

PrEP'ING TO PROVIDE PrEP TO PREGNANT WOMEN IN SOUTH AFRICA: WHAT DO WE KNOW AND WHAT WILL WE LEARN?

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Background around HIV risk in pregnancy and postpartum periods & PrEP use in pregnancy



Formative research studies and mathematical modelling



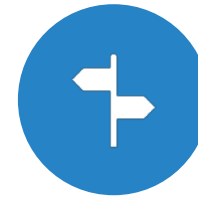
Introduction to our study: PrEP in pregnancy and postpartum period in Cape Town (PrEP-PP)



Study aims and conceptual model



Expected results

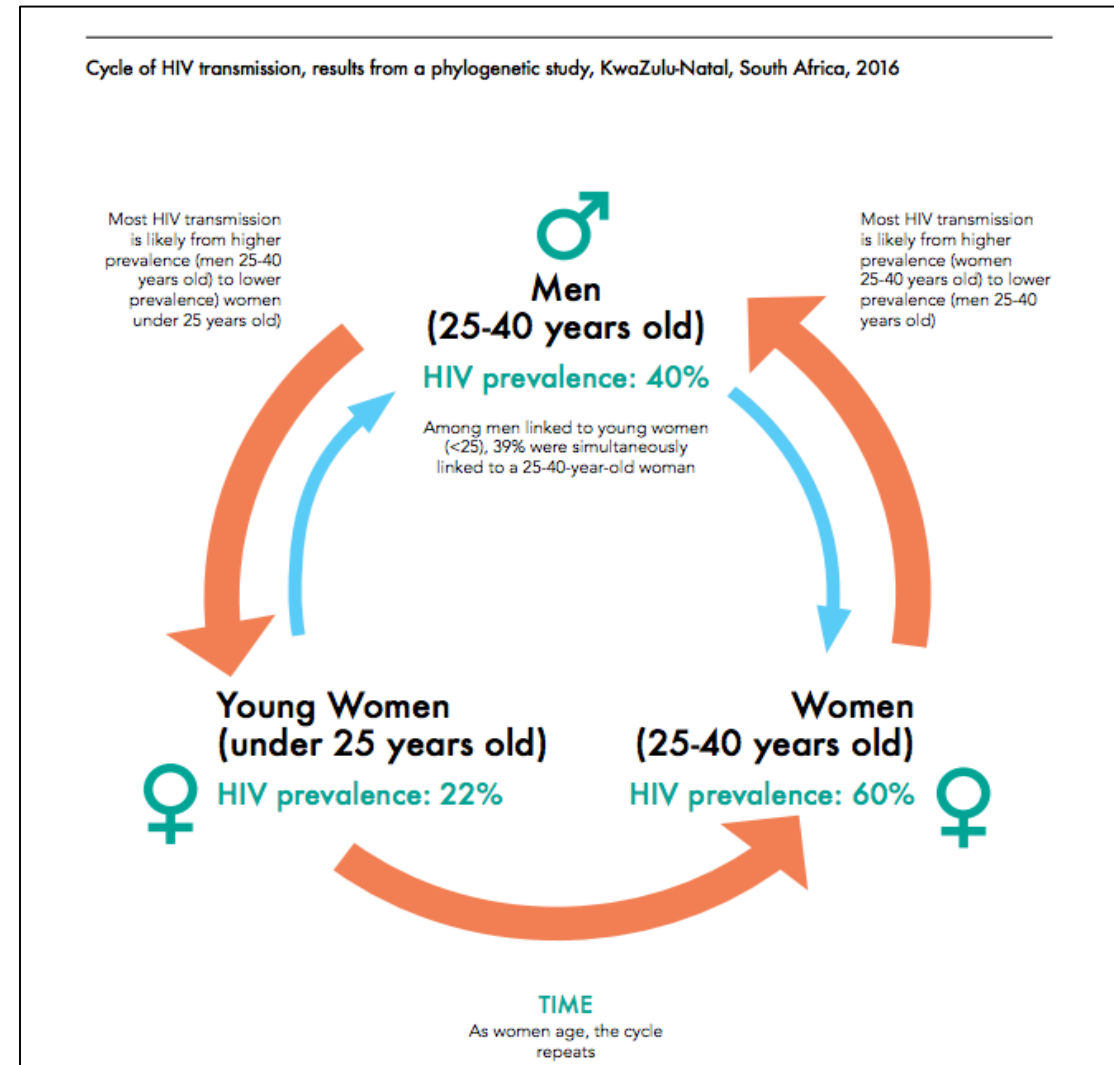


Future direction

OUTLINE

BACKGROUND: HIV & WOMEN

- Women account for more than half of the number of people living with HIV worldwide
- Young women (10-24) are twice as likely to acquire HIV than men their age
- HIV is the leading cause of death of women of reproductive age (15-44)
- In 2016, new infections among young women aged 15-24 were 44% higher than men their age
- In eastern and southern Africa, young women make up 26% of new HIV infections but only 10% of the population



•UNAIDS (2017) [Ending AIDS: Progress towards the 90-90-90 targets](#)

•UNAIDS (2017) ['When women lead change happens: Women advancing the end of AIDS'](#)

•Dellar, R.C. et al (2015) ['Adolescent girls and young women: key populations for HIV epidemic control'](#) JIAS 18

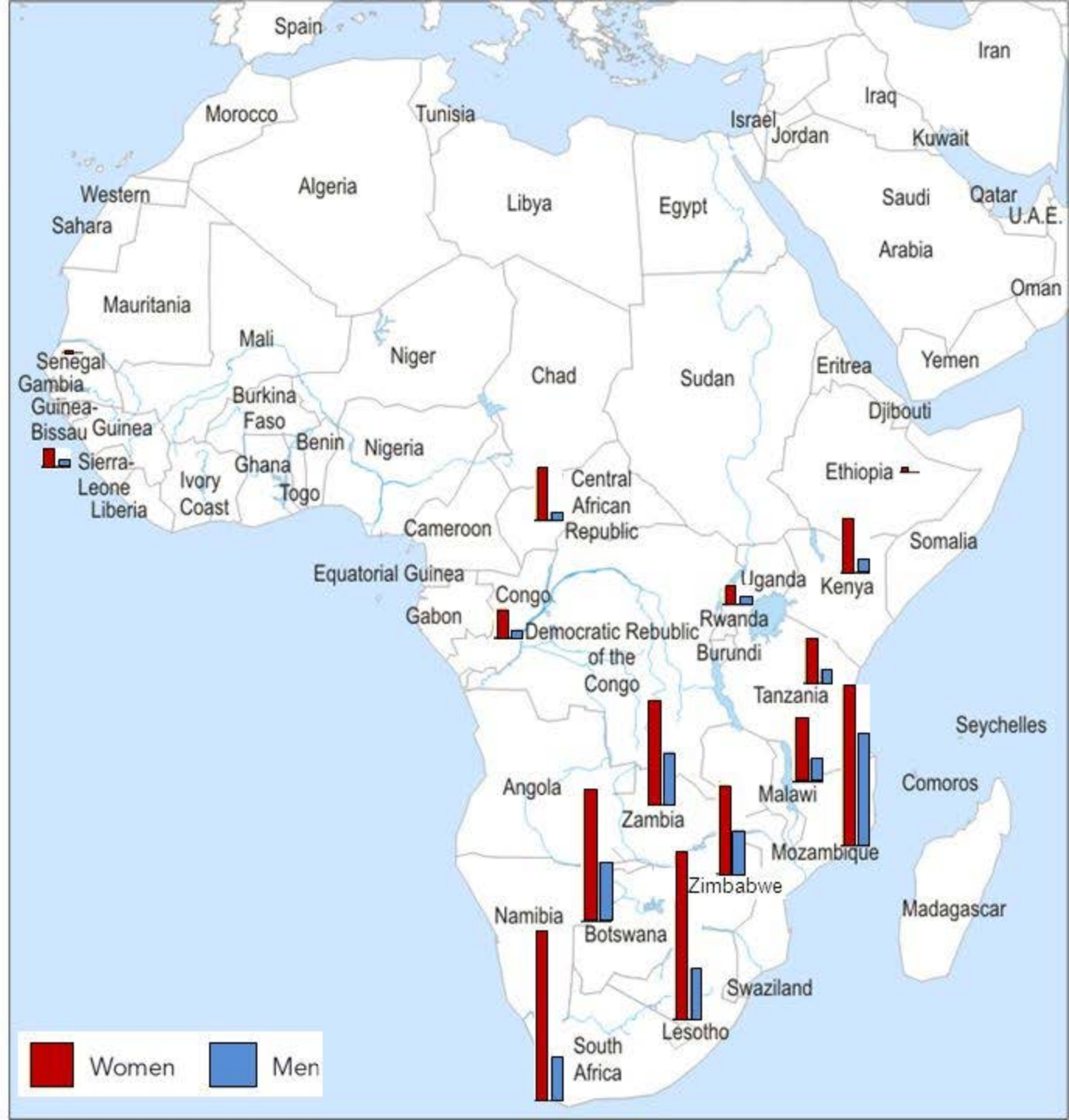
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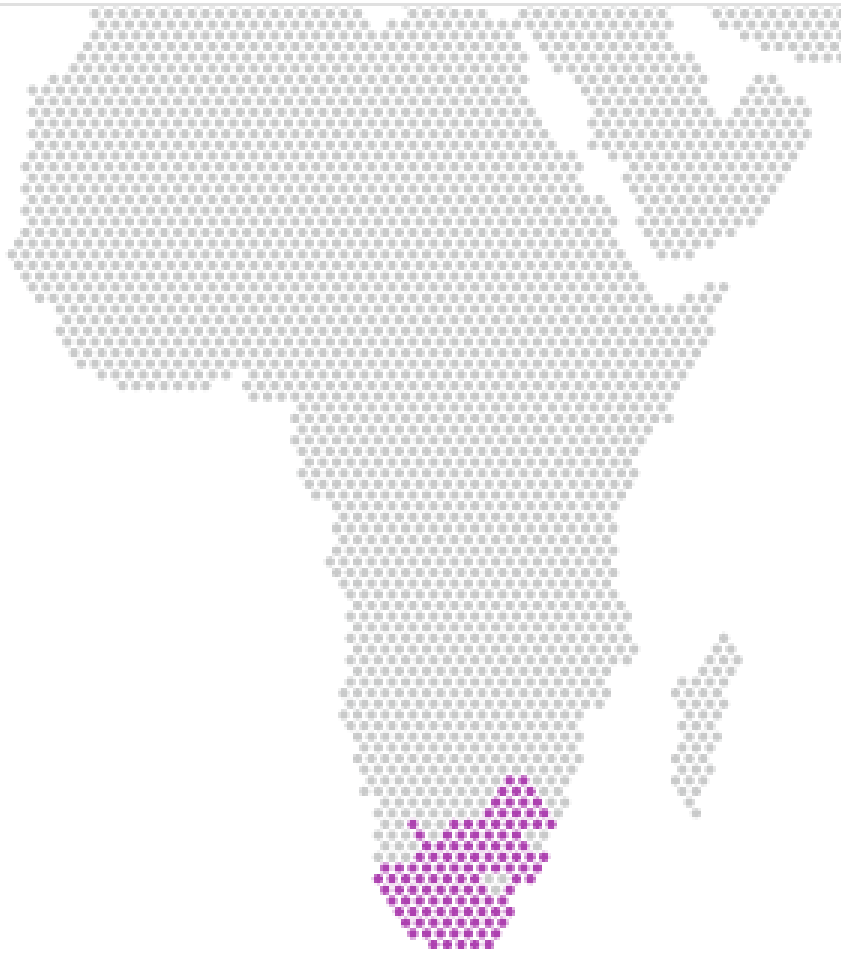
T de Oliveira et al, Lancet HIV, 2017

High burden of HIV in young women in Africa:

HIV in 15–24 year men and women (2008–2011)

Young women have up to 8 times more HIV than men





South Africa (2017)

7.2m people living with HIV

18.8% adult HIV prevalence (ages 15-49)

270,000 new HIV infections

110,000 AIDS-related deaths

61% adults on antiretroviral treatment*

58% children on antiretroviral treatment*

*All adults/children living with HIV

Source: UNAIDS Data 2018

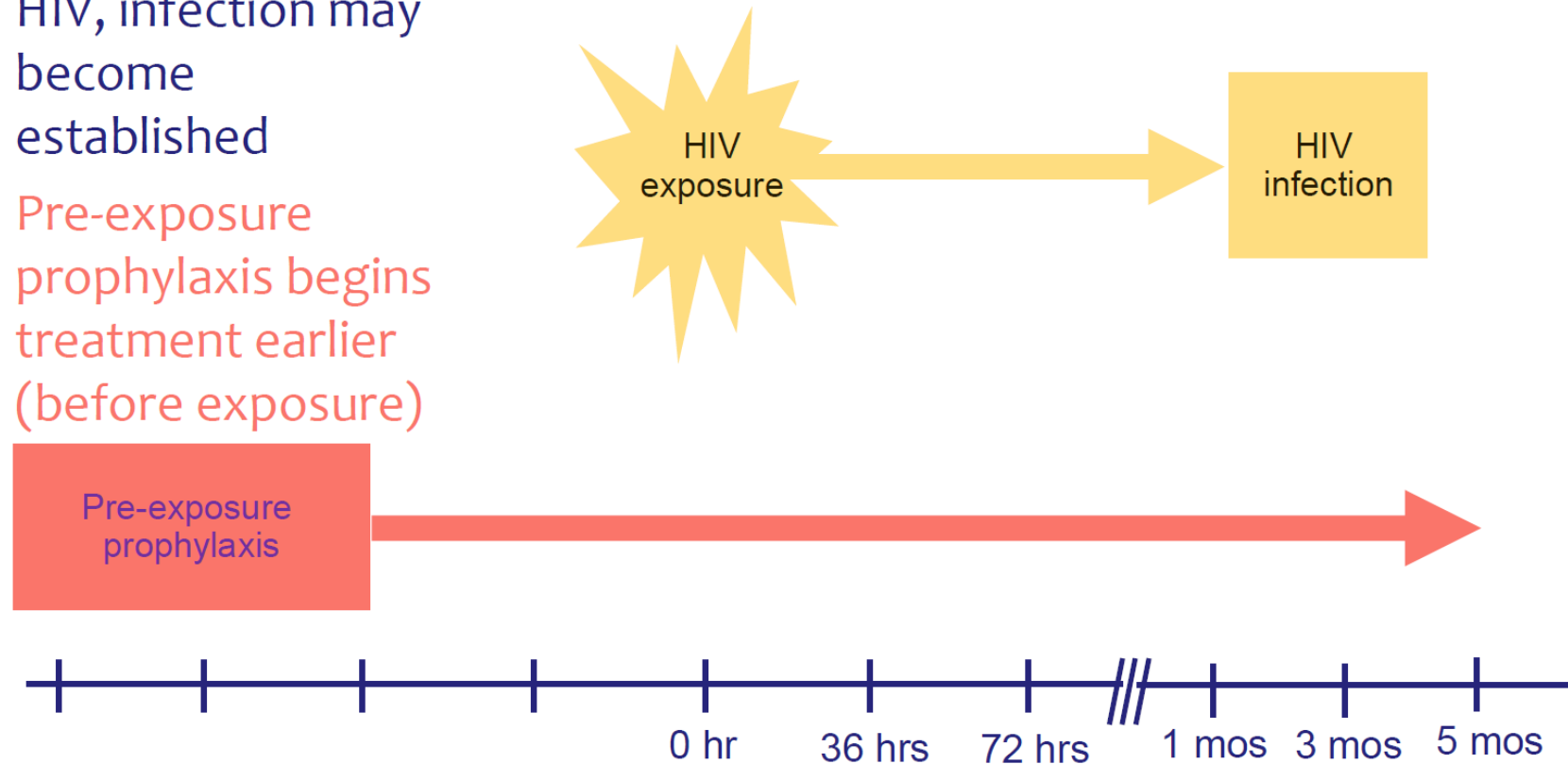
HIV RISK IN PREGNANCY

- Much has been done to reduce mother-to-child transmission (MTCT) of HIV, but more needs to be done to *eliminate* MTCT
- **HIV incidence continues to be very high during and after pregnancy**
 - In South Africa it is estimated that maternal HIV incidence was 3.3 per 100 woman-years [1, 2]
 - Mothers who seroconvert after their first antenatal visit account for approximately 34% of vertical transmission [2]
- Increased biological susceptibility and behavioral factors increase HIV risk [3]
- In a recent meta-analysis, **odds of MTCT was higher in women with incident vs. chronic HIV infection** in the postpartum period (OR=2.9, 95% CI=2.2, 3.9) or in pregnancy and postpartum periods combined (OR=2.3, 95% CI=1.2, 4.4) [4].



How does PrEP prevent HIV infection?

- After exposure to HIV, infection may become established
- Pre-exposure prophylaxis begins treatment earlier (before exposure)



WHO RECOMMENDATIONS FOR PREP USE DURING PREGNANCY AND BREASTFEEDING (2018)

- Oral PrEP should be offered to all people at substantial risk of HIV infection ($>3\%$ HIV incidence), including pregnant breastfeeding women
- The choice to start, continue or discontinue PrEP when a woman is pregnant should be made by the woman, following discussion of the risks and benefits with her healthcare provider
- No safety-related rationale for disallowing PrEP use during pregnancy or breastfeeding

IS PrEP USE SAFE IN PREGNANCY AND BREASTFEEDING?

- TDF-containing ART recommended by WHO as a 1st-line PMTCT regimen for pregnant HIV-infected women
- 26 studies in HIV-infected and 7 in HIV-uninfected women **found no difference between mothers with and without prenatal TDF use in:**
 - Pregnancy incidence
 - Stillbirth/pregnancy loss
 - Preterm delivery <37 weeks
 - Low birth weight <2500g
 - Small for gestational age
 - Birth defects

Why should pregnant and breastfeeding be offered PrEP?

- During pregnancy, biological factors increase susceptibility, and social and behavioral factors can **increase exposure to HIV infection**



Increased Biological Susceptibility

- Elevated hormone levels related to cervical inflammation
- Untreated STIs associated with cervical inflammation
- Changes in the vaginal microbiome associated with genital inflammation
- Nutritional deficiency and lowered immunity



Increased Behavioral Exposure

- Behavior changes in women and male partners during the pregnancy/ postpartum period
- Less condom use, intimate partner violence

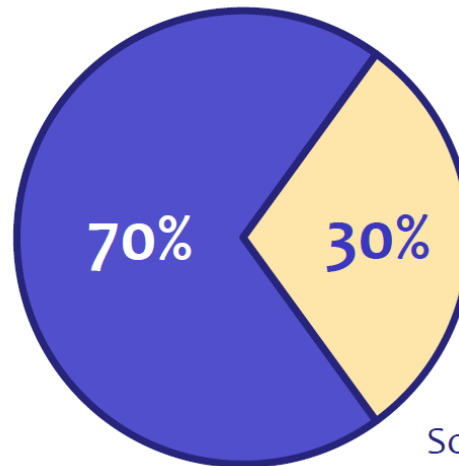
Source: WHO TECHNICAL BRIEF: Preventing HIV during pregnancy and breastfeeding in the context of PrEP

Why should pregnant and breastfeeding be offered PrEP?

- Pregnant and breastfeeding women who acquire HIV at this time have a **greater risk of transmitting HIV to their infant**

Contribution of maternal HIV infections to mother-to-child transmission of HIV

Chronic HIV
(infected with prior HIV to pregnancy/breastfeeding)



Acute HIV
(infected with HIV during pregnancy/breastfeeding)

Source: WHO TECHNICAL BRIEF: Preventing HIV during pregnancy and breastfeeding in the context of PrEP; Dinh et al 2015; Johnson et al 2012

YOU ARE EITHER AFFECTED
OR
INFECTED WITH HIV/AIDS:

**FORMATIVE RESEARCH AND MODELLING
THE IMPACT OF PREP ON HIV PREVENTION**

STUDY 1: SEX IN PREGNANCY AND POSTPARTUM PERIOD (SEX-PP)

- Cross-sectional study among HIV-uninfected (HIV-) and HIV-infected (HIV+) pregnant and postpartum women in an informal settlement in Cape Town
 - N= 377 women (56% pregnant; 44% post-partum; 60% HIV-)
 - Mean age= 28-years
 - 43% were in a relationship with the father of the index pregnancy
- We collected survey data to evaluate factors for HIV acquisition and transmission in pregnant & postpartum women
- We reported descriptive and multivariable logistic regression results for factors associated with risky sex during and after pregnancy stratified by serostatus



RISK FACTORS FOR HIV ACQUISITION IN PREGNANCY AND IMPLICATIONS FOR ONGOING RESEARCH

Table 1: Results from a study on sexual behavior and PrEP awareness in Gugulethu (n=363 pregnant or postpartum women) [74]

	Pregnant women	Postpartum women
Father of baby is casual partner or no relationship	10%	13%
Don't know HIV status of partner	45%	31%
Heavy drinking (>6 drinks on >1 occasion)	12%	8%
>1 sex partner	16%	15%

Implications for future research:

- 10-13% of women were **not in a relationship**
 - **Couples counseling & testing** challenging if pregnant women are not in a relationship/ don't live with the father of their child
- Almost half of pregnant women **did not know if they were in a serodiscordant relationship**
 - Couples HIV testing is not readily available and should be integrated into intervention
- High proportion of women had **>1 partner** during pregnancy
 - Need to involve all sex partners in HIV prevention in pregnancy (not just primary partner)
- **Alcohol use during pregnancy** was reported by 12% of pregnant women (27% in HIV-negative women), of whom 57% reported drinking 5+ drinks on >1 occasion

SEX-PP RESULTS 2: CONDOMLESS SEX WAS FREQUENT IN PREGNANCY

- 98% of women reported sex during pregnancy (10% reported anal sex), but less than 1/3 reported consistent condom use
- HIV-negative pregnant and postpartum women (vs. HIV+ pregnant/postpartum women) **had:**
- increased odds of condomless sex during pregnancy** ($\alpha\text{OR}=3.24$, 95% CI=2.03, 5.17) and
- decreased odds of knowing their partner's serostatus** ($\alpha\text{OR}=0.27$, 95% CI=0.09, 0.34) adjusting for age and alcohol use.

RESEARCH ARTICLE

Sexual risk during pregnancy and postpartum periods among HIV-infected and -uninfected South African women: Implications for primary and secondary HIV prevention interventions



ORIGINAL STUDY

Sexual Behaviors of Human Immunodeficiency Virus-Infected Pregnant Women and Factors Associated With Sexually Transmitted Infection in South Africa

Dvora Joseph Davey, PhD,*†‡ Remco P.H. Peters, MD,§¶|| Noah Kojima, BA,† Maanda Mudau, MPH,** Lindsey De Vos, BA,** Dawie Olivier, MPH,** James A. McIntyre, MD,*§ Jeffrey D. Klausner, MD,†‡ and Andrew Medina-Marino, PhD**

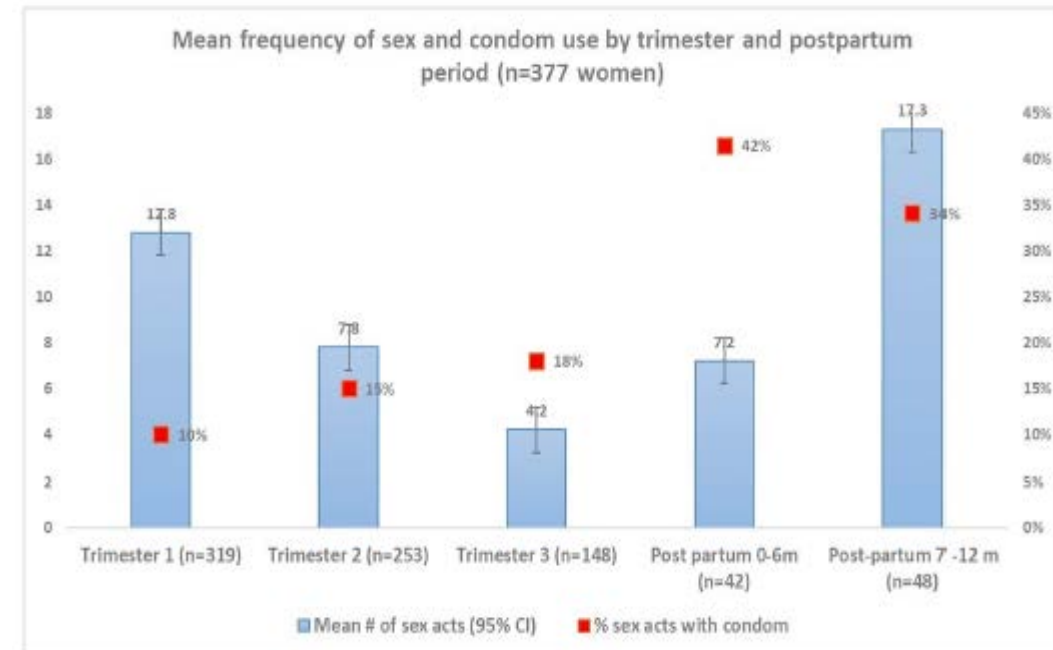


Fig 1. Mean frequency of vaginal sex acts per month by pregnancy vs. postpartum status and self-reported condom use (n = 377 women).

Frequency of reported sex varied significantly across pregnancy trimester and between pregnancy and postpartum periods, with greatest mean sex acts in the first trimester of pregnancy and >6 months postpartum.

SEX-PP RESULTS 3: KNOWLEDGE AND ATTITUDES ABOUT PrEP IN PREGNANT WOMEN

- Our recent study of pregnant and postpartum women found that 33% had previously heard of PrEP, most from their clinic
- Older women, women reporting >1 sex partner in the past year and unintended pregnancy were associated with PrEP knowledge
- Results from in-depth interviews showed that most mothers reported hypothetical willingness to use PrEP because of concerns over HIV acquisition and onward MTCT
- While mothers presented a clear desire to protect themselves from HIV once pregnant, they also reported:
 - Lack of control over sex and condom use
 - Socio-cultural beliefs that could be barriers to HIV prevention uptake, like “condomless sex is good for the baby”

QUALITATIVE RESEARCH ABOUT PrEP IN PREGNANT WOMEN

RESEARCH ARTICLE

Risk perception and sex behaviour in pregnancy and breastfeeding in high HIV prevalence settings: Programmatic implications for PrEP delivery

Dvora Joseph Davey^{1,2,3}*, Elise Farley¹, Catriona Towriss¹, Yolanda Gomba¹, Linda-Gail Bekker¹, Pamina Gorbach², Steven Shoptaw², Thomas Coates², Landon Myer¹

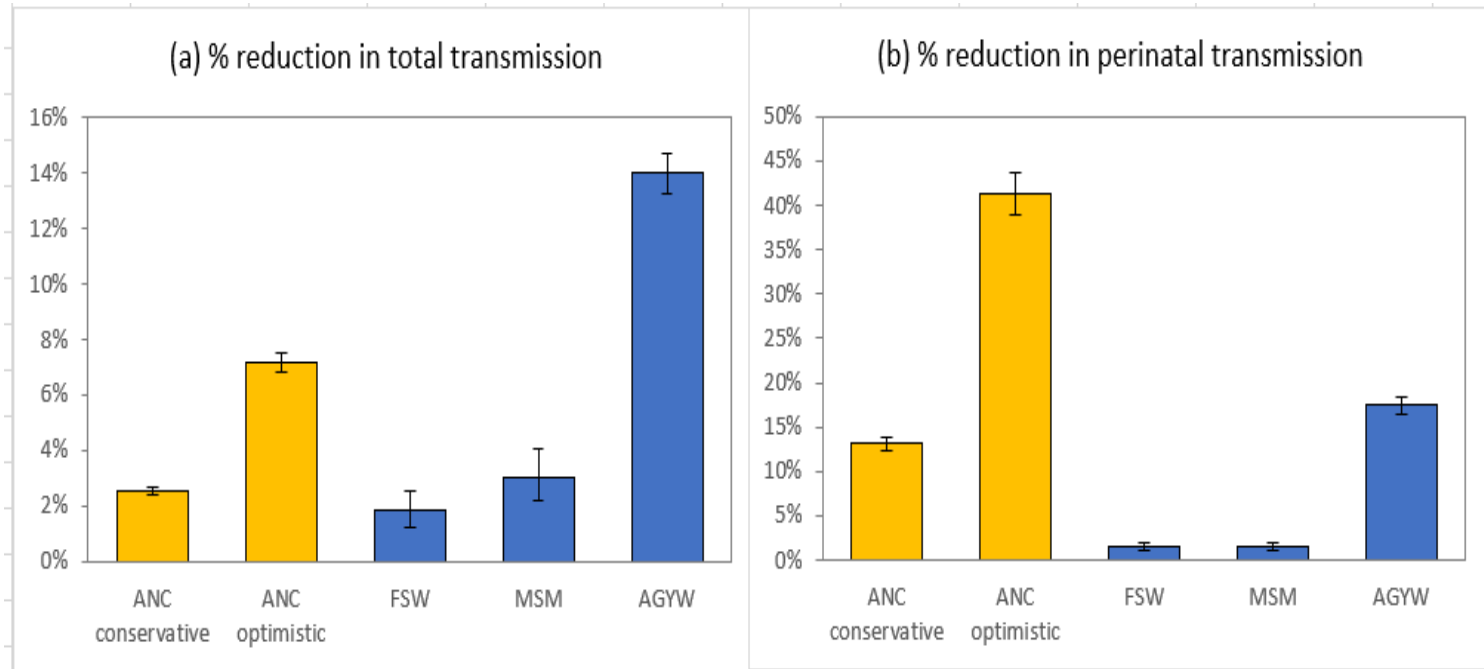
Some barriers and facilitators to potential PrEP uptake in pregnant women that we will address in our study:

It's a new drug and I don't know what it will do. You know how sensitive babies are.	Pregnant, 20 yrs
It's suitable because we know HIV is a lot here in South Africa. We should prepare ourselves. We don't know what men will do the next day. I would say we will just have to take up this opportunity because it might change your whole life. I would advise that all the women in South Africa should use it (PrEP).	Pregnant, 20 yrs
I would not be sure how it would affect the baby. . . because its pills. I think it's those with multiple partners (should take PrEP). Yes I would use it because they say a pregnant woman get infected easily. Even when breastfeeding, it would act as extra protection. They say breast milk has vitamins and nutrients for the baby so it would do the extra job on the side.	Pregnant, 32 yrs
I am not a pill person. Pills make me sick, especially you say it has side effects. But I would like to use it because I don't think there is a person who does not want to protect themselves from HIV. I would be afraid of one thing. Maybe. . . I don't know how ARVs look like. . . if I use it someone will think it's ARVs	Pregnant, 22 yrs

STUDY 2: EVALUATION OF POTENTIAL IMPACT OF PrEP IN PREGNANCY

- To estimate the potential impact of introducing PrEP for pregnant and breastfeeding women, we used the Thembisa model, a demographic and HIV model for South Africa using two scenarios:
 1. **Conservative scenario:** we set the model assumptions to match the experience reported in the Kenyan PrEP programme for pregnant women (estimated probability of PrEP uptake=32% and 11% in high-risk and low-risk women respectively)
 2. **Optimistic scenario:** PrEP is assumed to be initiated by 80% of all pregnant women (both high-risk and low-risk).
- In both scenarios, women are assumed to remain on PrEP for an average duration of 2-years (covering pregnancy and breastfeeding).
- Scenarios are compared in terms of reduction in total HIV incidence and reduction in perinatal HIV transmission

EXPECTED REDUCTIONS IN HIV INCIDENCE DUE TO PrEP, 2020-2030, UNDER DIFFERENT ENHANCED PrEP PROMOTION SCENARIOS



Our model demonstrates important infections averted in South Africa including:

- 2.5% (95% CI: 2.4-2.6%) in the conservative scenario

- 7.2% (95% CI: 6.8-7.5%) in the optimistic scenario between 2020-30 (**Figure 1a**).

In the absence of policy change around PrEP, **76,000 new cases of mother-to-child transmission** are expected to occur

With PrEP provision to pregnancy and breastfeeding women MTCT is expected to be reduced by:

- 13.2% (95% CI: 12.5-14.0%) in the conservative scenario

- 41.4% (95% CI: 39.1-43.8%) in the optimistic scenario (**Figure 1b**).

STUDY 3: EVALUATION OF PREGNANCY SYMPTOMS AND ART SIDE EFFECTS IN PREGNANT WOMEN ON ART: **METHODS** (D. DITULLIO- UCLA MED STUDENT)

Objectives: evaluate the ART-symptoms and attribution in HIV-positive pregnant/recently pregnant women on ART

- ART was used as a proxy for PrEP in HIV-negative pregnant women to inform design of future PrEP studies in pregnant women

Population: Sub-study that enrolled n=31 pregnant HIV-positive women on ART enrolled in another study evaluating STIs in pregnancy at a public Midwife Obstetrics Unit in Cape Town, South Africa

- Group A: began ART during current pregnancy (n=11)
- Group B: began ART prior to current pregnancy (n=20)

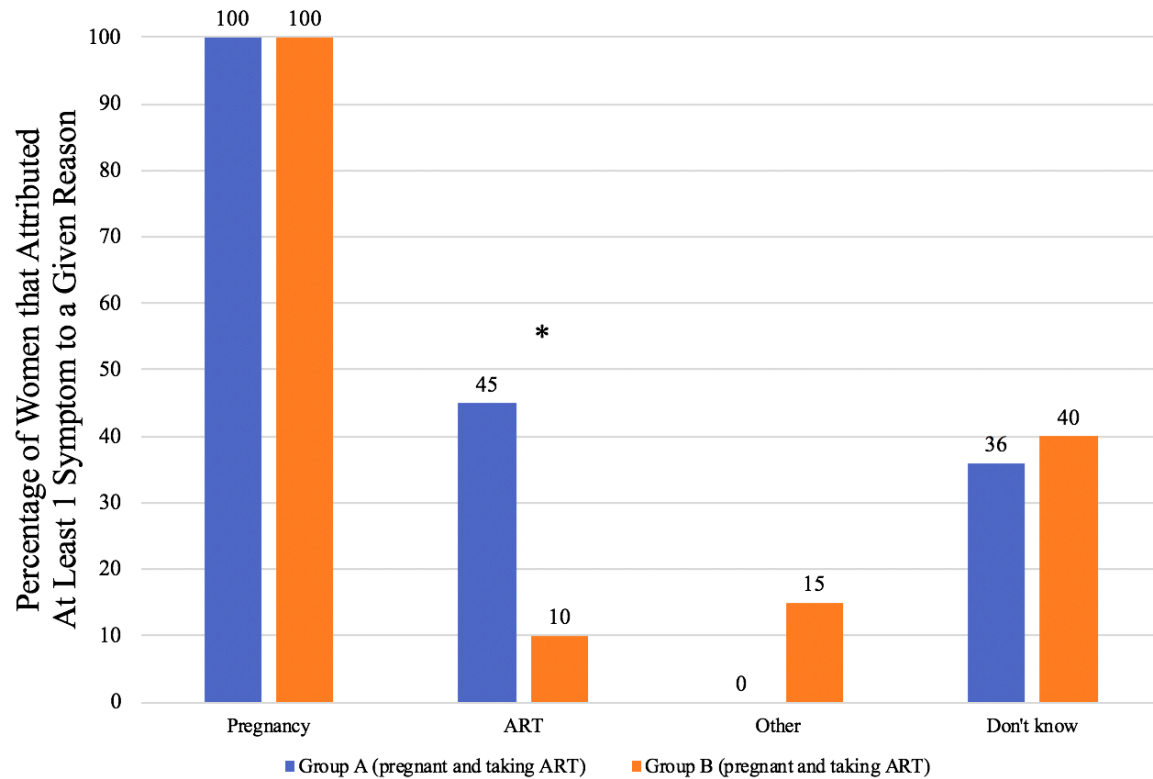
Metric	Group A	Group B
Average amount of time on ART (weeks)	6.63	265.3
Average gravidity	1.67 (n=9)	2.16 (n=19)
Average gestational age (weeks)	19.56 (n=10)	23.39 (n=18)

Mixed methods survey administered by the study counselor in isiXhosa during the participants' other study visits over the course of 4 weeks

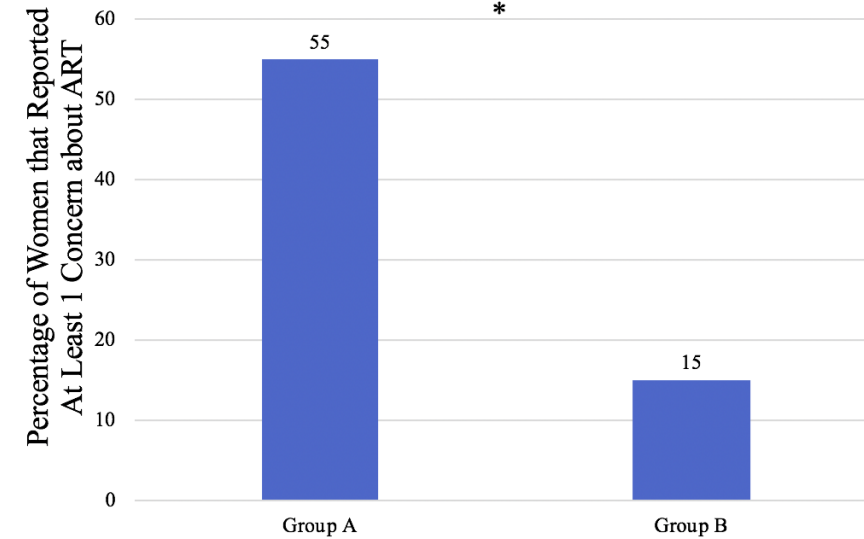
- Assessed the presence and attribution of the following symptoms: nausea, vomiting, stomach pain, diarrhea, headache, dizziness, changes in mood, joint pain, loss of appetite, strange dreams, difficulty sleeping, fatigue, other

EVALUATION OF PREGNANCY SYMPTOMS AND ART SIDE EFFECTS IN PREGNANT WOMEN ON ART: KEY FINDINGS

Comparison of Symptom Attribution by Group



Comparison of Frequency of Concerns about ART



Group A - started ART during pregnancy
Group B - started ART prior to pregnancy

* p<0.05

Women who initiated ART during their current pregnancy were more likely to attribute symptoms experienced to ART and express concerns about ART compared to women who initiated ART prior to their current pregnancy.

Concern	Percentage of women in Group A	Percentage of women in Group B
Side effects	27%	5%
Amount of medical visits*	36%	0%
Taking medication every day	27%	10%
Effects on unborn baby*	45%	10%
Effects on born baby*	36%	5%
Disclosure of HIV status	27%	5%

EVALUATION OF PREGNANCY SYMPTOMS AND ART SIDE EFFECTS IN PREGNANT WOMEN ON ART: **IMPLICATIONS AND FUTURE DIRECTIONS**

- Potential for **mis-attribution of pregnancy symptoms to symptoms of ART** in HIV-positive, which may be even the same or more pronounced in HIV-negative women taking PrEP.
- This finding, along with the greater number of concerns reported by those who started ART during pregnancy, highlights the **importance of adequate counseling about PrEP and ART initiation during pregnancy (and mostly short-term side effects)** to allow for proper management of expectations and to potentially improve adherence.
- In our next study we will provide targeted counseling about mostly transient side effects and evaluate side effects (and potential impact on adherence) in a cohort of pregnant women
- Our study will help determine the optimal way to inform patients about PrEP risks and benefits and address concerns about side effects that may contribute to poor adherence.

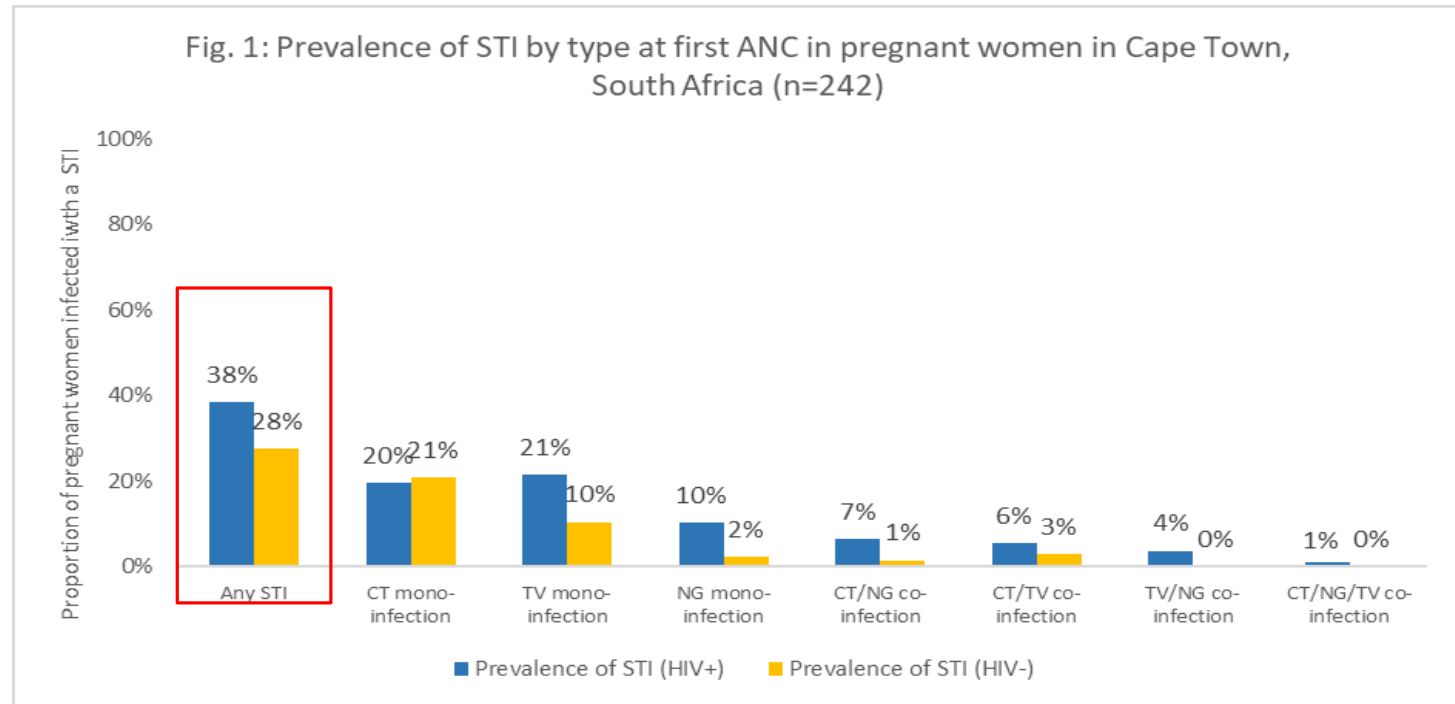
STUDY 4: SEXUALLY TRANSMITTED INFECTIONS IN PREGNANT WOMEN (STIP) — *STUDY ONGOING (D. SHABSOVITCH & D. DITULLIO- UCLA MEDICAL STUDENTS)*

Cohort study of 242 pregnant women to evaluate prevalence, incidence of treatable STIs and correlates of having a STI at 3 time points (1st antenatal visit, 3rd trimester, & 1 week postpartum)

At baseline:

- 44% of women were HIV-infected
 - 33% started ART at their first ANC visit.
- 47% of women were married/cohabiting.
- Almost all women reported vaginal sex during pregnancy (93%)
- Prevalence of any STI was 32
- STI-related symptoms in women diagnosed were reported infrequently

D Joseph Davey, et al. STD, Under Review



In a multivariable logistic regression model **being unmarried or not cohabiting** with the father of the child (aOR=2.00, 95% CI= 1.06, 3.76), **being HIV-positive** (aOR=1.93, 95% CI=1.03, 3.61), and **having recent symptoms of STIs** (aOR=6.86, 95% CI=2.16, 21.8) were associated with being diagnosed with a STI, adjusting for maternal age and gestational age.

OTHER ONGOING OR PLANNED STUDIES OF PREP IN PREGNANCY



Daya Moodley, CAPRISA
(ClinicalTrials.gov Identifier:
NCT03227731)

Clinical trial randomizing PrEP to pregnant women to evaluate renal function, pregnancy outcomes, bone health and infant growth in n=842 women in Durban, SA



Lynn Matthews, Harvard
(ClinicalTrials.gov Identifier:
NCT03194308)

Evaluating safer conception interventions (which may include PrEP in a small sub-set) in peri-conception in Durban, SA



Ben Chi, UNC (Impaact 2009)

Pharmacokinetics (PK), Feasibility, Acceptability, and Safety of PrEP for Primary HIV Prevention during Pregnancy and Breast Feeding in Adolescents and Young Women

- RCT recruiting 300 women in 4 countries (South Africa, Zimbabwe, Malawi, Uganda) followed until 6 months
- PK component in 40 women in 2 groups (ANC vs PNC)

Following our formative research, our team's focus has been on on **PrEP Implementation Science** – how best to evaluate PrEP delivery in real-world settings to inform policy and bring PrEP to those who need it – quickly.

OPINION

Delivering preexposure prophylaxis to pregnant and breastfeeding women in Sub-Saharan Africa: the implementation science frontier

**Dvora L. Joseph Davey^{a,b,c,d}, Linda-Gail Bekker^e, Pamina M. Gorbach^b,
Thomas J. Coates^c and Landon Myer^{a,d}**

AIDS 2017, 31:000–000

Keywords: breastfeeding, HIV prevention, pregnant, preexposure prophylaxis,
Sub-Saharan Africa

PREP-PP IS A NEW ROI FUNDED BY NIMH (OCT 18-2023)

Study team:

Co-Principal investigators:

Dr. Thomas Coates, UCLA

Dr. Landon Myer, University of Cape Town (UCT)

Co-investigators:

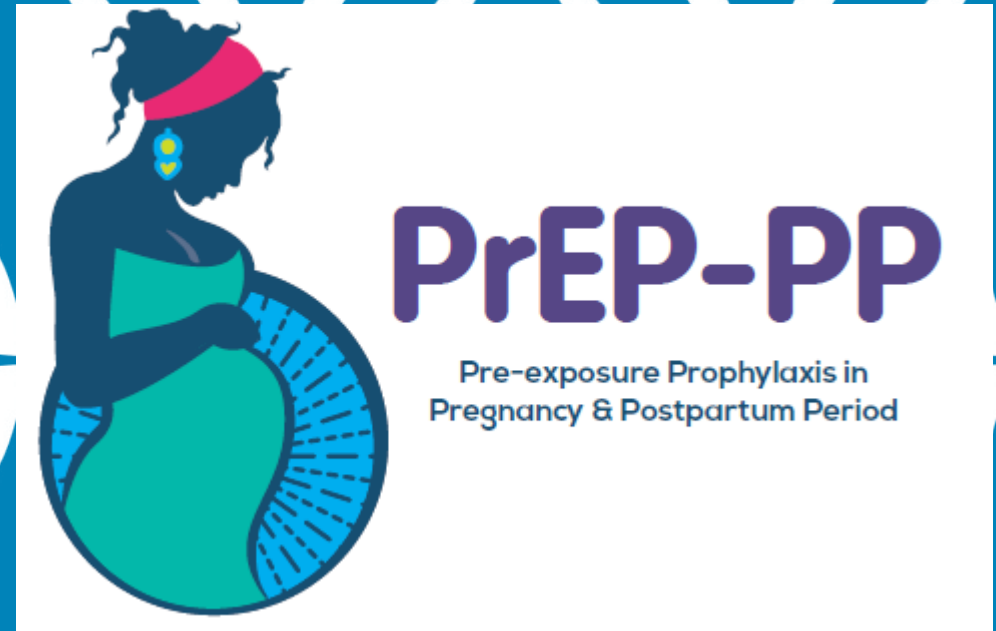
Dr. Dvora Joseph Davey, UCLA & UCT (Epidemiologist)

Dr. Pamina Gorbach, UCLA (Behavioral epidemiologist)

Dr. Linda-Gail Bekker, UCT (PrEP expert & Clinician)

Dr. Leigh Johnson, UCT (Mathematical modeler)

Dr. Maia Lesosky, UCT (Statistician)

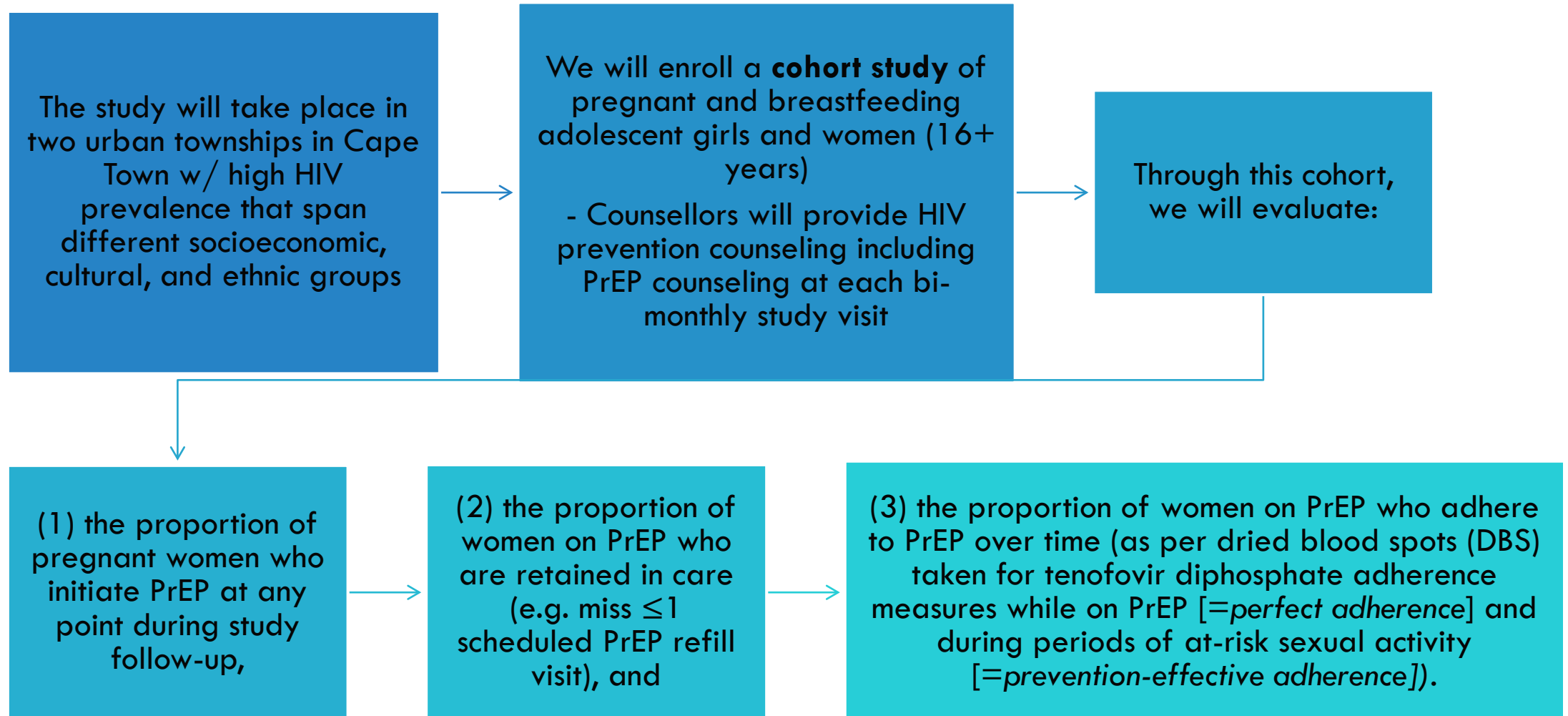


BACKGROUND

- HIV incidence in pregnant/breastfeeding women very high
- PrEP in pregnancy and breastfeeding women is limited to small pilot projects in Kenya and 2 ongoing clinical trials
- Our team has received a new R01 from NIMH for 5 year study to evaluate PrEP uptake, adherence in pregnant and breastfeeding women in Cape Town
- I received a K01 from the Fogarty International Research Science Development Award for formative work in the cohort
- Current PrEP policy in South Africa is limited to sex workers, men who have sex with men and adolescent girls and young women
 - We received support from the Deputy Director-General for Health in South Africa, demonstrating strong government interest in evaluating potential for PrEP in pregnancy



PrEP-PP STUDY DESIGN

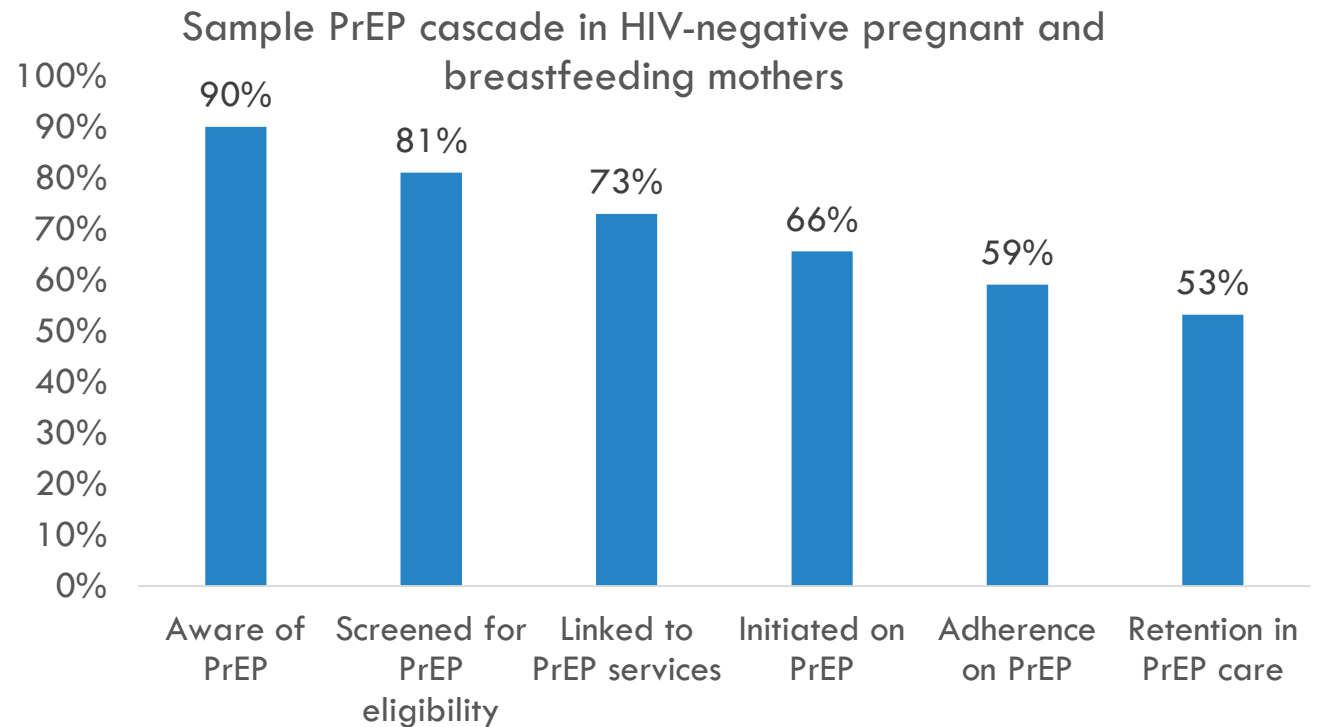


PrEP-PP AIM

1: EVALUATE THE PrEP CASCADE

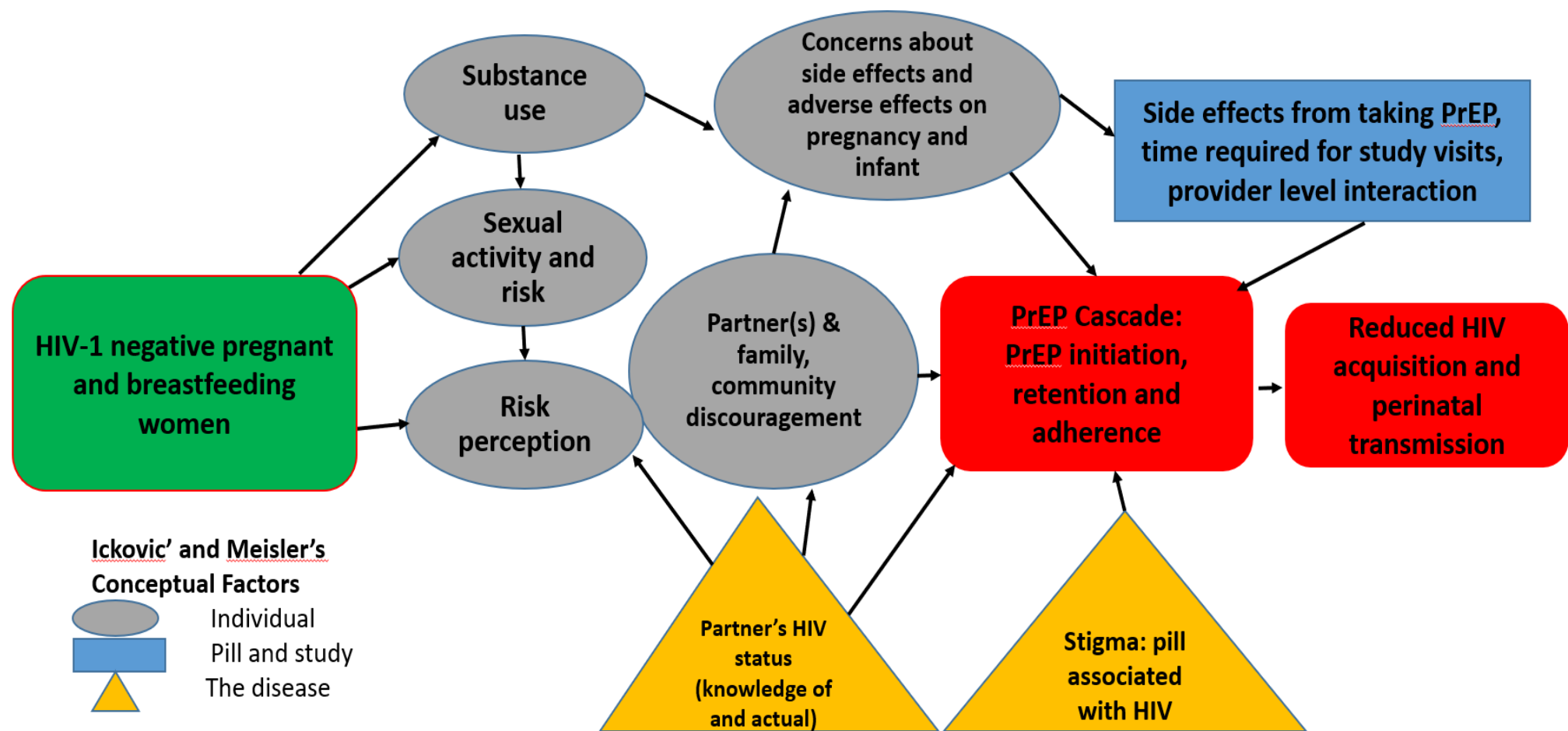
In a cohort of 1200 women followed until 12 months post-partum, we will evaluate what proportion of HIV-negative pregnant and breastfeeding women will:

- (1) opt to take PrEP
- (2) remain on PrEP and in study
- (3) adhere to PrEP



PrEP-PP AIM 2: EVALUATE WHO TAKES PrEP AND WHO ADHERES TO PrEP AND WHY?

Evaluate individual, pill/study and disease related factors associated with the PrEP cascade (initiation, retention and adherence)



PrEP-PP AIM
3:
MATHEMATICAL
MODEL
INFORMING THE
POTENTIAL
IMPACT OF PrEP
IN PREGNANCY

What is the potential impact of PrEP in pregnancy on HIV prevention and MTCT in South Africa?

Simulate the impact of improvement in the PrEP cascade on HIV infections averted (maternal and perinatal) in South Africa

INNOVATIONS IN PrEP-PP



We will include adolescent, pregnant and breastfeeding girls 16-19 years old who are at elevated risk because of pregnancy+ age+ behavioural/clinical risk factors



Our study is an open label non-randomized study



We will integrate PrEP counselling and provision into existing antenatal and postnatal care services (including peer support models)



We will measure both implementation and clinical outcomes through 12 months postpartum

Adherence to PrEP using DBS & self-reported measures

Clinical outcomes: HIV seroconversion, including perinatal infection, side-effects, infant health

EXPECTED RESULTS



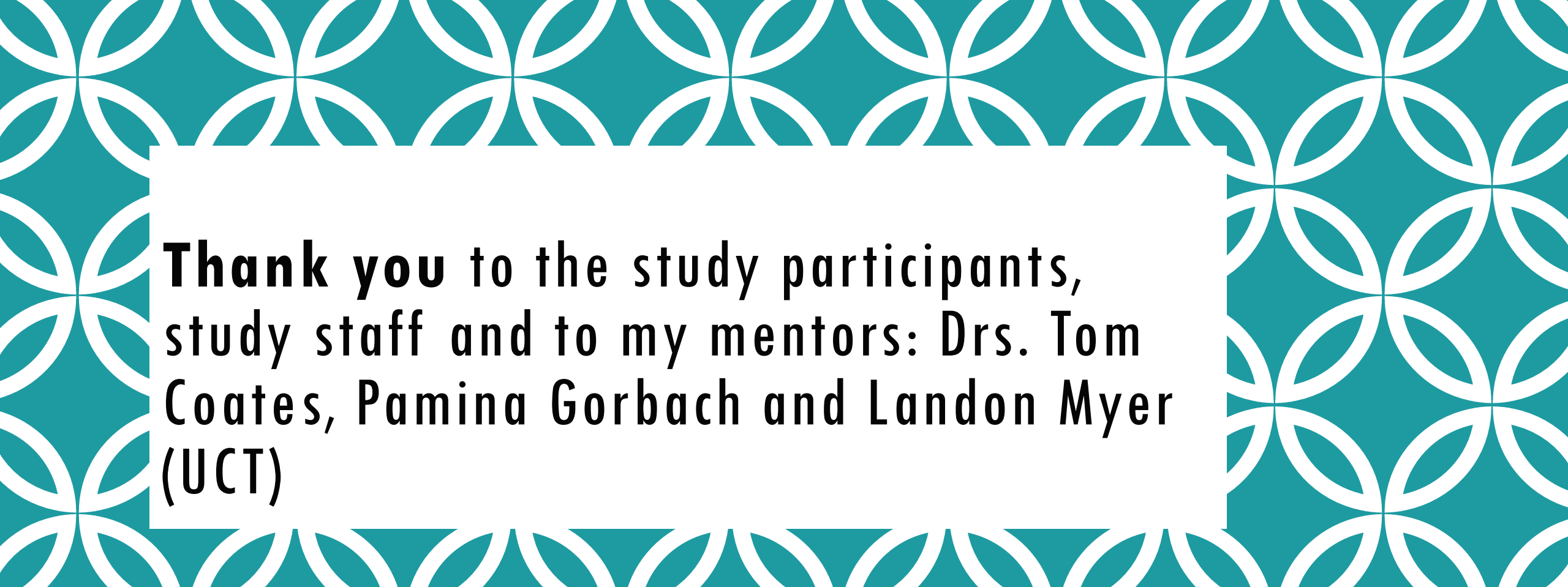
We will evaluate PrEP initiation and adherence in real-world clinics to better inform the roll out, marketing and service delivery



If our study is effective we will advocate for the South African Department of Health to update their policies to include pregnant and breastfeeding women in the national PrEP policy and roll out in 2021 and beyond

FUTURE COLLABORATION

- Opportunities to come work with our team in Cape Town as an Epidemiologist Intern this summer
- Other opportunities for PhD student dissertation research
- Other collaboration with ongoing research at UCLA and UCT



Thank you to the study participants,
study staff and to my mentors: Drs. Tom
Coates, Pamina Gorbach and Landon Myer
(UCT)



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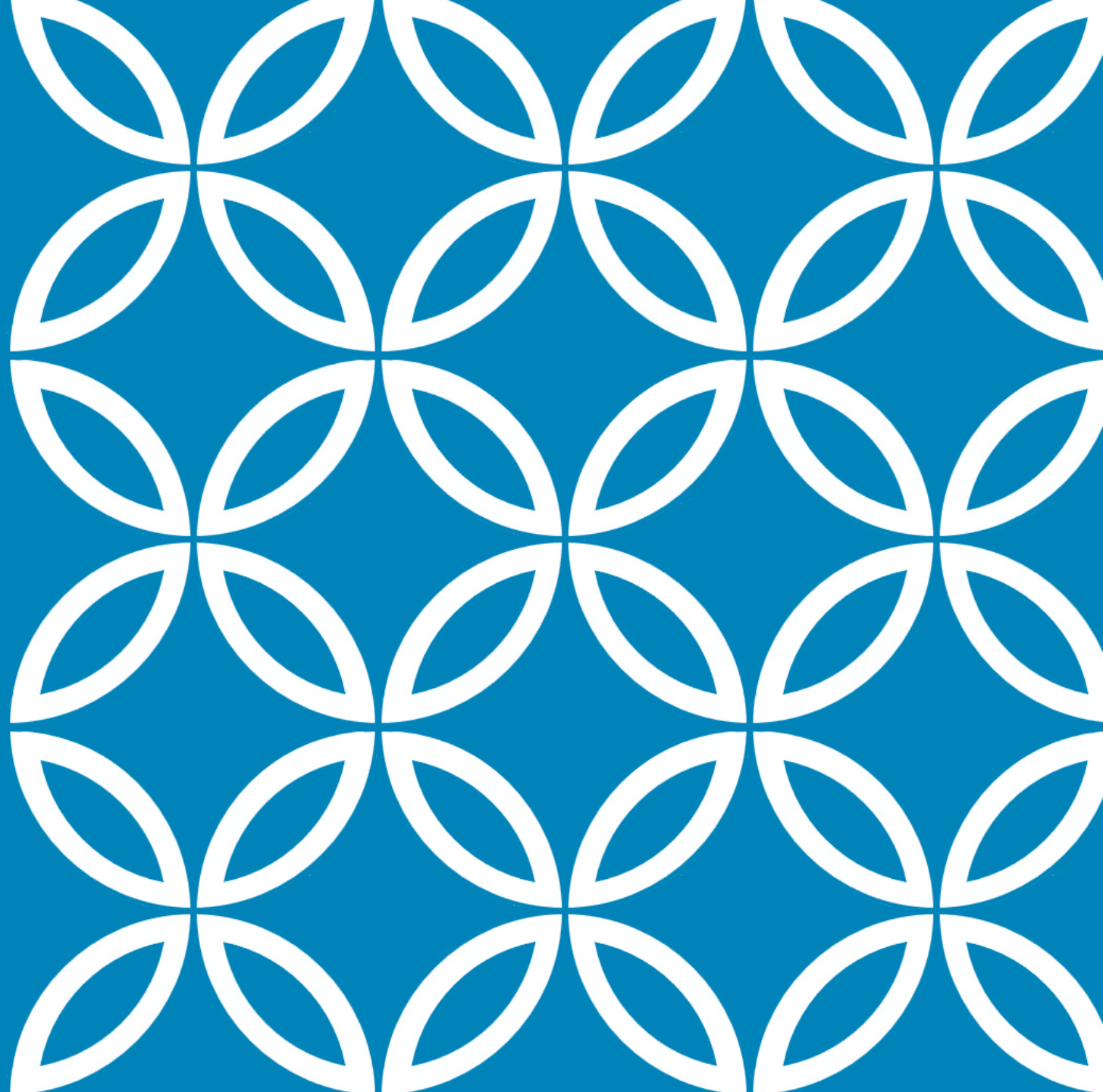
- **Fogarty International Center of the National Institutes of Health under Award Number K01TW011187**

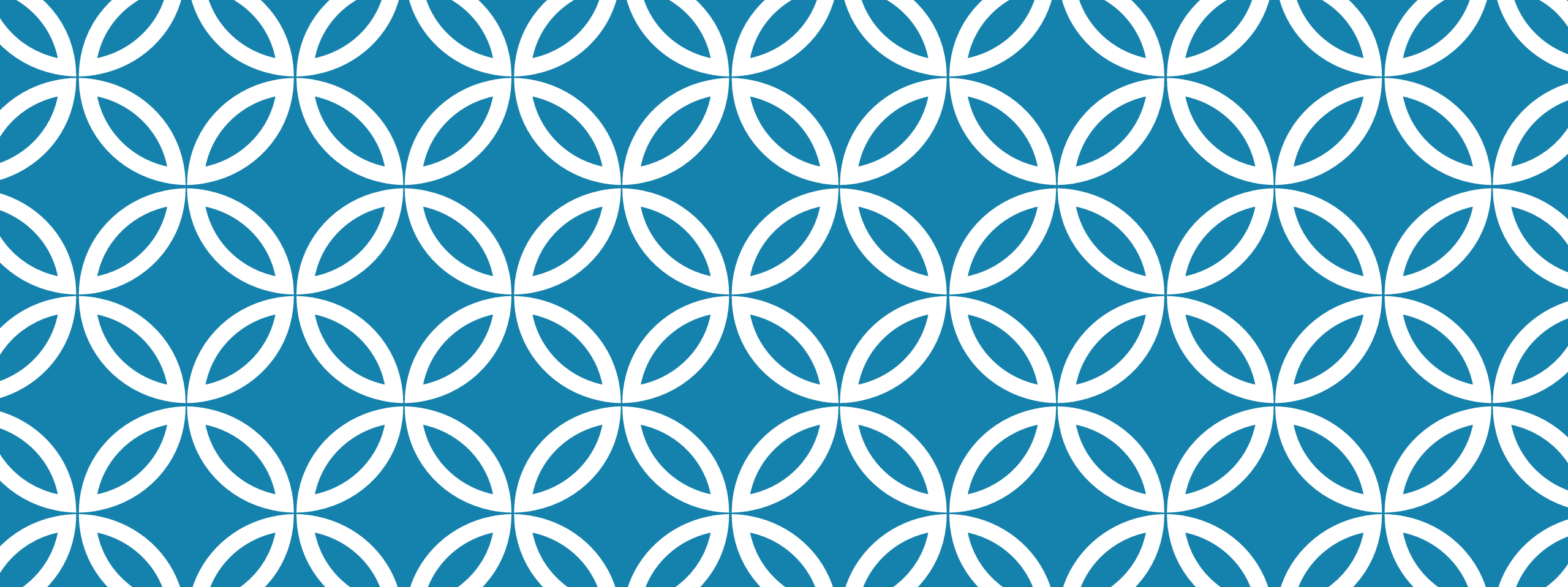
- **Post-doctoral support was from NIH-NIAID-T32DA023356 (PIs: Currier and Gorbach) and from UNC Training in global HIV prevention research (NIH/FIC R25TW009340: PI: Chi)**

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Study drug will be provided by **Gilead Pharmaceuticals.**

**QUESTIONS?
DISCUSSION**





THANK YOU!

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