

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".

ASPIRE

A Study to Prevent Infection
with a Ring for Extended Use

Jared Baeten MD, PhD

Thesla Palanee-Phillips, PhD

ASPIRE Protocol Team Meeting

October 2015





Meeting overview

- Welcome back!
- Today, we'll cover:
 - Updates on ASPIRE & The Ring Study
 - Looking forward to results and to HOPE (hopefully!)
 - Inspection readiness
- But, first, where we've been and where we are going in ASPIRE

Outline



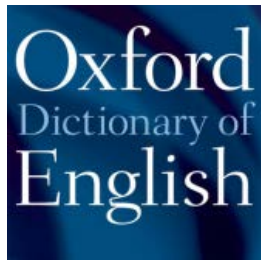
Where we have been and where we are going – mostly in pictures

We planned a study



- 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

We learned the meaning of ASPIRE



aspire(as·pire)

Pronunciation: /ə'spī(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.

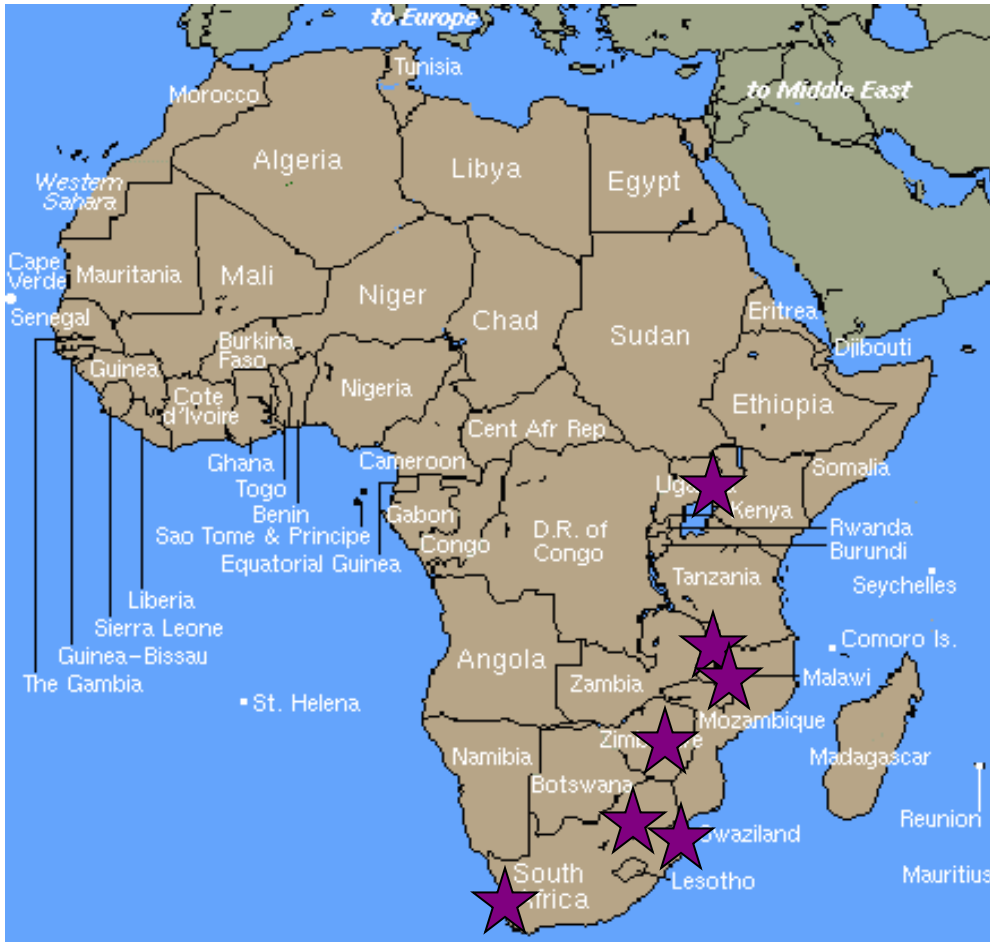
We started!

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).



We worked in 15 Sites across 4 countries



Blantyre
Lilongwe
Malawi

Cape Town
Durban (7 sites)
Johannesburg
South Africa

Kampala
Uganda

Harare/Chitungwiza (3 sites)
Zimbabwe

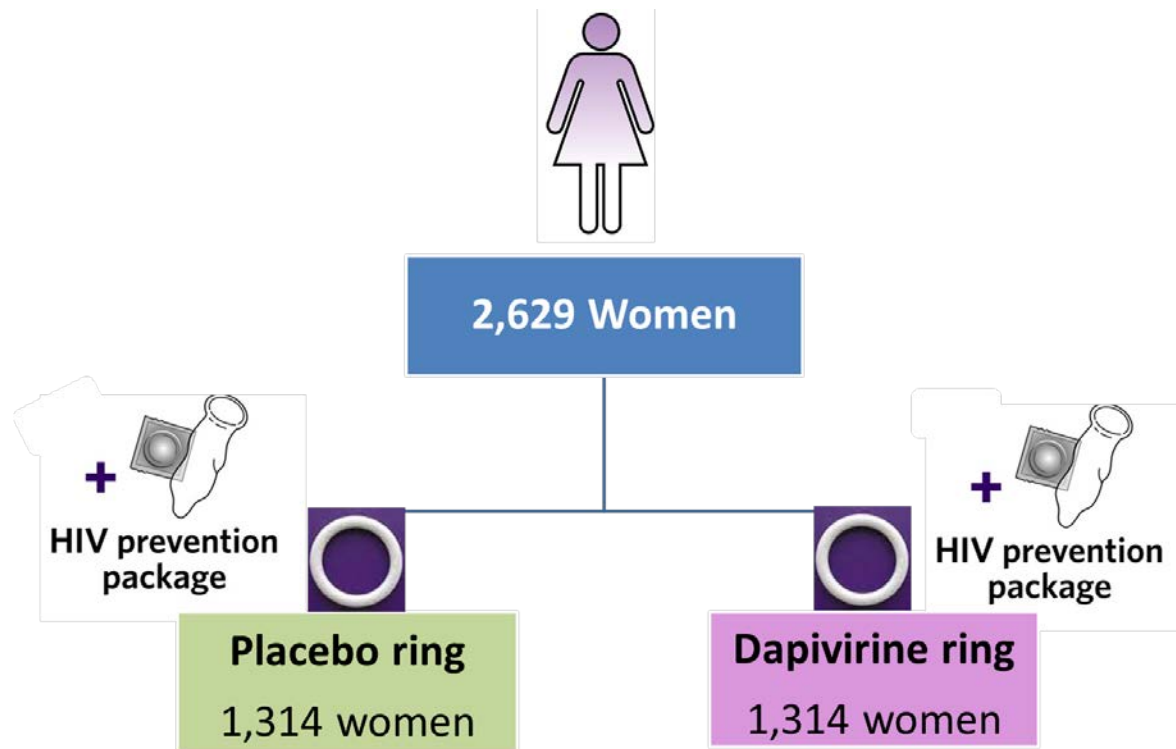
We learned how to explain the ring



We went to the community



We provided exceptional prevention services



We worked together



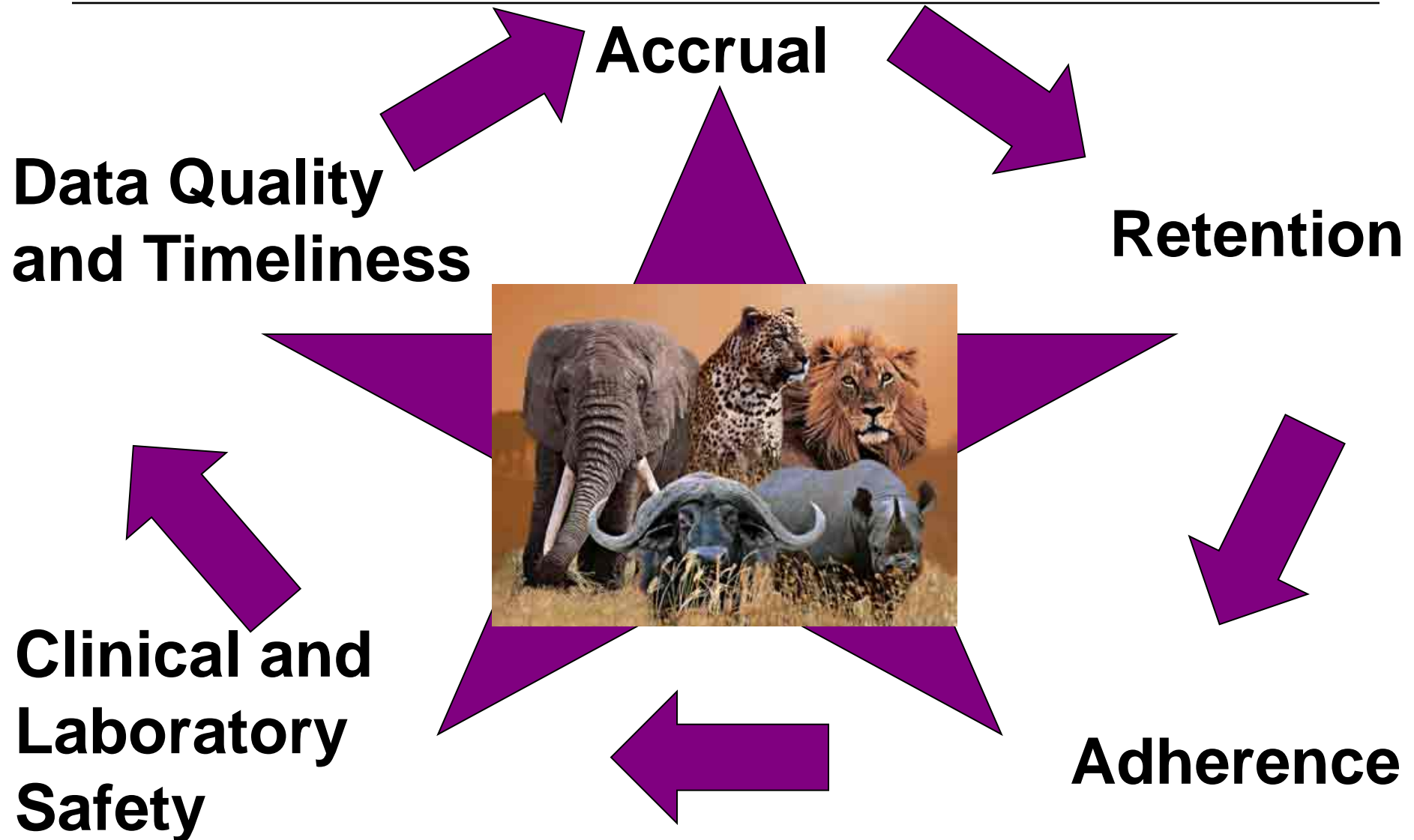
The Ring Study (IPM 027)



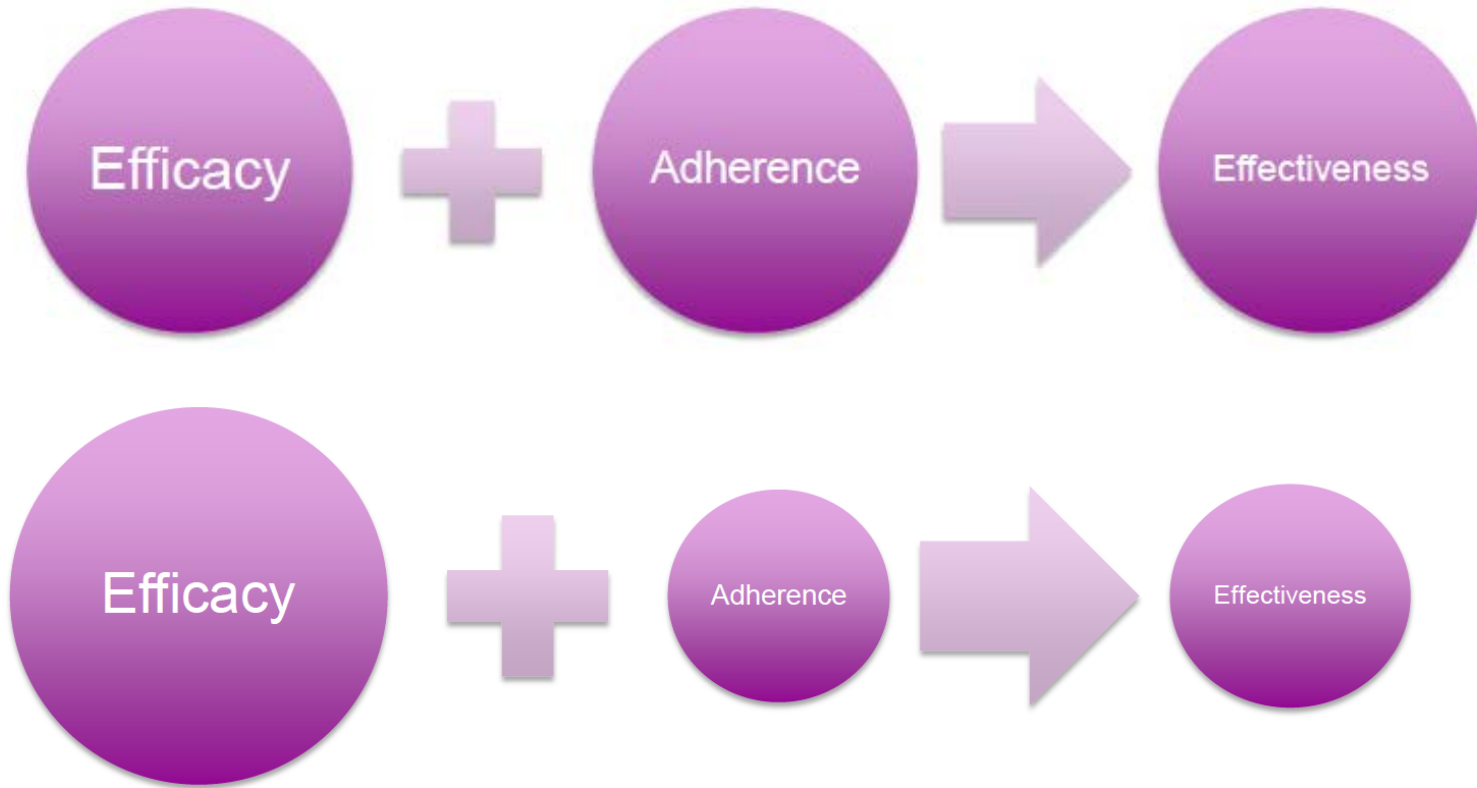
ASPIRE (MTN-020)

Objectives	Long-term safety and efficacy	Safety and effectiveness
Study design	Double-blind, randomized (2:1), placebo-controlled	Double-blind, randomized (1:1), placebo-controlled
Endpoints	Expected ~96 endpoints, 2 year on investigational product	Endpoint driven: ~120 endpoints
Enrollment	Total: 1959 women, ages 18-45 Active arm: ~1300	Total: 2629 women, ages 18-45 Active arm: ~1315
Regulatory requirement	3000 women on dapivirine ring for at least 1-year follow-up 1500 women on dapivirine ring for 2-year follow-up	
Participant follow-up	2 years + 6 weeks following ring discontinuation	Minimum 1 year + 4 weeks following ring discontinuation
Research sites	7 IPM research center partners in South Africa and Uganda	15 MTN research centers in Malawi, South Africa, Uganda, Zimbabwe

We defined our Big Five

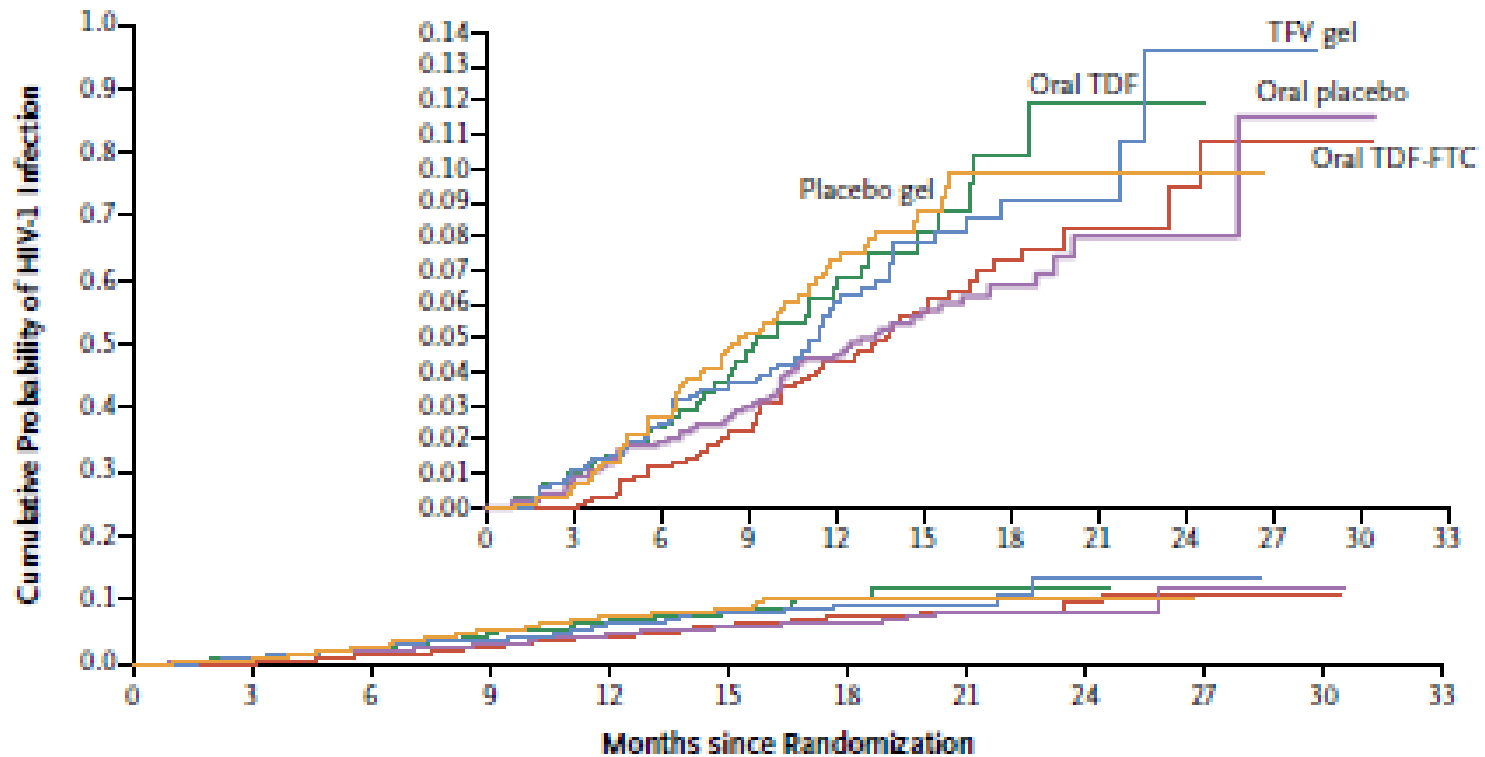


We thought about adherence



No adherence = no HIV protection

And then we thought a lot about adherence



VOICE Primary Efficacy Results



Adherence is Everything

Jared Baeten MD PhD
Thesla Palanee PhD

ASPIRE Adherence Meeting
Durban, South Africa
14 March 2013

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

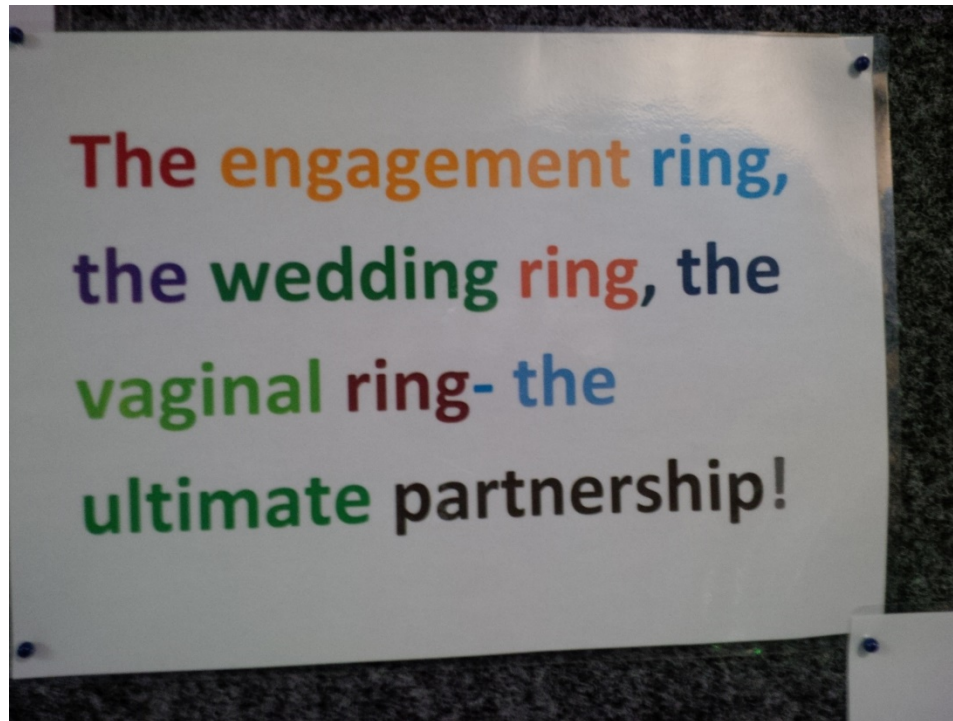
We did amazing participant engagement



Client focused
Invited ppt. to talk
Welcoming environment
Eye Contact/good body language
Good listening skills
Counselor support of plan/goal
Ppt. came up w/own strategies
A conversation/flexible



We did amazing participant engagement



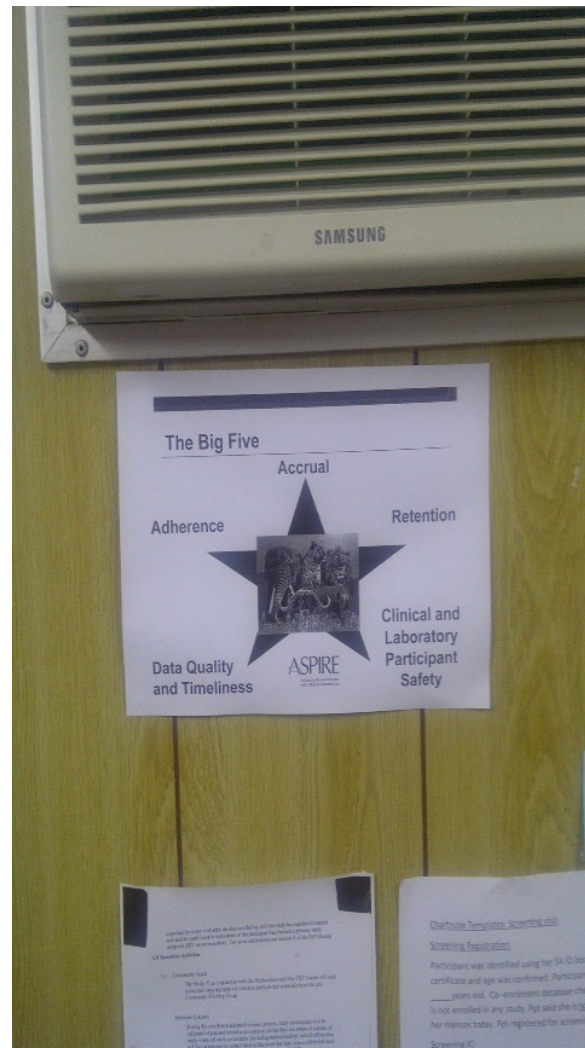
We did amazing participant engagement



We looked at returned rings



We made our Big Five a reality



We became a team



We continuously worked in communities



We completed accrual 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 OCT2012	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



We had amazing retention

**OVERALL >91% of all
expected visits**

**>97% of visits excluding
early terminations**

We reminded the world that PrEP is not one size fits all



Pill



Gel



Vaginal film



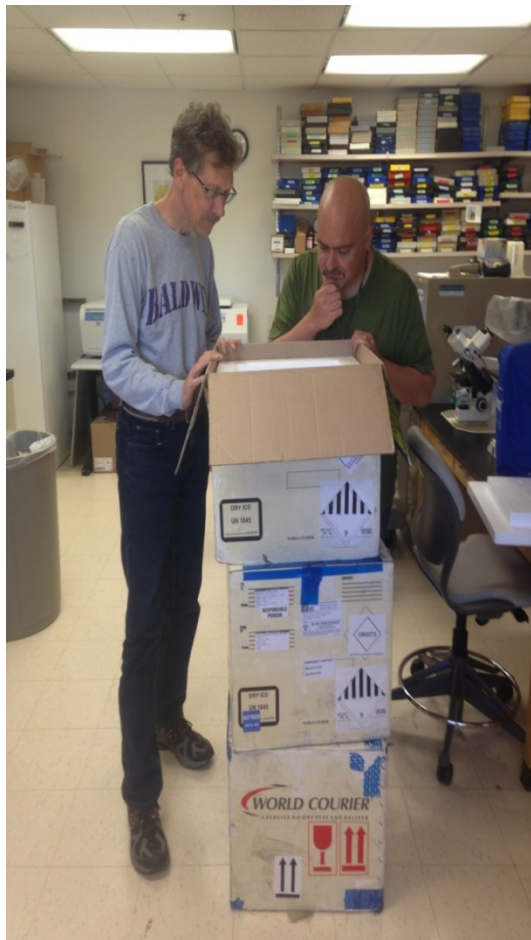
Vaginal ring



Injectable

- ✓ Tenofovir-based PrEP is a first proof-of-concept.
- ✓ Ultimate goals: multiple options, long acting, safe, effective, low cost and user-friendly
- ✓ Maximize choice & optimize effectiveness

We shipped a lot of samples



We did a lot of phone calls





We 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.

We have amazing data

- >600,000 CRF pages.
- >150,000 samples, including >20,000 plasma samples tested.
- >40,000 rings dispensed, returned, and tested.
- 248 IDIs, 12 FGDs.

We planned

2012

2013

2014

2015

2016

IPM 027 (The Ring Study)



Results?

MTN-020 (ASPIRE)



Results

Supporting Safety and PK Studies

Dapivirine Ring Regulatory Consultations

We planned for results

EFFICACY IS CLEAR

Great news!

Results clearly show dapivirine ring is safe and effective

Move to implement HOPE

HOPE

Out of ASPIRE, there is HOPE

EFFICACY WITH QUESTIONS

Good news (?)

Results show dapivirine ring is safe and effective

Decision about HOPE not straightforward

HOPE

Out of ASPIRE, there is HOPE

RESULTS UNCLEAR

Results don't provide clear answers - additional analysis needed?

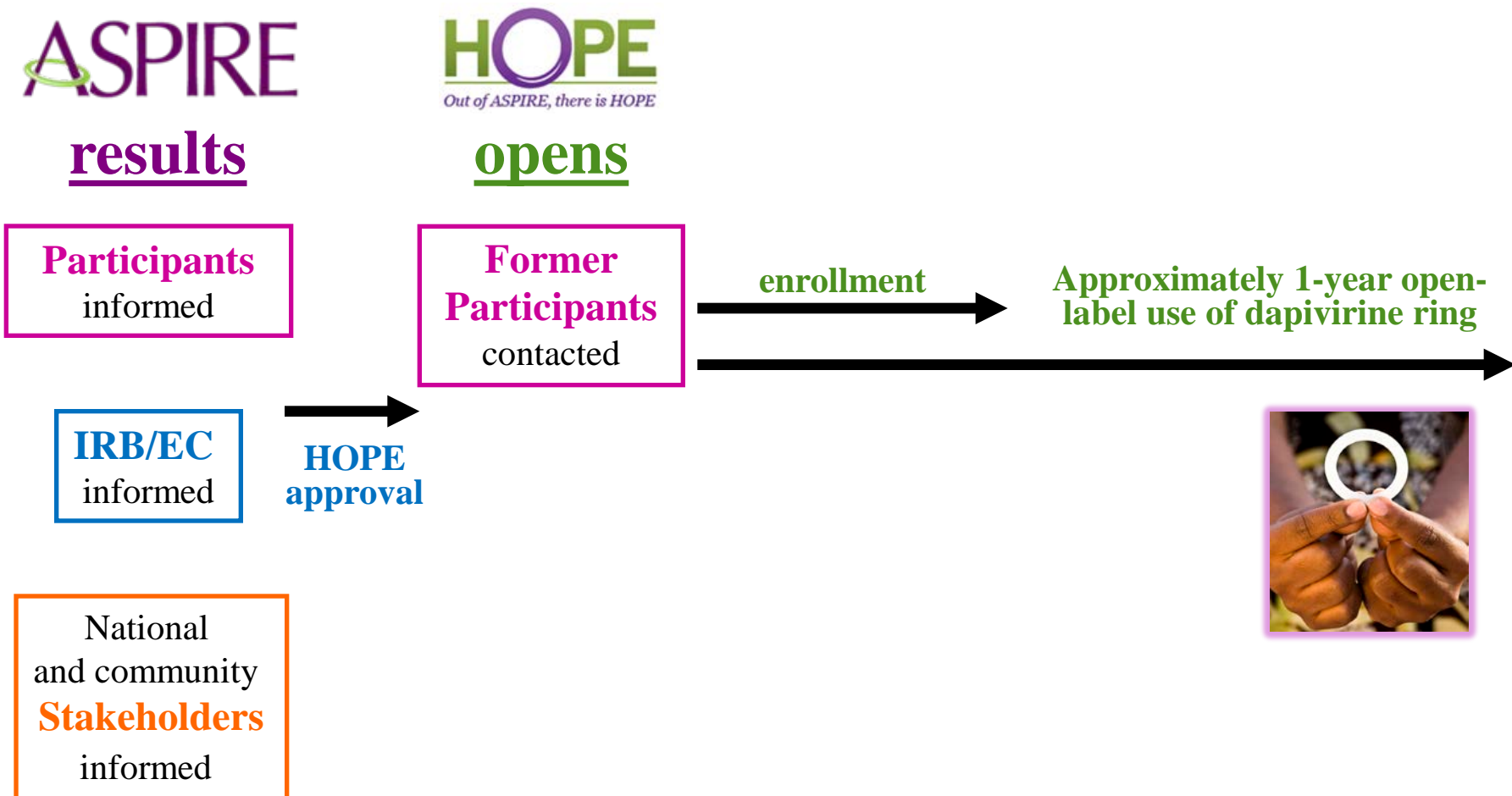
INSUFFICIENT EFFICACY

Results answer the questions - dapivirine ring is safe but not effective

ASPIRE

A Study to Prevent Infection
with a Ring for Extended Use

We planned for success



We are a team



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES



Participants and communities

University of Zimbabwe,
School of Medicine



Acknowledgements

MTN is funded by NIAID (UM1AI068633, UM1AI068615, UM1AI06707), NICHD and NIMH, all of the U.S. National Institutes of Health

