

The CARE PrEP Study (MATRIX-007)

Evaluating the safety of CAB-LA, the dapivirine ring and oral PrEP during pregnancy

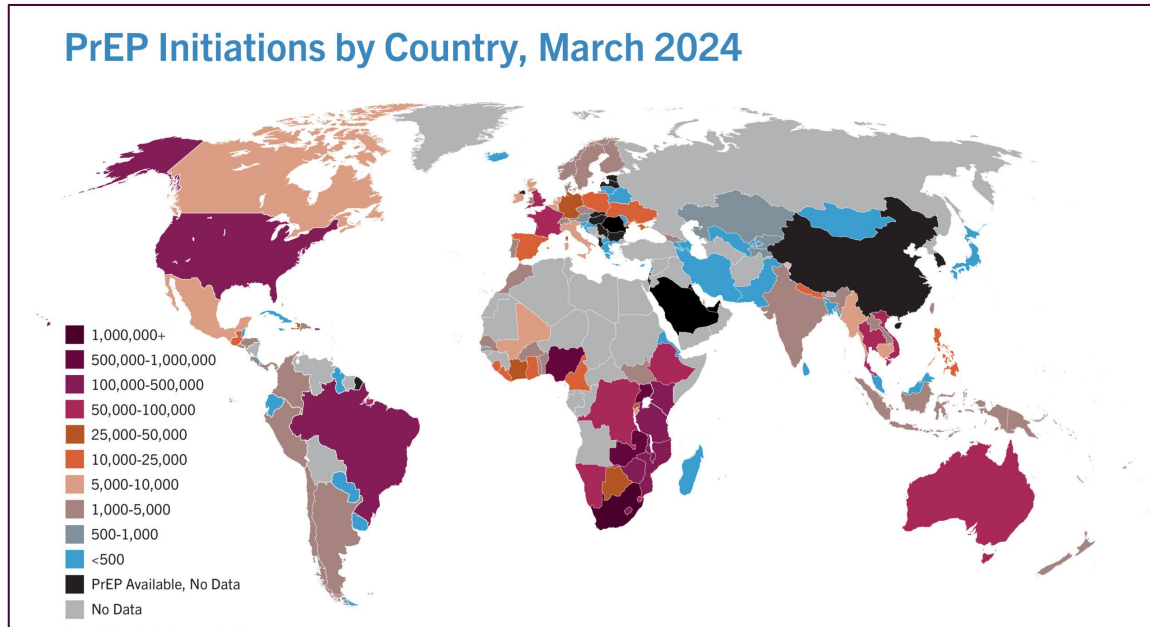
Njambi Njuguna

FHI 360

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Background - Global PrEP uptake



Source: AVAC Global PrEP Tracker

- 6.7 million PrEP initiations
- Almost all oral PrEP
 - DVR – 2,000
 - CAB-LA– 12,000
- Numerous clinical trials and demonstration projects underway
 - Few intentionally include pregnant or breastfeeding populations

What we know - HPTN 084 OLE

CAB-LA EXPOSURE, BY GROUP

	Active CAB-LA n (% or IQR)	Prior CAB-LA n (% or IQR)	No CAB-LA n (% or IQR)
Total no. pregnancies	212	68	45
Total no. CAB injections pre-pregnancy			
None	20 (9%)	-	45 (100%)
1 to 3	32 (15%)	11 (16%)	-
> 3	160 (75%)	57 (84%)	-

What we know - HPTN 084 Conclusions

- Maternal, pregnancy outcomes were consistent across non-randomized exposure groups and with expected background rates.
 - No maternal deaths or HIV infections
 - Similar rates of poor pregnancy outcomes
 - Infant growth parameters similar across exposure groups
- CAB-LA was well tolerated in pregnant women
 - Pregnancy-related AE rates similar across groups
 - Gestational hypertension rates similar to background rates
 - Weight gain similar across groups and within normal range for pregnancy

Is this enough?

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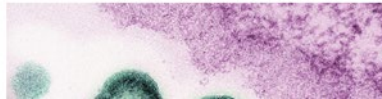
NEWS RELEASES

Tuesday, July 23, 2024

Long-acting injectable cabotegravir for HIV prevention is safe in pregnancy

NIH-sponsored study supports cabotegravir use throughout period of reproductive potential.

Long-acting injectable cabotegravir (CAB-LA) was safe and well tolerated as HIV pre-exposure prophylaxis (PrEP) before and during pregnancy in the follow-up phase of a global study among cisgender women. The analysis of outcomes from more than 300 pregnancies and infants will be presented at



- These data about the safety of CAB-LA for PrEP in pregnant women are reassuring but....
- IS THIS ENOUGH?

Not enough

Remember:

- Pregnant and breastfeeding women were excluded from participation in Phase III trials of the dapivirine ring and CAB-LA in order to “protect”
- If participants fell pregnant, they stopped using the product right away

Does this mean we know nothing about the dapivirine ring and CAB-LA in pregnancy and breastfeeding?

- We know a lot about the dapivirine ring....
- Two studies (DELIVER and B-PROTECTED) demonstrated safety of the dapivirine ring during pregnancy and breastfeeding
- But what we know about the safety of CAB-LA is not enough for some countries to decide whether to offer it to pregnant and breastfeeding populations

History of ARV-based HIV prevention

PrEP product	Efficacy results	Years after efficacy results						
		1	2	3	4	5	6	7
Oral PrEP	2010	2 years		3 years			2 years	
DVR	2016	4 years				1 year	?	
CAB -LA	2020	1 year	½ yr	?				



Time to approval by regulatory body



Time to WHO recommendation



Time to WHO recommendation for pregnant populations

What kind of data are needed?

Regulatory bodies in country and WHO require **high quality data** to support product use in pregnant populations

- Maternal ultrasound for accurate dating
- Surface exam of the newborns to assess fetal malformations
- Abstraction of medical records by medical personnel to identify other significant medical conditions which could be associated with maternal outcome
- Ensuring data are collected by appropriately qualified personnel

WHO 2023 London Consortium Core Endpoints

Birth Outcomes

Stillbirth

Preterm birth <37 weeks

Very preterm birth <32 weeks

Birthweight

Small for gestational age (<10th %ile), if possible

Congenital anomalies at birth (routine reporting)

Miscarriage (<20 weeks; <28 weeks)

Maternal Outcomes

Mortality during pregnancy, birth, and in facility

Neonatal/Infant Outcomes

Neonatal death (in facility)



A TALE OF TWO STUDIES

CATALYST

The CATALYST study, under the MOSAIC project, will use mixed methods to characterize and assess the implementation of an enhanced service delivery package providing choice of PrEP products among women at PEPFAR delivery sites in **Kenya, Lesotho, South Africa, Uganda, and Zimbabwe.**

Offered PrEP methods

- Oral PrEP
- Dapivirine ring (PrEP ring)
- CAB-LA (CAB PrEP)



STUDY DESIGN

- Implementation of **an enhanced service delivery package that supports choice** among the PrEP products that have regulatory approval in each country, such as oral PrEP, dapivirine ring and CAB-LA
- Includes components at the individual, provider, facility and community levels
- Uses **quality improvement methods** to refine components and identify a core service delivery package for PrEP choice

OBJECTIVE 1

Characterize the implementation of an enhanced service delivery package for PrEP choice and assess individual-, provider-, facility-, community- and health system-level facilitators and barriers to the implementation process

OBJECTIVE 2

Describe patterns of PrEP use and use effectiveness in the context of PrEP choice and assess sociodemographic and contraceptive use correlates of PrEP use patterns

OBJECTIVE 3

Describe clinically relevant indicators among PrEP users, including rates of HIV infection and drug resistance among PrEP users who acquire HIV following PrEP exposure

MATRIX-007 (CARE PrEP)

- **Full title:** Safety Evaluation following Exposure to Cabotegravir-, Dapivirine- and Tenofovir-based PrEP during Pregnancy
- **Design:** Prospective cohort study
- **Population:** Approximately 500-800 participant mothers and babies from Lesotho, Zimbabwe, and Kenya with pregnancies exposed to an ARV-based HIV prevention method at the time of enrollment

500-800 PrEP exposed pregnancies

CAB PrEP



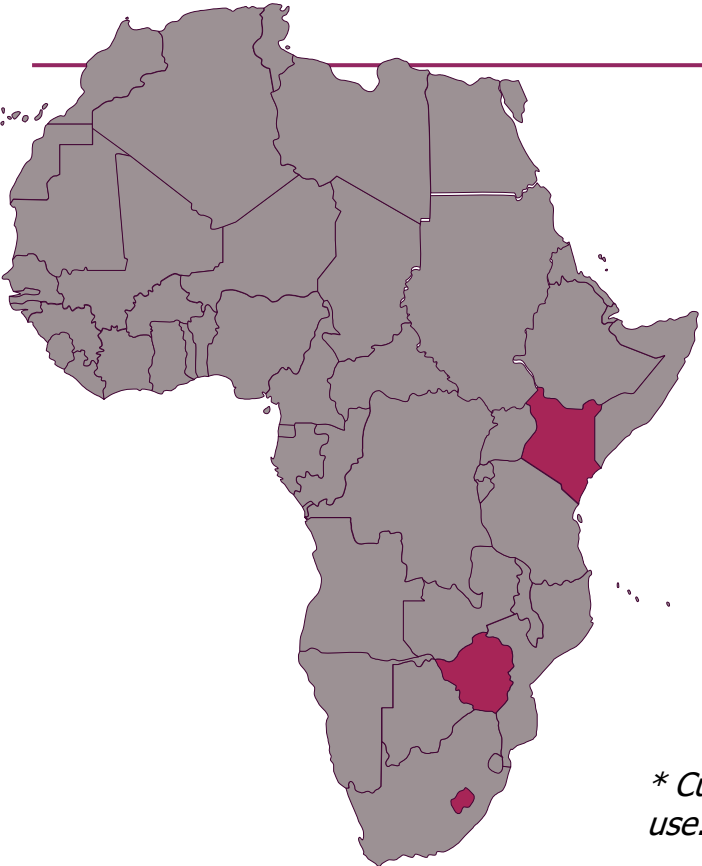
PrEP ring



oral PrEP



CARE PrEP Countries and PrEP during Pregnancy



Implementing in 3 CATALYST countries with high pregnancy rates and access to maternal and child health services

Approved PrEP options for pregnant populations currently vary by country

	Oral PrEP	PrEP Ring	CAB PrEP
Kenya	✓	✓	TBD
Lesotho	✓	✓	✗
Zimbabwe	✓	✗	✓*

** Current CAB users who become pregnant may choose to continue use. CAB cannot be initiated during pregnancy.*

Objectives and Endpoints

Primary endpoints

- Describe pregnancy outcomes of women exposed to PrEP products (oral, ring, CAB)
- Describe selected infant malformations resulting from pregnancies exposed to PrEP products (oral, ring, CAB)

Secondary endpoints

- Describe selected complications during pregnancy
- Describe frequency of infant deaths
- Describe infant growth parameters.

CARE PrEP and CATALYST Comparison

	CATALYST	CARE PrEP (MATRIX-007)
Study Products	Offering PrEP ring and CAB PrEP in addition to site-offered oral PrEP	None. All PrEP is offered through CATALYST
Pregnancy Outcome Data		
Gestational age dating	Self-report/ antenatal card (ANC) card if provided by participant	Ultrasounds provided by study
Source documents for pregnancy-related data	Self-report, ANC and delivery records if provided by participants	Additional access to ANC, delivery, pediatric records at health facilities
Documenting complications observed during pregnancies	Not systematically collected	Systematically collected; secondary study objective
Infant health data, including congenital anomaly identification	None. No data collected beyond pregnancy outcome	Surface exams and records review at birth, 3-months, and 6-months

Visit Schedule



**ENROLLMENT/
MOTHER**



**ANTENATAL
QUARTERLY/
MOTHER**



**PREGNANCY
OUTCOME/
MOTHER AND
INFANT**



**POSTNATAL 3-
MONTH/ MOTHER
AND INFANT**



**POSTNATAL 6-
MONTH/
MOTHER AND
INFANT**

Pregnancy Visits

- **Gestational age dating (ultrasound scan)**
- Pregnancy/medical history
- ANC record review
- Blood pressure
- HIV testing
- Syphilis testing

Pregnancy Outcome Visit

- Pregnancy outcome record review
- Pregnancy/medical history review
- Maternal HIV testing, blood pressure
- **Infant physical exam**

Infant visits

- **Infant physical exam**
- Breastfeeding assessment
- Records review
- Medical history review
- Maternal HIV testing, review

Where are we now?

- **Timeline:** expected enrollment from Oct 2024.
- **Activities:** All 3 countries engaged, staff recruited, protocol IRB submissions imminent, study training kicked off this week, site set up
- **Kenya** : CAB-LA registered, CAB-LA guidelines to be formulated
- **Future impact:** add to existing data on PrEP among pregnant and breastfeeding populations, and serve as a template for obtaining pregnancy safety data for future drug rollouts

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Questions and Discussion

The CARE PrEP (MATRIX-007) Study

- How is Kenya's Ministry of Health making HIV prevention among pregnant and breastfeeding women a priority outside of PMTCT programming?
- CARE PrEP will have results in 2026 or later. Given the encouraging results of the HPTN-084 study showing safety among pregnant women using CAB, what recommendations would you consider for use among these populations in Kenya, especially now that guidelines are in the process of being written?

- Will the results of a study like CARE PrEP be useful to Kenyan stakeholders responsible for deciding whether these products can be used by pregnant women?
- How would you advise we disseminate CARE PrEP study findings to policy-makers and healthcare providers to ensure they are translated into practice?