Conference (AIDS 2012).



January 2012:
SSP
Development
meeting



July
Activation

October
2: 'Oh
Oh
ASPIRE'
song
debuted at
the MTN
Regional
Meeting

2013: Enrollment, Adherence and Retention

February 2013: First round of PK specimens shipped; First qualitative interview

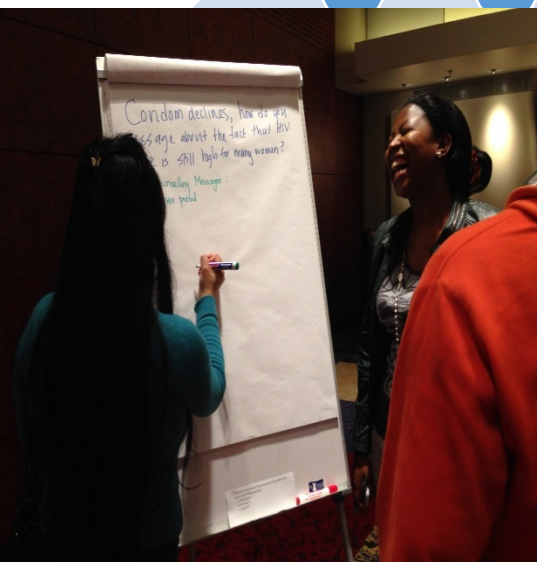
Client focused
Invited ppt. to talk
Welcoming environment
Eye Contact/good body language
Good listening skills
Counselor support of plan/goal
Ppt. Com...



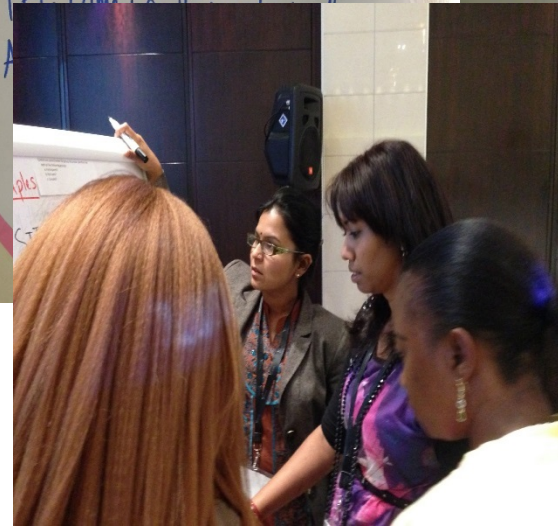
November 2013: No one contraceptive method with >50% use (all sites combined)

"GOOD FIT" ASPIRE PARTICIPANTS
REQUIRES PARTNER STUDY & RING-USE DISCLOSURE &
PARTNER'S ACCEPTANCE
ACTIVE INTEREST IN HIV PREVENTION & MTN020
- ASKS QUESTIONS

STATIONS TO CLINICAL STAFF
VALUE and CONTRIBUTION TO STUDY AND



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2014: Continuing Strong

New contraceptive implant free to women in SA, says Motsoaledi

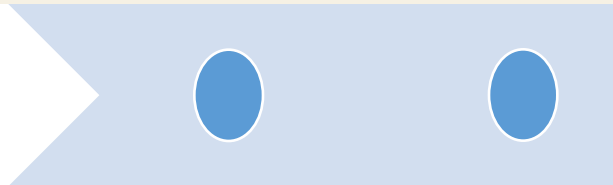
ASPIRE Phase III trial of a vaginal ring for HIV prevention completes enrollment of 2,629 women

MTN's trial testing dapivirine ring on track to finish next year; IPM's sister Phase III trial ongoing



ons:

Department of Health
People: Aaron Motsoaledi



April 2014: First batch of rings shipped for testing



Health Minister Aaron Motsoaledi briefs the media media after

A SMALL contraceptive device installed under the skin will be made available free of charge to all women from next week, Health Minister Aaron Motsoaledi told MPs on Wednesday.



2015: Looking Ahead



September 2015: Final FHI 360 assessment visit conducted



June 2015:
Final participant visit for ASPIRE



August 2015:
Database lock



End 2015:
Results!

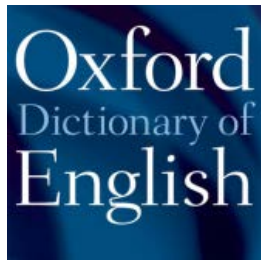




ASPIRE

Looking Ahead

What does ASPIRE mean?



aspire(as·pire)

Pronunciation: /ə'spɪ(ə)r/

verb:

direct one's hopes or ambitions toward achieving something:

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

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**

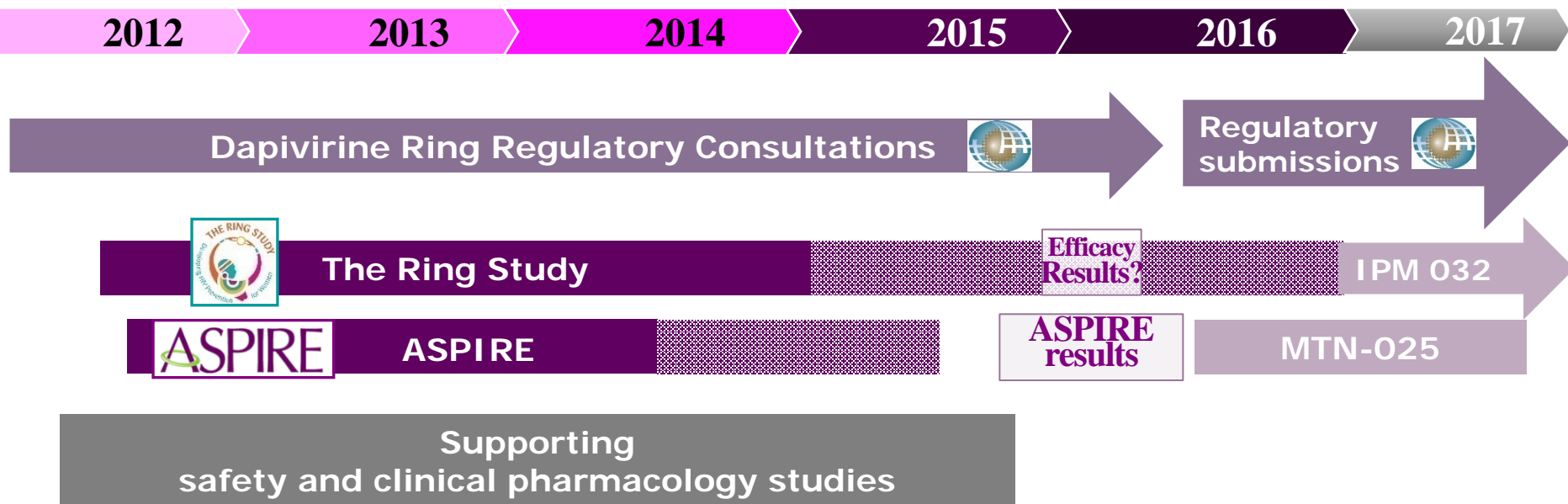


dream:

Quote from the qualitative component of ASPIRE:

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.

Dapivirine Ring Timeline



End of follow-up

- We anticipated that the required number of HIV seroconversions for the protocol will be accrued in Q2 2015 - this permitted us to initiate study close-out.
- Close-out was planned as an orderly exit of participants between March and June 2015, followed by rapid data cleaning and database closure (August 2015).
- Results planning is already underway. Tentative plan (with lots of steps to get there) is a results unblinding in November 2015, with public release soon after.



Much to do in the next months

How can we keep retention and adherence as priorities until the last day of data collection?

How can we make data cleaning as efficient as possible?

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

Countdown has begun!



What we have learned

- ❑ Women are interested in a ring for prevention.
- ❑ Real-time adherence monitoring can be done in a trial, and women are adherent to a ring.
- ❑ Women want prevention options.
- ❑ Contraceptive options matter.
- ❑ Male involvement, in many different ways, is part of prevention in women.



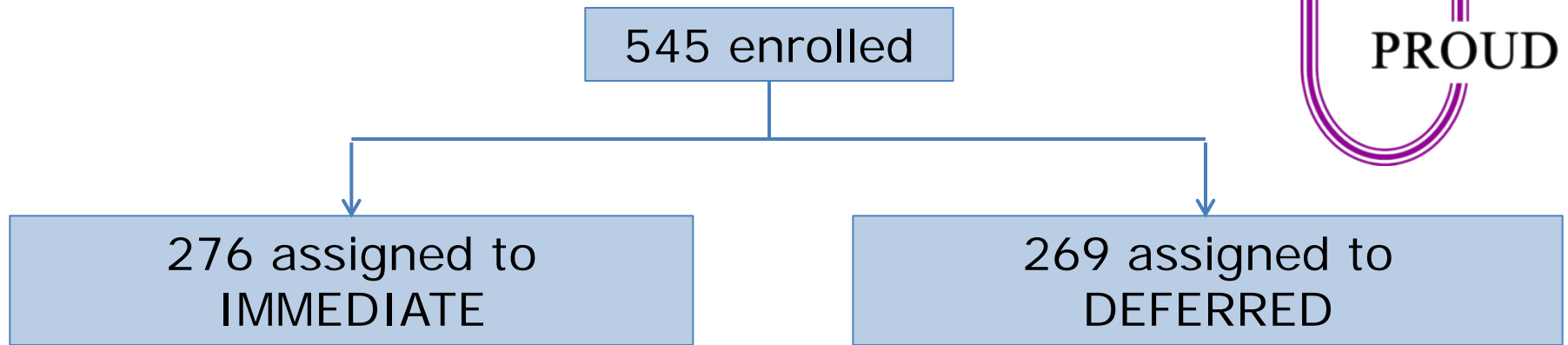
Much more to learn

- Efficacy and safety of the dapivirine ring for prevention.
- Whether HIV protection is greater when adherence is greater.
- Safety of the ring in women who become pregnant, and then safety in pregnancy and lactation and in other populations.
- Use of the ring in real-world settings....



In real-world settings, PrEP works

- New data – including from CROI 2015 – show us that PrEP really can work in open-label studies that follow clinical trials.



Group	No. of infections	Incidence (per 100 PY)
Immediate	3	1.3
Deferred	19	8.9

Efficacy = 86% (90% CI: 58 – 96%)

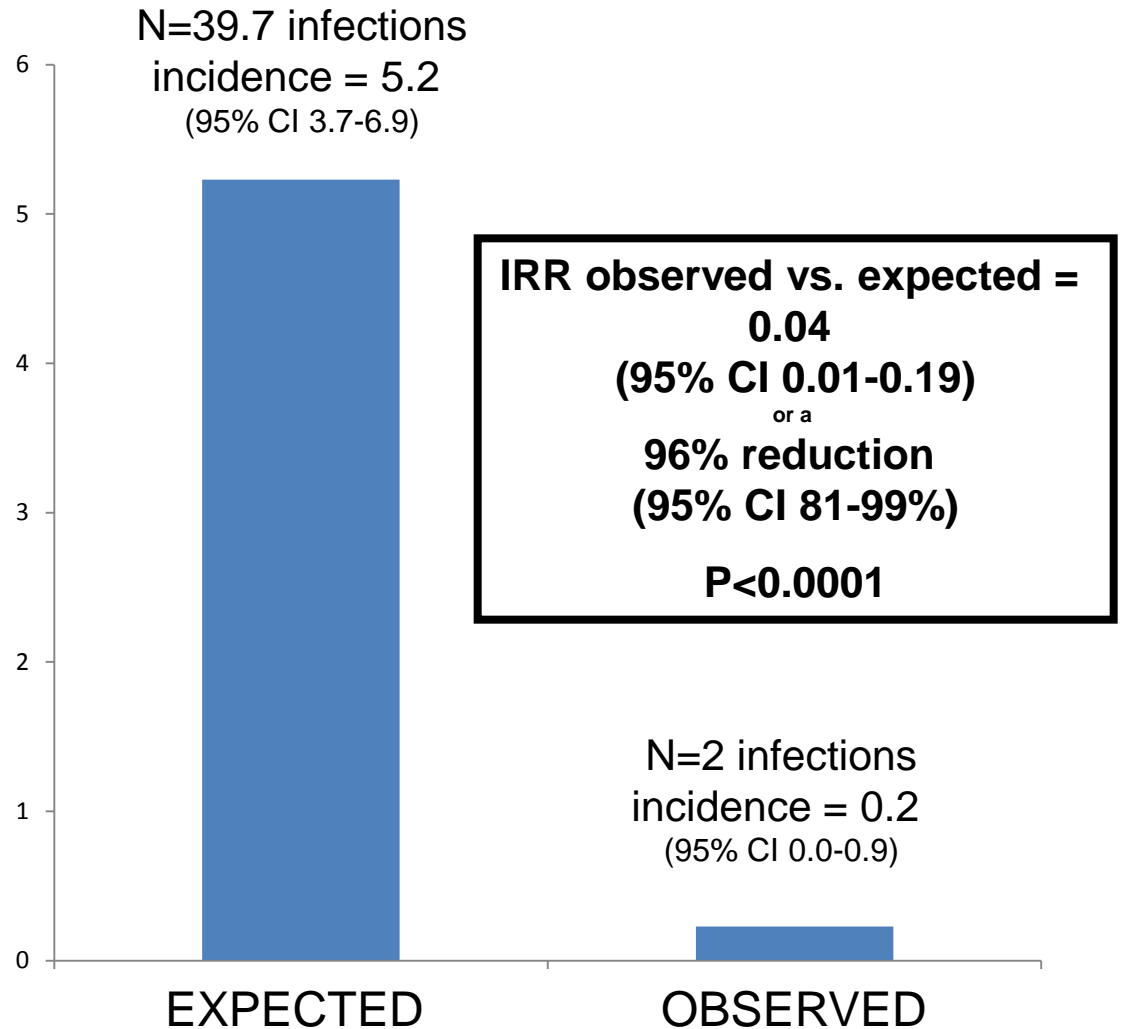
P value = 0.0002

Rate Difference = 7.6 (90% CI: 4.1 – 11.2)

Number Needed to Treat = 13 (90% CI: 9 – 25)

Partners Demonstration Project

- Only 2 HIV infections observed in 1013 high-risk serodiscordant couples, compared with nearly 40 infections expected.
- The observed incidence is a **96% reduction** compared to expected.

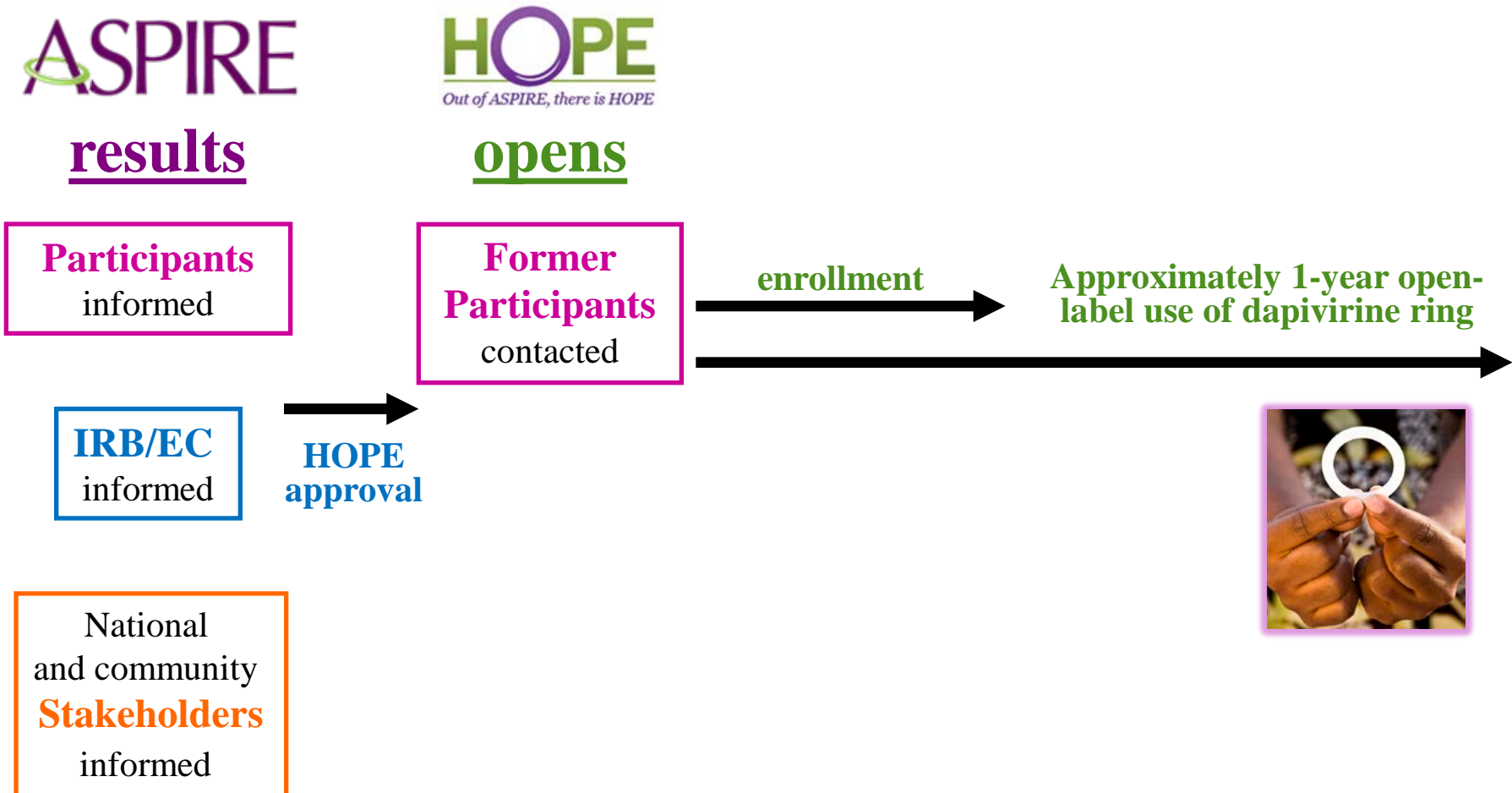




In real-world settings, PrEP works

- New data – including from CROI 2015 – show us that PrEP really can work in open-label studies that follow clinical trials.
- Because people want prevention tools that work.

Out of ASPIRE ... HOPE





**THE
WORLD**

**IS
WATCHING**

ASPIRE

A Study to Prevent Infection
with a Ring for Extended Use

Thank you



Malawi College of
Medicine – JHU
Research Project



Participants and communities

University of Zimbabwe,
School of Medicine



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