MATRIX-003

Trial to Assess Acceptability and Safety of Two Placebo Intravaginal Ring (IVR) Designs

Kathryn T. Mngadi
Protocol Co-Chair
Aurum Tembisa Clinic 4 CRS
Johannesburg, South Africa

Surina Reddy
Protocol Co-Chair
Wits RHI Research Centre CRS
Johannesburg, South Africa

MATRIX Investigators Meeting (28 Aug – 1 Sep 2023)
Southern Sun Rosebank, Johannesburg, South Africa

PEPFAR

USAID
FROM THE AMERICAN PEOPLE

MATRIX
Advancing R&D of Innovative HIV Prevention Products for Women

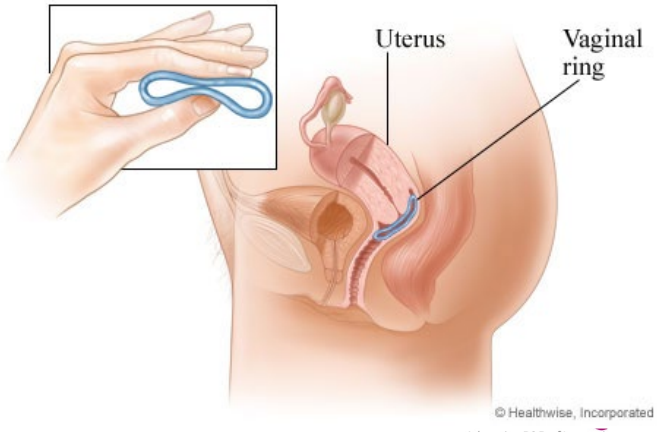
Presentation Outline

- Introduction
- Study sites
- Study team
- Study overview
- Progress
- Acknowledgements

Intravaginal Rings (IVR)

- IVRs are flexible torus-shaped, long-acting drug delivery systems (contraceptive rings e.g. NuvaRing)

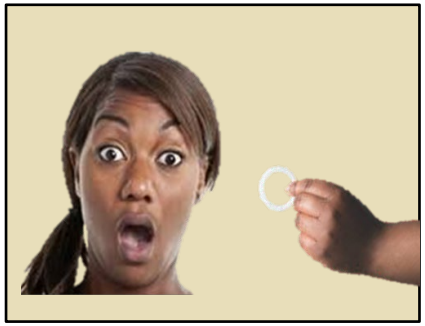
- They have the advantage of being:
  - female-controlled
  - not coitally dependent and not dependent on daily use
  - completely reversible and
  - easily inserted/removed without assistance

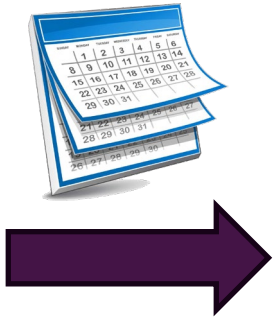


IVR for PrEP

- Vaginal ring as PrEP - Dapivirine vaginal ring (MTN-020, MTN-025, IPM027, IPM032)

Scary! (Initially)





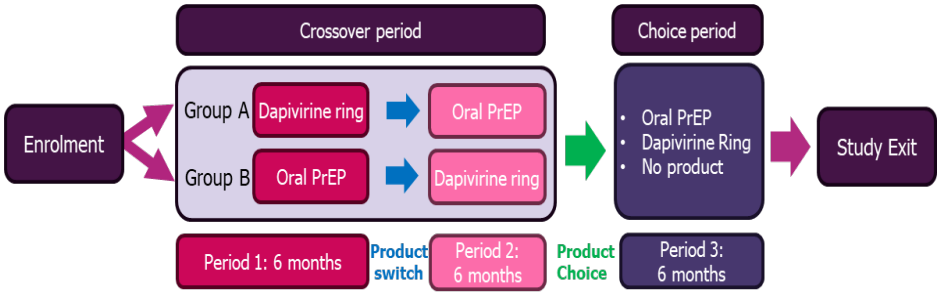
Discrete, easy to use and more comfortable

- Recommended by WHO as an additional HIV prevention option for women >18 years
- Approved for use/under regulatory review in multiple countries in SSA
- **Exciting new option for HIV prevention** allowing more choice for women

MATRIX

IVR for PrEP

- MTN-034/REACH (crossover trial of oral PrEP and Dapivirine vaginal ring among AGYW (aged 16-21)



- Ring was well-tolerated and highly acceptable
- Drug levels in crossover and choice periods showed partial to high adherence
- 67% chose the ring in the choice period

Rings are a viable, promising new prevention method for this key population

- Overall, ring users have expressed preferences for long-acting methods preventing both HIV and pregnancy, with few side effects, and the potential for use without partner knowledge

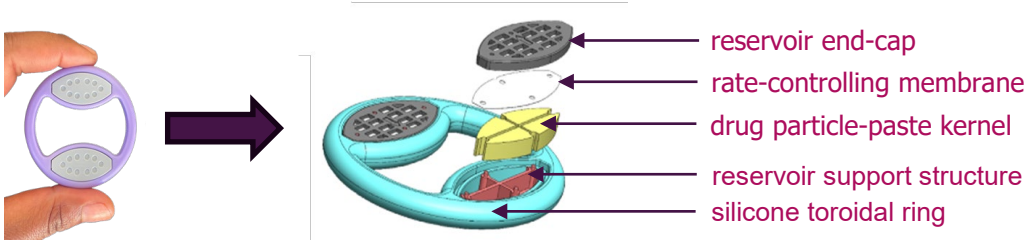
MATRIX

MATRIX-003

ONERING
Dual-Purpose Ring to Prevent HIV and Pregnancy

OAK CREST INSTITUTE OF SCIENCE

- **MATRIX-003** will gather acceptability, usability, and safety data of 2 placebo prototypes of a new type of ring (OCIS OneRing) which differ in firmness
- The rings' size is similar to that of approved devices and multiple clinical trials (like the dapivirine vaginal ring), but the design is different as it includes two cassettes (cartridges)



- Designed for simultaneous delivery of two medications (non-ARV antiviral and non-hormonal contraceptive) for HIV and pregnancy prevention
- Each participant will use each ring for ~28 days - allow assessment of ring use and preference for the different rings (without the impact of drug related side effects)

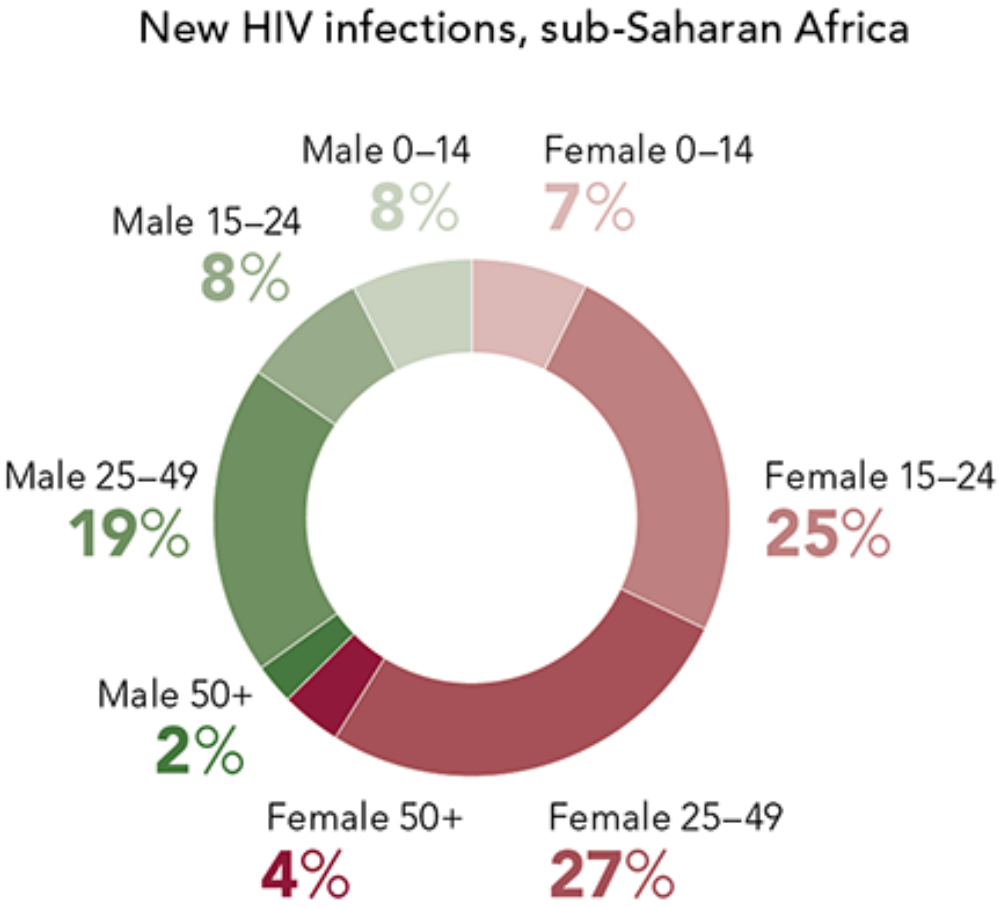
MATRIX-003

- This data collected in **MATRIX-003** will guide the final design of a dual-purpose vaginal ring that
  - Contains non-ARV and non-hormonal drugs that act locally – fewer side effects, less concern about viral resistance, rapid return to fertility
  - Could offer long-term protection from both pregnancy and HIV (30 days)
  - Women can use discretely and insert and remove themselves
  - Goal is low cost and easy to manufacture

MATRIX

MATRIX-003

- The dual-purpose aspect of this new ring could potentially drive uptake and adherence among women
- This is of particular importance among women and AGYW in SSA who remain at substantial risk of acquiring HIV



Source: UNAIDS epidemiological estimates, 2021 (https://aidsinfo.unaids.org/).
Note: Due to rounding, the percentages do not add up to 100%.

Study Sites

Pittsburgh
(United States)

Aurum-Tembisa
(Johannesburg)

HHRC
(Zimbabwe)

Wits RHI
(Johannesburg)

CAPRISA-Vulindlela
(Durban)

MATRIX

Study Team

Protocol Co-Chairs:

Kathryn T. Mngadi, MBChB, MSc Clin Trials, MPhil Pall Med, Dip HIV Man SA, Dip Epi
Aurum Tembisa Clinic 4 CRS

Surina Reddy, MMedSci
Wits RHI Research Centre CRS

CRS Investigators:

Pitt/MWRIF CRS - USA

Catherine Chappell, MD
Site IoR

Ingrid Macio, PA-C
Site Investigator

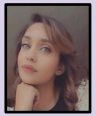
HHRC – Zengeza CRS - Zimbabwe

Nyaradzo M. Mgodi,
MBChB, MMed
Site IoR

Sheu Matimbira,
MBChB
Site Investigator

The Aurum Institute – Tembisa #4 CRS - SA

Kathryn T. Mngadi,
MBChB,
Site IoR



Sabiha Shaik,
MBBS,
Site IoR

Wits RHI Research Centre CRS - SA

Nkosiphile Ndlovu,
MBChB,
Site IoR

Thesla Palanee-Phillips,
PhD,
Site Investigator

CAPRISA – Vulindlela CRS - SA

Gabriella Benadé,
MBBCh, Site IoR

OCIS:

OAK CREST INSTITUTE OF SCIENCE

Marc M. Baum,
PhD,
OCIS PI

John A. Moss,
PhD,
OCIS PI

Peter A. Anton,
MD,
OCIS PI

Amy Adler,
RN, MSN, FNP,
OCIS Clinical Ops Manager

USAID:

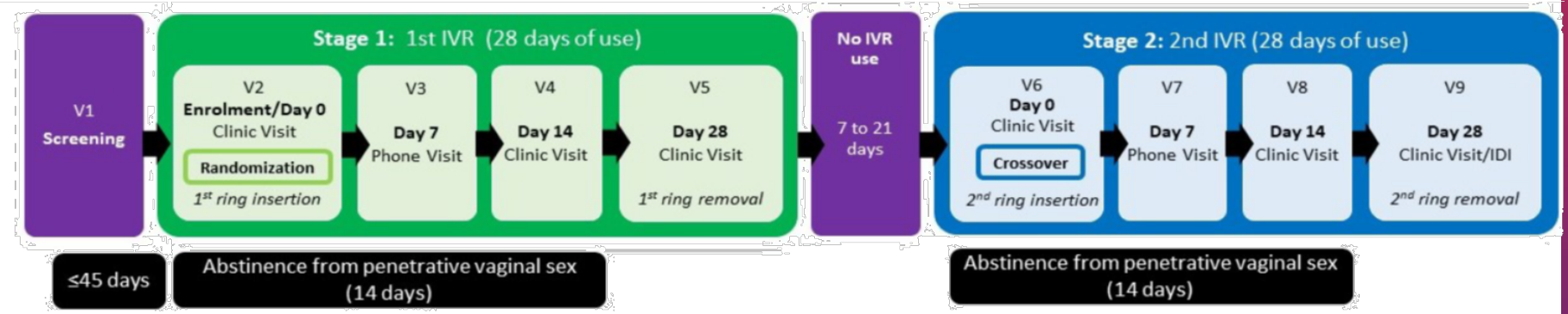
Mary Latka,
PhD, MPH,
Chief: Microbicides Branch

Shannon Allen,
PhD,
MATRIX
Agreement Officer

Chelsea Solmo,
MATRIX Senior,
Technical Advisor

Study Overview: Study Design

- Randomized, partially blinded, crossover trial with 2 arms, each assigned a different sequence of placebo IVR (A then B or B then A)
- The two IVRs differ slightly in flexibility or hardness
- Each participant will use each placebo IVR for ~28 days each, with 7-21 days between the two product use periods



Study Overview: Study Design

- **Population:** HIV-negative adult (18-45 years old) persons assigned female sex at birth, and selected sexual partners
- **Sample size:** ~100 participants across 5 study sites,
  up to 30 sexual partners for an IDI
- **Accrual period:** ~3-5 months.
- **Study duration:** Total study duration will be ~5-8 months
  Participants will complete ~9-11 weeks of follow-up

Study Overview: Objectives and Endpoints

Primary objective	Secondary objective	Exploratory objectives:			
Acceptability	**Safety**	**Participant acceptability, attitudes and experiences**	**Sexual partner attitudes & experiences**	**Vaginal microbiota**	**Social harms & benefits**
To compare the acceptability of two placebo IVR types *Preference for and satisfaction using each IVR*	To compare the safety of two placebo IVR types *Urogenital Grade 2 or higher AEs deemed related to each study product*	To explore dimensions of acceptability of two placebo IVRs and participants' attitudes towards and experiences with each IVR. *Responses to Qs and IDIs*	To explore sexual partners' attitudes towards and experiences with participants' IVR use. *Sexual partner responses during IDI*	To assess the impact of placebo IVR use on the vaginal microbiome *Change from baseline*	To describe reported experiences of social harms and social benefits over the course of IVR use. *Participant or sexual partner self-report*

Study Overview: Participant Inclusion Criteria

- Aged 18 to 45 years (inclusive) at Screening
- Assigned female sex at birth
- Able and willing to provide written informed consent and adequate contact information
- Able to abstain from other intravaginal products or practices for the duration of the study
- Able to abstain from penetrative vaginal intercourse for the first 14 days of each product use period
- Having reliable access to a private phone for scheduled phone contacts.
- HIV-uninfected and not pregnant or breastfeeding

Study Overview: Participant Inclusion Criteria

- Not having an STI (TV, GC, CT or Syphilis at Screening and (per participant report) not treated for potential STI within past 12 months
- Protected from pregnancy starting at least 2 weeks before Screening and continuing for the duration of study participation by an effective contraceptive method (except diaphragm, NuvaRing, or spermicide)
- Per participant report, is either
  - not currently sexually active or
  - in a mutually monogamous relationship with only one partner who is not known to be HIV positive or to currently have an STI

Study Overview: Participant Exclusion Criteria

- Coenrolment in other studies
- If the participant indicates intention to do any of the following during study participation:
  - Become pregnant or breastfeed
  - Relocate away from the study site
  - Travel away from the study site for a time period that would interfere with product resupply and/or study participation
- Diagnosed with UTI, PID or RTI requiring treatment*
- Has a Grade 2 or higher pelvic exam finding*
- Known adverse reaction to silicone (ever)
- Use of stimulants/illicit injection drug use in the past 12 months

MATRIX

Study Overview: Participant Exclusion Criteria

- Use of PEP or oral PrEP in the past 4 weeks or any prior use of long-acting systemic PrEP (including cabotegravir or islatravir)
- Use of antibiotic, steroid, or antifungal (oral or intravaginal) therapy in the past 14 days
- Having had a hysterectomy
- Having had a gynecologic or genital procedure within 21 days
- Has Grade 2 or higher Aspartate aminotransferase (AST), alanine transaminase (ALT), creatinine, or Hemoglobin lab results
- Investigator/designee discretion

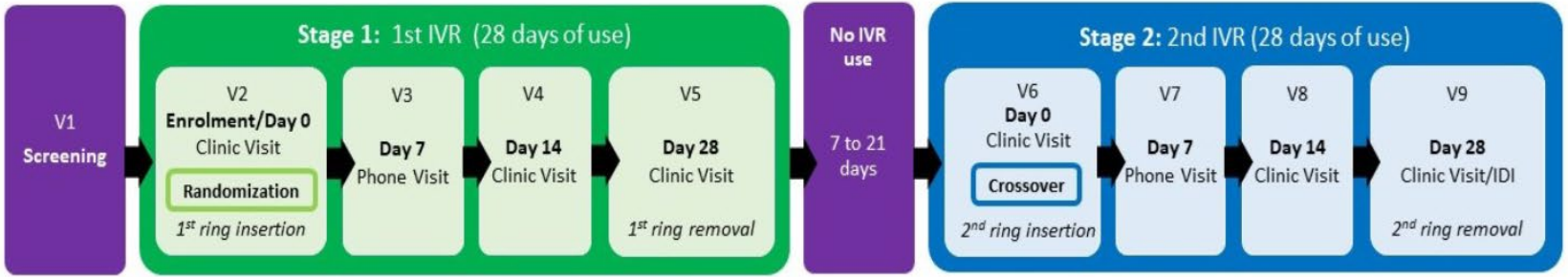
Study Overview: Partner Inclusion Criteria

- Identifies as a sexual partner of a MATRIX-003 participant
- Identified by participant as a sexual partner during MATRIX-003 and for whom the participant has given permission to contact
- Able and willing to provide written informed consent
- Able and willing to complete the required study procedures.
- Must be 18 years old or above at the time of their study participation

MATRIX

Study Visits

- Participants will have 7 clinic visits and 2 telephonic contacts over 9 weeks



- Procedures will include:
  - HIV pre and post-test counselling,
  - Collection/review of medical/ menstrual history, con meds and AEs
  - Physical, pelvic and/or digital exams

- Specimen collection will include:
  - Saliva (HIV test) – at sites with certification
  - Blood (HIV, Syphilis, safety tests, storage)
  - Urine (pregnancy, dipstick testing)
  - Pelvic swabs (Chlamydia, Gonorrhoea, Trichomonas, Wet mount, Gram Stain, microbiota, pap smear tests, storage)

MATRIX

Study Visits

- Questionnaire completion about
  - general health and medications
  - what they think about the product
  - whether they are having any problems with or after insertion
  - whether they can feel the ring

- IVR insertion
  - The IVR will be inserted by participants at the clinic with clinical staff guidance and instructions - If they fail after 2 attempts clinical staff will assist
  - Post insertion clinical staff will check to ensure placement is correct
  - Participant will be asked to walk and squat to ensure there is no discomfort

- IVR removal
  - Participants will be asked to self-remove IVRs at the clinic - If they fail after 2 attempts clinical staff will assist

MATRIX

Progress

- Selected protocol team and co-chairs
- Finalised trial sites
- Completed protocol development
- Finalised product development (OCIS)
- Drafted product insertion instructions with images (D2D)
- Initiated Study Procedure manual and CRF development (OCIS)
- Collected site documents for SAHPRA submission – in progress
- Preparing for IRB submissions (sites) - progress

MATRIX

Acknowledgements

MATRIX
Advancing R&D of Innovative HIV Prevention Products for Women

This program was made possible by the generous support of the American people through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID).

The contents in this presentation are those of the presenter and do not necessarily reflect the view of the U.S. President's Emergency Plan for AIDS Relief, the U.S. Agency for International Development or the U.S. Government.