

# Understanding (non-) adherence: VOICE and Ancillary Studies

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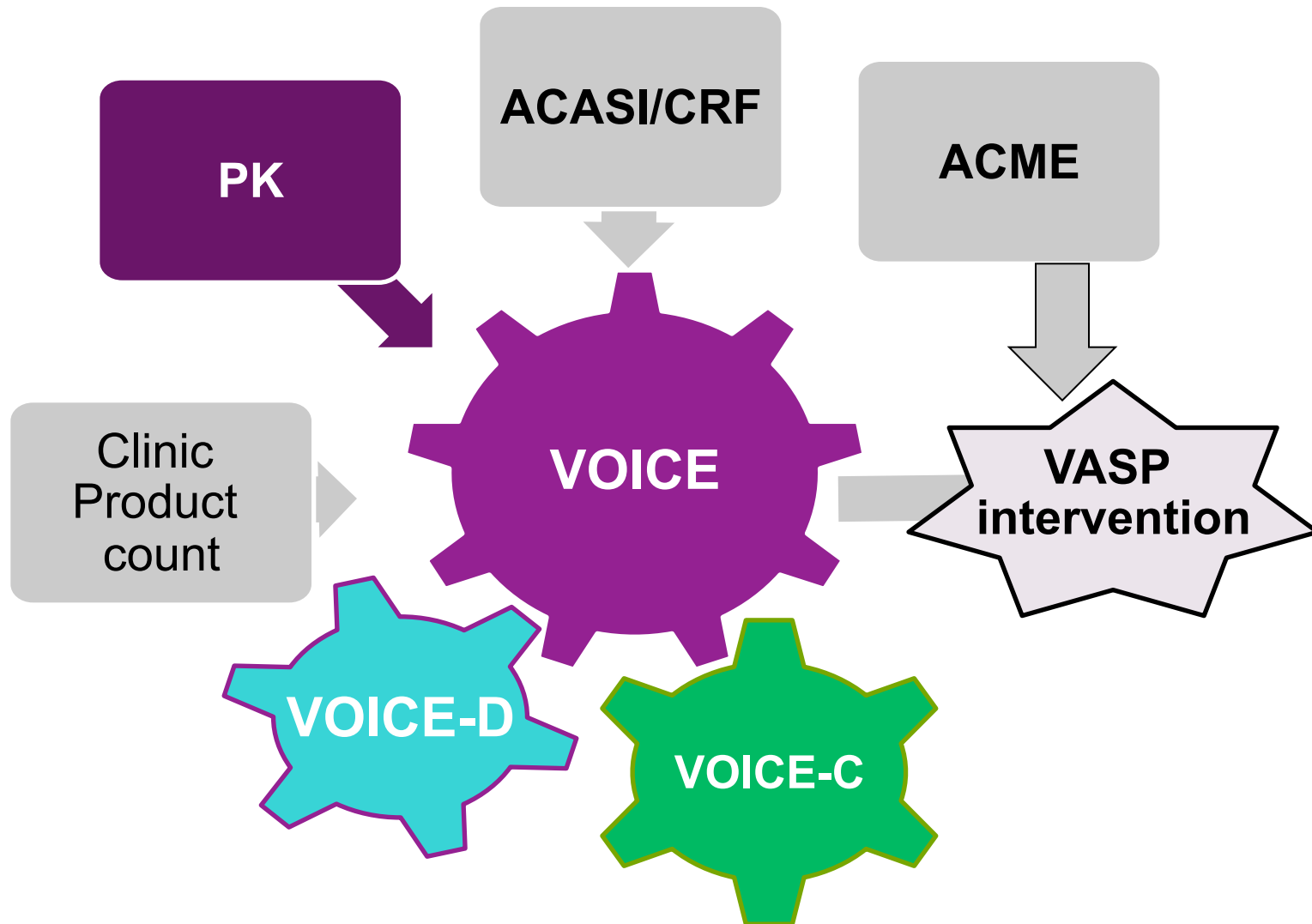


# Presentation Overview

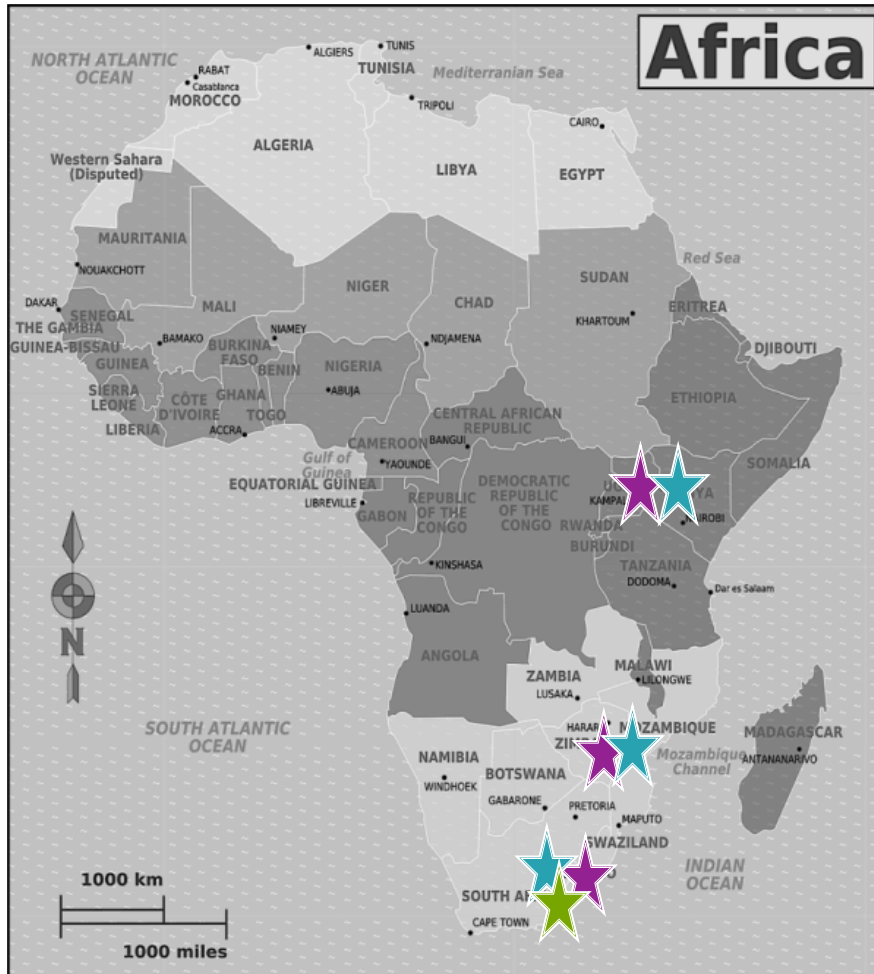
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1. VOICE and ancillary studies
2. VOICE-C: Design and key findings
3. VOICE-D: Design & preliminary findings
4. Concluding remarks

# Approaches to Assessing Use

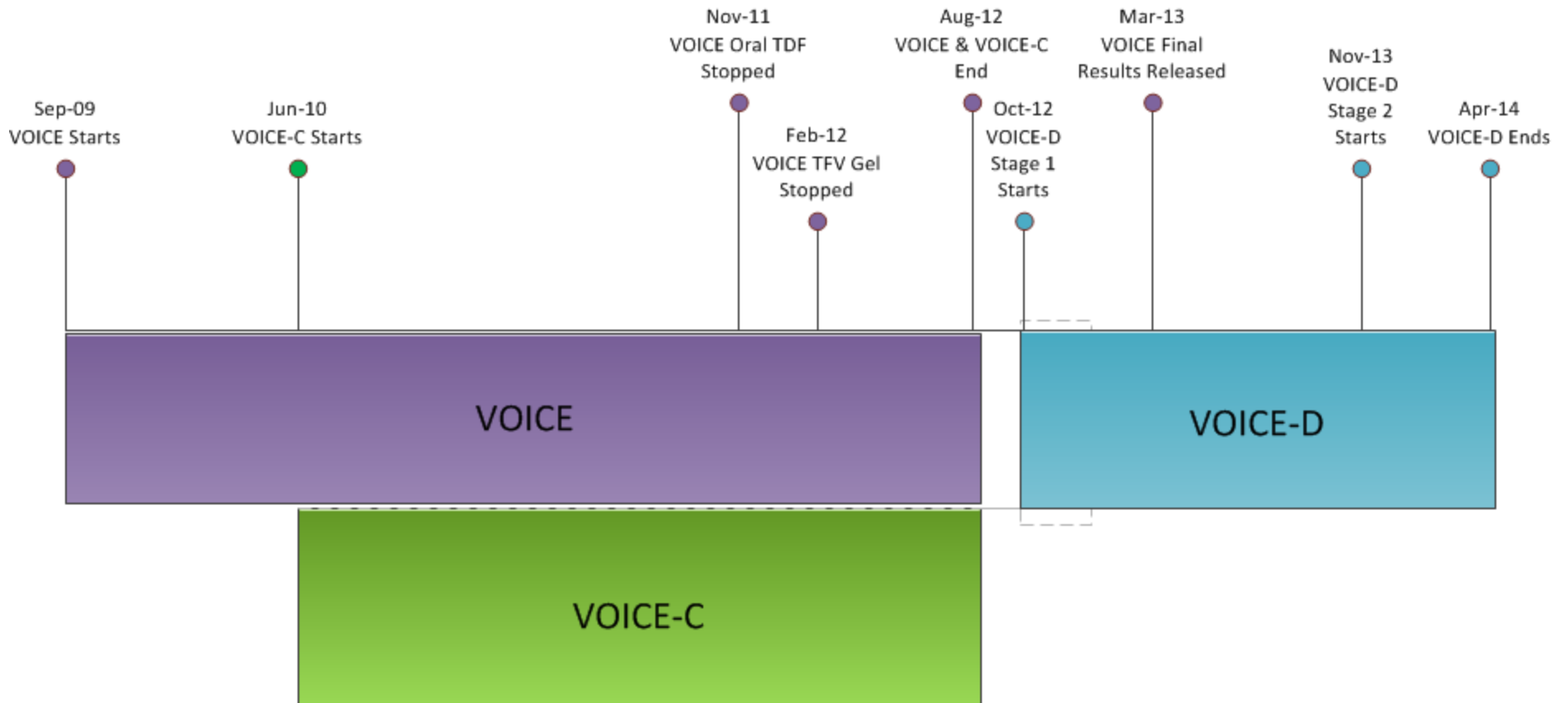


# VOICE, VOICE-C, and VOICE-D

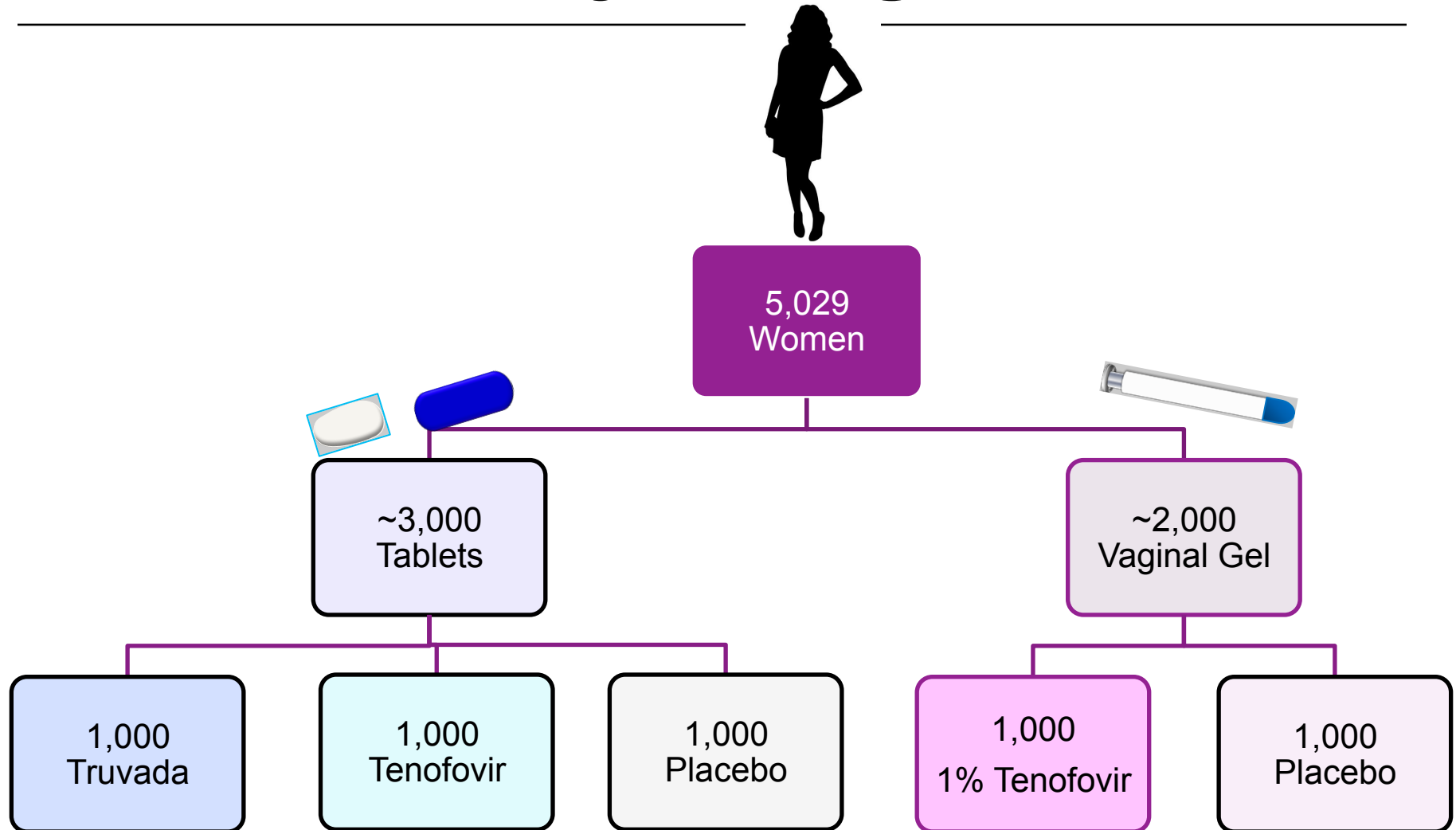


- **VOICE:**
  - N=5029 ♀
  - 3 countries, 15 CRS (sites)
- **VOICE-C:**
  - N=102 ♀, 22 ♂, 17 CAB, & 23 community stakeholders
  - 1 country, 1 CRS (Joburg)
- **VOICE-D:**
  - Stage 1, N=88 ♀
  - Stage 2, N=131 ♀
  - 3 countries, 5 CRS (Kampala, Chitungwiza, Durban)

# Timelines: VOICE, -C and -D



# VOICE: Study Design



# Final VOICE Results

**No demonstrated effectiveness of any of the 3 products, in the context of high HIV incidence**



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**FOR IMMEDIATE RELEASE**

## **Daily HIV prevention approaches didn't work for African women in the VOICE Study**

### **Truvada found not an effective strategy in this population**

**Young, single women were least likely to use tablets or gel, and more likely to get infected at very high rates**

**ATLANTA, March 4, 2013** – Results of a major HIV prevention trial suggest that daily use of a product – whether a vaginal gel or an oral tablet – does not appear to be the right approach for preventing HIV in young, unmarried African women.

Of the three products tested in the VOICE Study – tenofovir gel, oral tenofovir and oral Truvada® – none proved to be effective among the 5,029 women enrolled in the trial; most participants did not use them daily as recommended. Drug was detected in less than a third of blood samples from women who were assigned to use either Truvada or oral tenofovir and in less than a quarter of samples from women designated to use gel. Moreover, those least likely to use their assigned products, single women under age 25, were also the most likely to acquire HIV. Incidence in these young women approached nearly 10 percent in some of the study sites in South Africa. a

# Adherence from 3 Different Measures

<b>VOICE</b>	<b>TDF</b>	<b>FTC/TDF</b>	<b>TFV Gel</b>
<b>Total percent of doses reportedly taken*</b>			
<b>Returned Product Counts</b>	87%	92%	86%
<b>Self Report (7 days)</b>	90%	91%	90%
<b>Adherence based on plasma TFV detection</b>			
Percent of <i>samples</i> with TFV detected averaged across women (mean)	<b>30%</b>	<b>29%</b>	<b>25%</b>

\* Mean across all women's proportion of adherence estimated by these measure



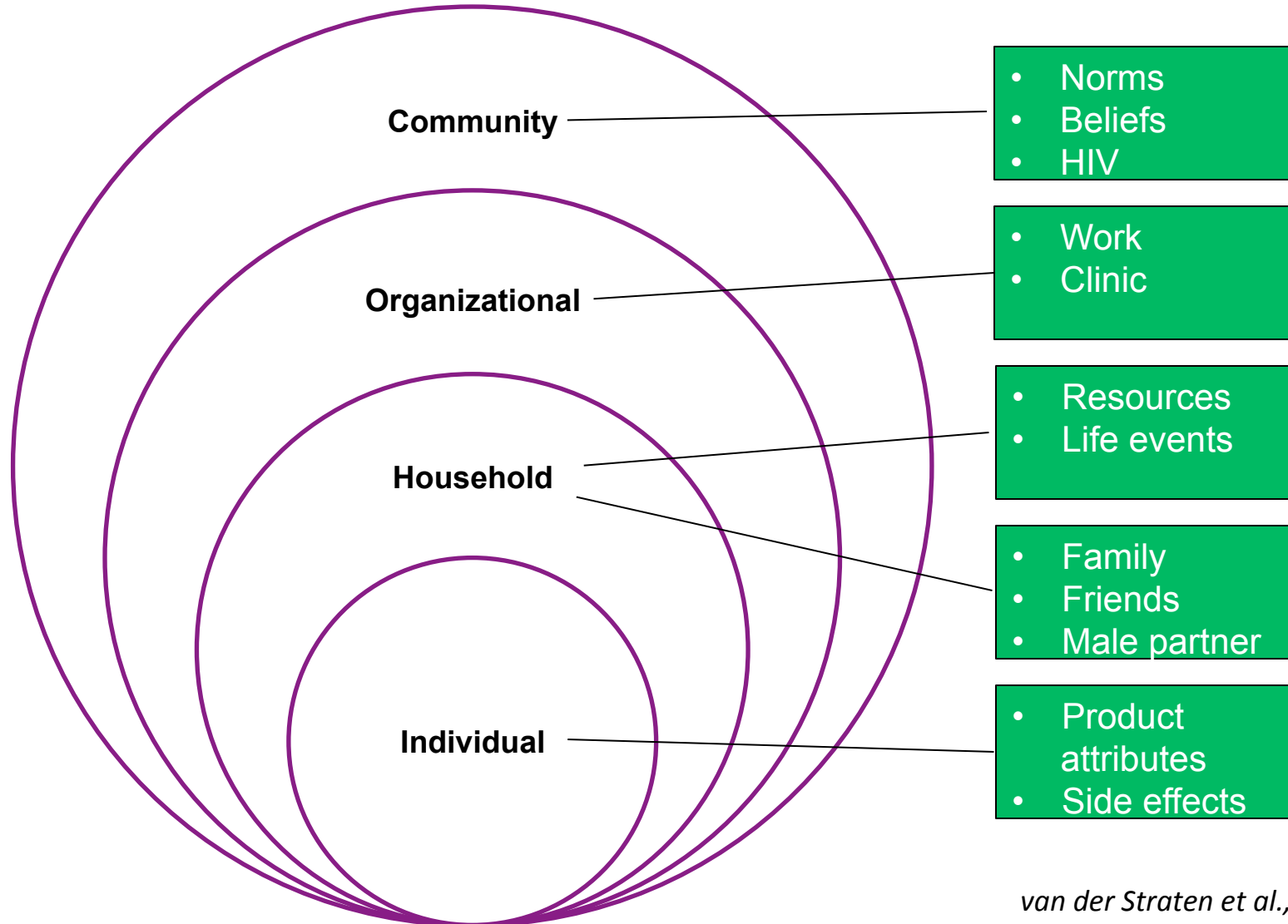
# VOICE-C Design & Approach

- *Design:* Exploratory sub-study of VOICE using multiple qualitative research methods at Wits-RHI (Joburg) site

Study Population	N	Selection	Data Collection Method
Female VOICE Participants	102	Random	<ul style="list-style-type: none"><li>• IDI</li><li>• EI</li><li>• FGD</li></ul>
Male Partners of VOICE Ppts	22	Systematic: permission requested of ♀ partner	<ul style="list-style-type: none"><li>• IDI</li><li>• FGD</li></ul>
CAB Members	17	Purposive	<ul style="list-style-type: none"><li>• FGD</li></ul>
Key Community Stakeholders	23	Purposive	<ul style="list-style-type: none"><li>• FGD</li></ul>

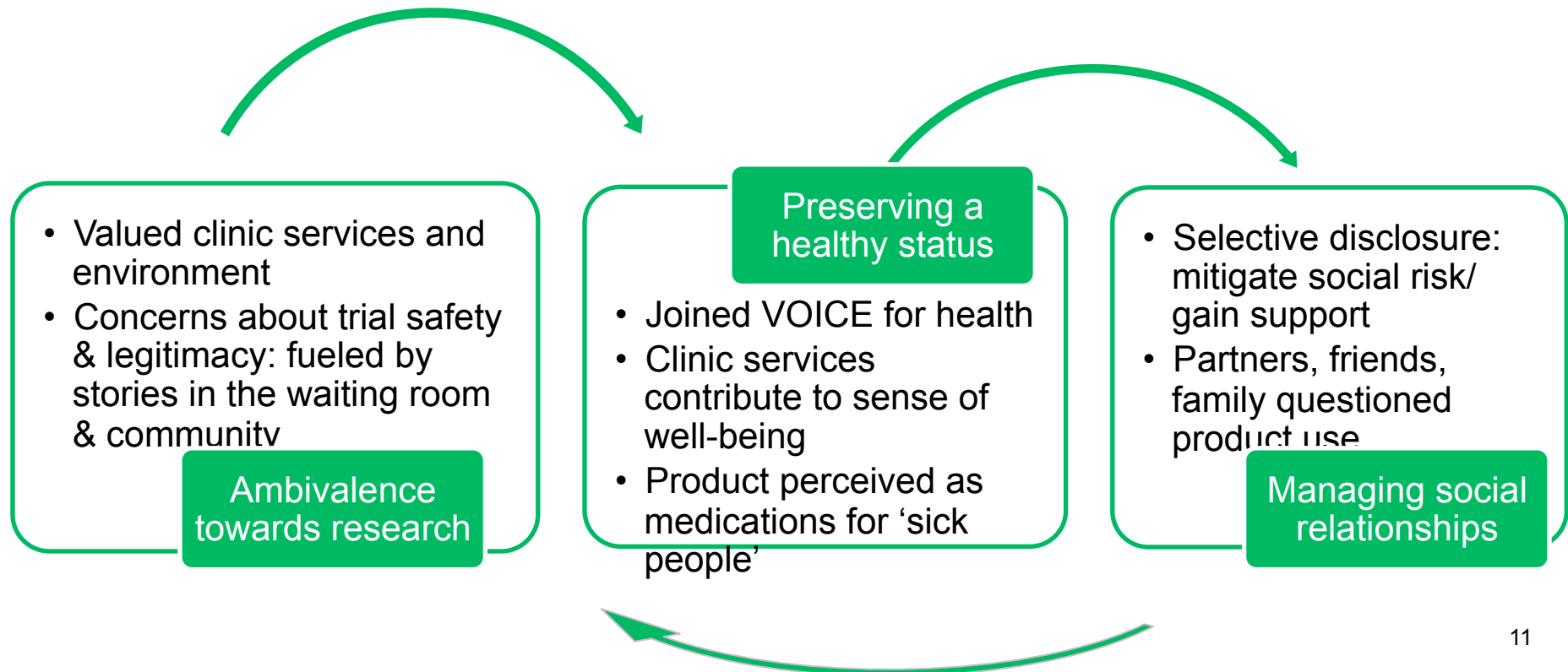
IDI=in-depth interview; EI=ethnographic interview; FGD=focus group discussion

# Socio-Ecological Framework (SEF): Levels of Influence on Adherence

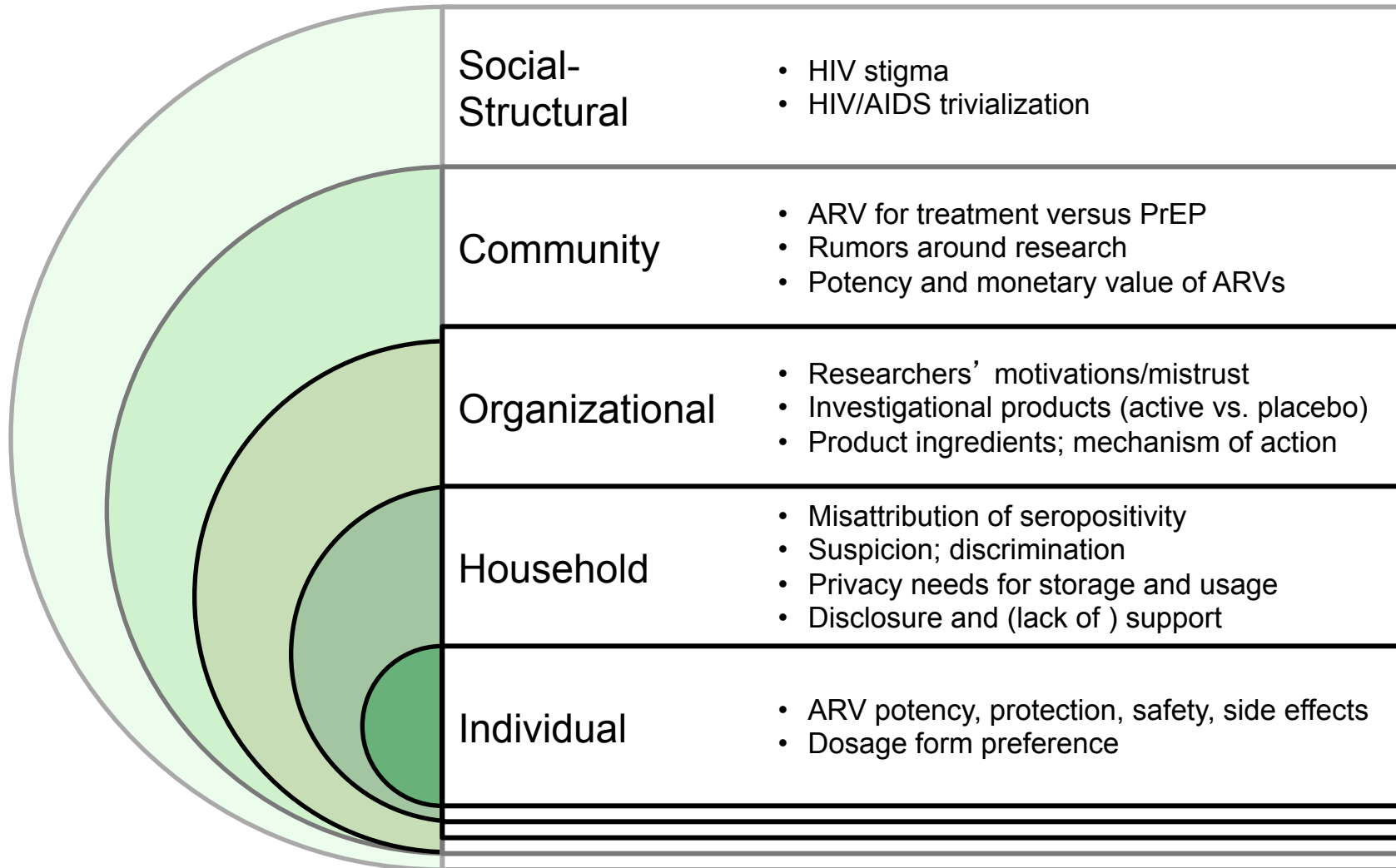


# VOICE-C Key Findings

- Demographics similar to VOICE ppts at Johannesburg site
- Difficult to acknowledge product non-use, even in qualitative IDIs
- Themes influencing product experience:



# Factors affecting perceptions about ARV for PrEP



# VOICE-D Stage 1 Design & Approach

□ *Design:* Qualitative exploratory study

Sample* (N=88)	Selection	Data Collection Method**
Former VOICE participants on product >3 months	Pre-selected based on: <ul style="list-style-type: none"><li>• Anal sex report (ACASI)</li><li>• HIV status (+ and -)</li><li>• Study product (tablets &amp; gel)</li></ul>	<ul style="list-style-type: none"><li>• IDI</li></ul>

\*Sample revised after study activation to maximize the number of participants in active arms

\*\* Filed Staff not involved with VOICE, and IDI conducted at a neutral location



# Stage 1 Preliminary Findings

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- ❑ Participants largely did not admit to personal non-adherence but spoke widely of ‘other women’ not adhering
- ❑ Participants suggested that **presenting women with blood test results during the study (in “real time” )** would encourage honesty in reporting product use level
- ❑ Participants demonstrated inconsistent understanding of adherence questions, specifically the self-rating scale and its response categories

# VOICE-D Stage 2 Approach

□ *Design:* Qualitative exploratory study

Sample* (N=131)	Selection	Data Collection Method
Former VOICE participants on product >3 months	Pre-selected based on: <ul style="list-style-type: none"><li>• Plasma drug PK detection (low, inconsistent, high)</li><li>• HIV status (+ and -)</li><li>• Study product (tablets &amp; gel)</li></ul>	<ul style="list-style-type: none"><li>• IDI</li><li>• FGD (only with HIV-, low / inconsistent PK results)</li></ul>

\*Sample included participants who previously took part in Stage 1 (experienced) and who had not (naïve)

# PK Visualization: Teapot Tool








# Presentation of PK results

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- **Tea cup**: represents a “snapshot” of recent product use: was drug “on board” (i.e. in her blood) or not at a visit
- **Tea cup row**: the presentation is by design not specific to individual participant results. The order of full vs. empty cups is not representative of the participant’s pattern of drug detection.
- **Teapots**: presents overall drug detection (“product use”) category



# Preliminary Observations

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## □ PK Results

- Can be made understandable through pictorial tool
- Reactions vary, but generally participants are not offended by results and have accepted them
- Some examples of reasons for refuting results:
  - Used it initially, only stopping after several months
  - Took purposely product just before clinic visits
  - Took products consistently
  - Blamed alcohol or medication use on drug not showing up
  - Believed to be on placebo
  - Tested while pregnant
- Willingness to discuss adherence challenges and product disposal/handling



# Study Teams and Key Roles

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## VOICE-C

- **Chairs:** Ariane van der Straten, Jonathan Stadler
- **Wits RHI:** Sello Seoka, Florence Mathebula, Busisiwe Magazi
- **FHI 360:** Katie Schwartz, Kat Richards, Rhonda White
- **RTI/WGHI:** Elizabeth Montgomery, Miriam Hartmann, Helen Cheng, Catie Magee
- **MTN Core:** Beth Galaska Burzuk
- **DAIDS:** Lydia Soto-Torres

## VOICE-D

- **Chair:** Ariane van der Straten
- **Co-chairs:** Elizabeth Montgomery, Barbara Mensch
- **MRC:** Sarita Naidoo, Kubashni Woeber, Funeka Mthembu, Nozipho Vilakazi
- **UZ-UCSF:** Nyaradzo Mgodzi, Petina Musara, Imelda Mahaka, Oillia Munaiwa
- **MU-JHU:** Clemensia Nakabiito, Juliane Etima, Josephine Nabukeera, Teopista Nakyanzi
- **DTHF:** Zoe Duby, Thola Bennie
- **FHI 360:** Lisa Levy, Kristy Alston
- **RTI/WGHI:** Miriam Hartmann; Helen Cheng
- **MTN Core:** Beth Galaska Burzuk, Sonia Gor
- **DAIDS:** Jeanna Piper
- **NIMH:** Cynthia Grossman



**THANKS!**

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## THE TEAM ...



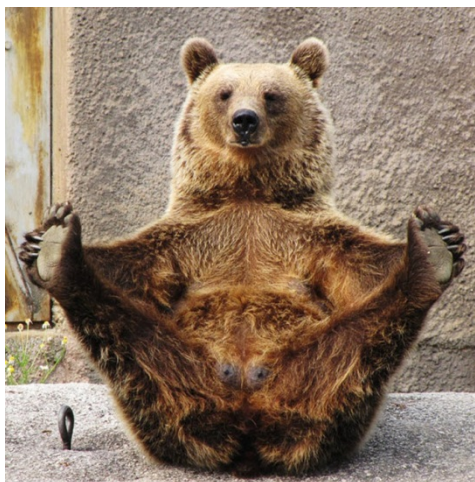
**Jeff Lucas**  
'Jeffers'



**Steve Kretschmer**  
'Kretschmer'



**Moushira El-Sahn**  
'Moushi'





**THE PRIMARY OBJECTIVE OF THIS RESEARCH IS TO IDENTIFY THE OPPORTUNITIES AND ASSESS THE POTENTIAL FOR MULTI-PURPOSE PREVENTION TECHNOLOGIES (MPTs) IN UGANDA, SOUTH AFRICA AND NIGERIA ...**

**... AND GET TO KNOW THE PEOPLE WHO WILL BE USING THEM ...**



BILL & MELINDA  
GATES foundation

**ACCEPTABILITY ...  
UNDERSTANDING AND  
FOCUSING ON THE WOMAN,  
HER NEEDS, HER LIFE, HER  
DECISIONS ...**

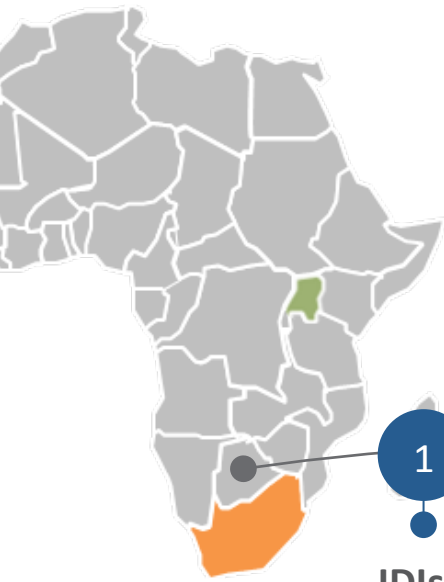
**A SALIENT DIMENSION FOR  
IMPLEMENTING SUCCESSFUL  
HIV PREVENTION STRATEGIES**





# WE QUALITATIVELY TALKED WITH 363 WOMEN, 80 MEN, 108 HCPs & 18 BRAND MANAGERS AND EXECUTIVES IN UGANDA, SOUTH AFRICA AND NIGERIA

From November 2013 – March 2014



1

**IDIs Women**  
~32 per country  
15 – 30 years  
90 minutes

2

**FGDs Women**  
12 focus groups with ~n=6 women in each group (total sample of 72 women) per country  
120 minutes

3

**IDIs Men**  
24 per country  
18 – 45 years  
60 minutes

4

**IDIs HCPs/nurses who prescribe and/or consult with women on contraception options/ HIV prevention**  
24 physicians  
12 nurses (HCW/ Nurses)  
60 minutes

5

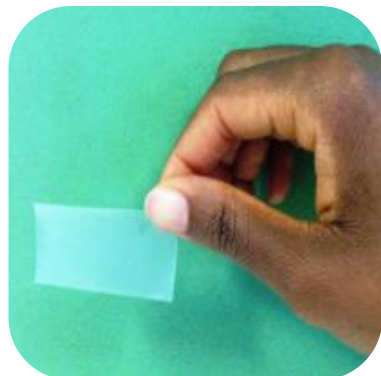
**IDIs Executives/ brand managers**  
45 minutes

→ **WE ARE CURRENTLY SETTING UP THE QUANTITATIVE PHASE IN ALL MARKETS ... TALKING WITH 1,500 WOMEN ACROSS UGANDA, NIGERIA AND SOUTH AFRICA**

- From April – July 2014 500 per country, 65 minutes
- 15 – 35 years, representative sample of country demographics
- Using mobile phone technology



# THERE WERE 4 MPTs TESTED ...



ON DEMAND INTRA-VAGINAL FILM

- A film used up to 12 hours before sex and another up to 12 hours after
- 70% effective against HIV infection
- 85% effective as contraceptive
- Possible side effects: vaginal itching, irritation, dripping, wetness



INTRA-VAGINAL RING

- A ring inserted up high into the vagina, used continuously for 60 days
- 70% effective against HIV infection
- 95% effective as contraceptive
- Possible SEs: vaginal itching, irritation, bleeding irregularities



INJECTABLE

- Two injections – one in the arm, and one in the buttocks every 3 months by a trained healthcare professional
- 70% against HIV infection
- 90% contraceptive
- Possible SEs: Bleeding irregularities, heavy or no bleeding
- 6-9 month gap conceiving



IMPLANT TYPE DEVICE

- Two transparent rods – both inserted into the upper inner arm – HIV rod every 6 months and contraceptive rod every 5 years by trained HCP
- 70% HIV and 90% contraceptive
- SEs: Bleeding irregularities for 6-9 months

- ALL: HIV TEST BEFORE AND EVERY 3 MONTHS DURING USE
- STORAGE: BETWEEN 15OC AND 30OC



## THERE ARE DIFFERENCES BETWEEN WOMEN IN SOUTH AFRICA AND UGANDA WHEN IT COMES TO THEIR HOMES, EXPERIENCES WITH SEX, CONTRACEPTION AND LOVE

- **Socio-economic Class and living arrangements:**

The majority of the women in Uganda have a similar experience; a younger sample, many are students, not married although in stable relationships, and did not have any children (although want 4 on average). Differences between social class were less pronounced. However, in South Africa differences were more stark – those in lower echelons share homes with immediate and extended family, are unemployed, with a child, and generally ‘complicated’ relationships.

- **Contraceptive awareness and use:**

Awareness and use of protection methods are broader in Uganda. In South Africa most women are exposed to injections or condoms. Consequently, their use is impacted but what is available and what they are aware of. However, where some women in Uganda use safe days/timing, only 3 women in South Africa do. However, condom use is higher in Uganda and slightly more consistent.

- **Advice and HCPs:**

Where women in Uganda actively seek advice from members of the healthcare community, South African women get in contact with clinic, namely due to the birth of their first child and normally, according to HCPs, are advised on the injection or condoms. Other women are essential sources of information.

- **The role of the partner:**

South African men play a limited role, they do not live with their partner (even if they are the father of the child), and are considered less knowledgeable with regard to contraception, communication is basic, and there is a strong level of distrust (men admit multiple partners) and sometimes violence (in lower SEC). Uganda men play a bigger role, sometimes initiators of condom use, and the purchasing power for contraceptives, however they do admit to promiscuity and women are also cautious, hence stronger use of condoms amongst young women.

## WOMEN ARE VERY MUCH ALIGNED IN TERMS OF WHAT THEY LOOK FOR IN AN IDEAL CONTRACEPTION AND THE IMPORTANT CHARACTERISTICS IT SHOULD HAVE

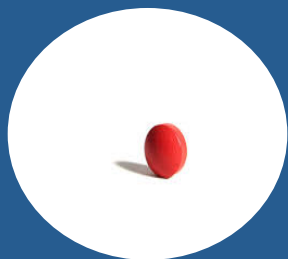
- The three most important characteristics for a contraceptive described by women are:  
**Good duration, Convenience/ Ease of Use and Low or no Side Effects**

When asked about the ideal contraceptive ....



### **Injection**

3 months to 5 years  
duration of protection [1<sup>st</sup>  
in Uganda, 3<sup>rd</sup> in SA]



### **A pill**

2 weeks to 1 year  
duration [2<sup>nd</sup> in  
Uganda & SA]



### **Drink (liquid/ syrup)**

Before sex [4<sup>th</sup> in  
Uganda, 1<sup>st</sup> in SA]



### **Gel**

To rub on before sex  
[Uganda mostly]

## NEARLY ALL CELEBRATE THE CONCEPT OF COMBINING A CONTRACEPTIVE WITH HIV PROTECTION



It's "like killing two birds with one stone"

"Women can protect themselves"

It will "give us peace of mind"



**THERE IS A HIGH LEVEL OF HIV AWARENESS, HOWEVER THIS DOES NOT NECESSARILY TRANSLATE INTO SAFE SEX PRACTICES ...**



# A QUARTER IN UGANDA AND UNDER A THIRD IN SA BELIEVE THEY ARE SOMEWHAT/ COMPLETELY AT RISK OF CONTRACTING A STI/HIV

Although, under half believe that they are not at all at risk of contracting a STI/HIV from current partner – *particularly from condom users in Uganda*

## Why?

Women voice a lack of trust with their partners

- At least a third explicitly in South Africa especially (and yet do not always use condoms "I don't know my partners' movements", "I am not with him all the day")

Many cannot do anything about it (a third):

- Women who are in relationships, married, stable, or after they get to know each other, where the man does not like using condoms ... in these cases, there is nothing to protect them, and convincing the partner for condom use will cause conflict ... "he will ask me why? Do you think I am sleeping around?"
- Some openly admit that they are at risk, but ... "faithfulness is all I have got" Implant, married, Uganda

More worryingly, a group (albeit smaller) seem ambivalent towards HIV, HIV is 'normal'...

- ... Like malaria (Uganda), or that it is better to get HIV than cancer as you live for longer (Uganda and South Africa).
  - Some are so sensitised that they are in fact desensitised: Thinking that it is inevitable, or that they can go on ARVs and it be managed



## Nearly all women suggest that they or the women in their communities would prefer to get HIV then get pregnant ...

- Younger girls would prefer HIV – not acceptable to get pregnant
- Older women would prefer to get pregnant – more acceptable, and have seen the impact of HIV





### Because:

- **The community response is VITAL to the fear of getting pregnant ...**
- Students/ younger women cannot get pregnant:
  - In Uganda: they will be kicked out/chased out of school; the parents will be disgraced
  - In SA: Financial instability and lack of ability to care
- Pregnancy shows physically, whereas HIV does not - you can hide it, take ARVs, no one will have to know ... getting pregnant is "like telling everyone you had sex" ... you can't see HIV





## SUMMARY: OUT OF ALL THE MPTs, SOME WILL REQUIRE MORE WORK IN ORDER TO ENSURE ADOPTION

	Resonance	Deployment	Barriers to be addressed	Key Maxims
	<b>High</b>	<b>Medium</b>	<b>Low</b> - Providers	Familiarity, Current use, Duration, Protection, Belief in efficacy, Bleeding, Pain, 6-9 months
	<b>High</b>	<b>Medium</b>	<b>Low</b> - Providers	Duration, Protection, Known, Bleeding, 6 months, insertion
	<b>Medium</b> <i>more preferred by men</i>	<b>Low</b>	<b>Medium-High</b> - Education, misuse, trust	Easy to use, Dissolves, Self admin, ST, Lower SEs, Sex unplanned, Insertion, Timing/ Frequency, Believability, Dripping, Irritation
	<b>Low</b>	<b>Low</b>	<b>Medium-High</b> - Education, design, trust, use	Duration, Self-admin, Lower SEs, Insertion, Removal, Falling out, Partner feeling it, Hygiene

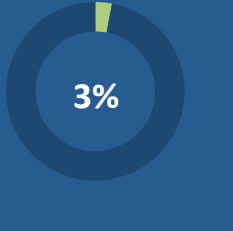
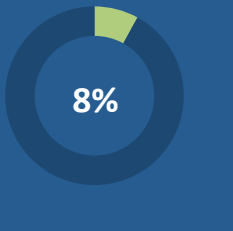
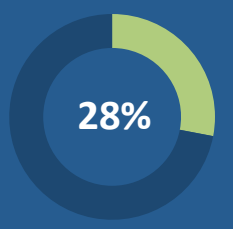
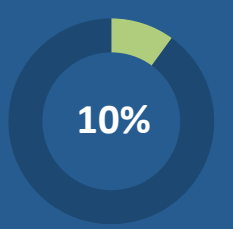
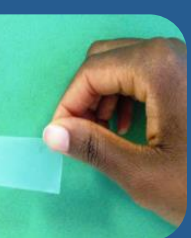
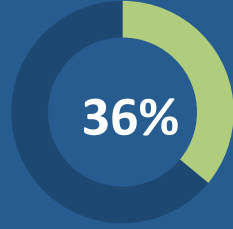
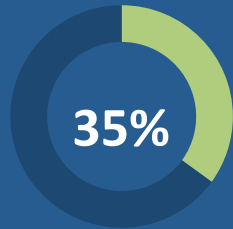
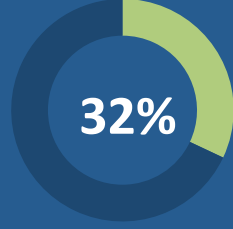
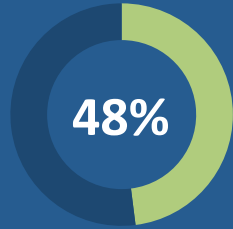


# THERE IS NO OVERALL LEADING MPT – THE IMPLANT AND INJECTION ARE TWO FAIRLY STRONG OPTIONS

## PREFERENCE:

SOUTH AFRICA

UGANDA



## WHY?

- A mostly neutral initial reaction in Uganda: 46% and a happy reaction in SA: 56%
  - Duration is the main driving force behind preference
  - Issues on irregular bleeding and the big and painful needle
- 
- A more neutral reaction in Uganda: 38% and a more happy reaction in SA: 46%
  - Preferred because it is similar to current with added benefits
  - Issues on irregular bleeding and the long waiting period to be able to conceive
- 
- More in Uganda give a happy face 42% while in SA more give a sad face 39% (neutral Uganda: 49% SA: 40%)
  - Easy of use and the fact that it dissolves is appealing
  - Concern on side effects (irritation, dripping) and 12 hour duration is too short for unplanned sex
- 
- Half of Uganda and 60% in SA give it a “sad face”
  - Several issues behind lack of appeal mostly hardness, big size, partner may feel it, and difficult to insert and remove
  - Reasons why few like it: Limited side effects and the fact that it is self administered



## AN IMPORTANT DEVELOPMENT IN CONTRACEPTION AND HIV PREVENTION, BUT ONE NEEDING MORE SUPPORT

- **There is universal acceptance of the concept of a MPT**
  - Women NEED contraceptive products and women are aware of HIV (but many cannot do anything to protect themselves)
- **However, no one MPT form is ideal**
  - Each MPT form has unique features, which appeals to different women and resonates to women's varying lifestyles or life stages, so one MPT will not be enough
  - Women's lifestyles are not uniform within and between countries; there is a need for options
- **Therefore, it will be important to support those MPT forms which answers women's needs, this may demand further investment and development as equally each MPT has unique features which are unappealing to women ...**
  1. The strategic intent of introducing the MPTs into South Africa and Uganda
  2. The level of acceptability
  3. The fact that women's needs change over lifetime and,
  4. The level of further investment needed to develop these MPTs



## THESE LEARNINGS WERE VITAL TO DEVELOPING THE QUANTITATIVE PHASE OF THIS RESEARCH

- To quantify across country representative samples what we saw during the qualitative phase
- To really gauge the level of risk women are taking
- To really know how acceptable each form is – and the reasons behind appeal/ lack of appeal
- To understand whether there are profiles of certain women who find specific MPTs more acceptable
- To understand whether or not, taking into account their perceptions of each MPT, negative and positive, they would use it if available (in particular the for the Intra-vaginal Ring and The Intra-vaginal Film)



THANK  
YOU



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# Rethinking HIV prevention in young African women

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# Challenges with HIV prevention for young women in SSA

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- HIV incidence of 6% in FemPrEP & VOICE
  - No efficacy of oral & daily topical tenofovir-based PrEP due to low adherence
  - High incidence in context of monthly visits & best available HIV prevention tools
- 2012 HSRC survey in South Africa
  - New infections more common in young women & informal urban settlements
  - Worrisome increases in youth reporting their first sexual experience occurred before age 15, adolescent girls reporting older partners, & having >1 sexual partner in past year

# Our objectives

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- Examine our assumptions & approaches to HIV prevention for young African women
- Engage experts in health psychology, adolescent health, behavioral economics, diffusion of innovation, social marketing, family planning delivery
- Identify gaps
- Prioritize research needs

# Two areas of focus

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- 1) Effective implementation of evidence-based interventions
  - HIV testing, behavior change, & emerging technologies (eg PrEP)
  - How to engage young women, help them assess their risk & motivate them to adopt prevention?
  
- 2) Design, development and evaluation of new biomedical prevention strategies
  - Long-acting PrEP, dual HIV prevention-contraceptive technologies
  - How to design products that women want & use?



# Some assumptions underlying HIV prevention for young African women

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- Human behavior is rational
- Information & awareness translate into motivation & behavior
- HIV prevention is a high priority for young African women
- Young women are able to accurately perceive their risk (which often is uncertain & is dynamic)
- Women need strategies under their control



# Past approaches to HIV prevention for young African women

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- Media campaigns have emphasized behavior change
- Behavioral interventions have changed knowledge in right direction, but had limited impact on self efficacy or attitudes
- Disease prevention model with HIV focus (rather than health promotion)
- Have been individually focused more than on community or structural factors
- Limited integration with family planning
- Few new tools or messages

# Potential reasons for limited prevention impact to date

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- Behavioral biases (self control, temptation, inattention, biased beliefs, hassle or channel factors)
- Information (i.e. not having the right information / enough information)
- Service delivery barriers (do not know where to access FP or HIV services, locations far away, concern re stigma)
- Structural barriers (poverty, unemployment)
- Concerns for social image, desire to conform to social norms
- Cultural factors (low power for women, expectations about sexual activity, pregnancy)

# Going forward with HIV prevention for young African women

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- Biomedical HIV prevention needs to engage wider disciplines
  - Risk experts, behavioral economics, health psychology, diffusion of innovation, structural interventions, FP delivery
  - Define gaps & prioritize new approaches
- Qualitative work to better understand what matters to & motivates young women
  - Health, contraception, & HIV prevention behaviors

# Going forward with HIV prevention for young African women

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- Demonstration projects of combination prevention
  - Interventions to increase partner testing & engagement, condoms, PrEP for those motivated (& adherence support), behavior/empowerment interventions
  - Provide in context of youth-friendly FP services
  - Learn from ‘early adopters’
  - Will help us prepare for expanded methods, as they become available (long-acting PrEP & MPTs)

# Key questions for demonstration projects of combination prevention for young African women

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- Risk perception
  - How to understand it, measure it, influence it?
- Willingness & motivation for HIV prevention
  - Can self-efficacy & locus of control be modified?
- Reasons to include PrEP in combination prevention
  - Uptake & adherence may be higher in context of known efficacy
  - Adherence : Role for 'nudges', incentives, & peer support?

# Acknowledgments

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- Collaborators
  - Jared Baeten, Linda Gail-Bekker, Elizabeth Bukusi, Sinead Delaney-Moretlwe, Ann Kurth, Margaret McConnell, Heidi van Rooyen
- Funder
  - BMGF (Lut VanDamme, Stephen Becker)
- Those who have shared their expertise & opinions