2nd Long-Acting Treatment and Prevention Conference

29 October 2024 | Johannesburg

LA medications: Where do they fit in for niche populations in an African context

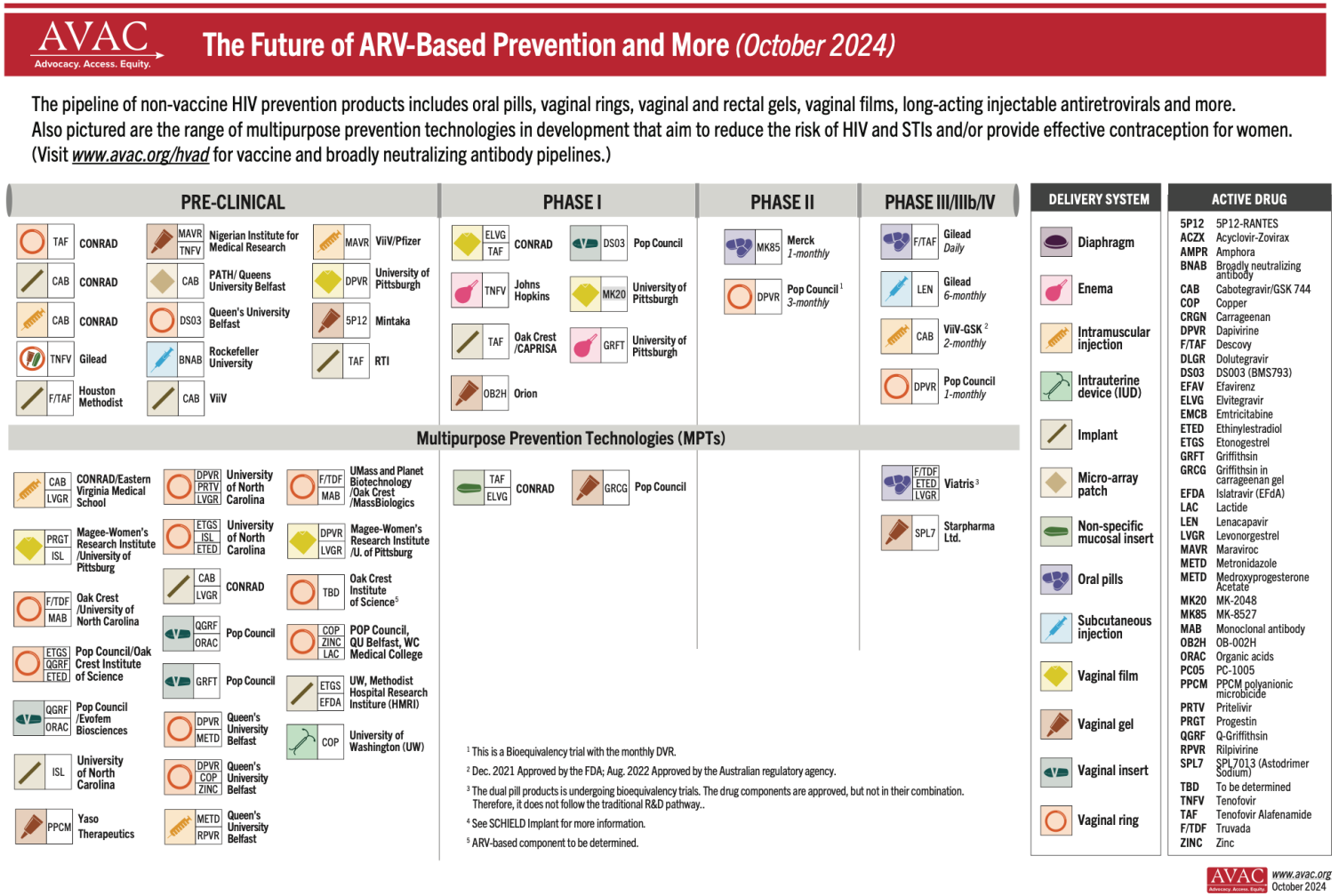
Lee Fairlie
Wits RHI

Much progress made in the past 4 decades regarding available ART for treatment and especially prevention

FDA Approval of HIV Me

1985-89	1990-94	1995-99	2000-04	2
1987 Zidovudine (NRTI)	**1991** Didanosine* (NRTI) **1992** Zalcitabine* (NRTI) **1994** Stavudine* (NRTI)	**1995** Lamivudine (NRTI) Saquinavir Mesylate* (PI) **1996** Indinavir* (PI) Nevirapine (NNRTI) Ritonavir (PI) **1997** Combivir* (FDC) Delavirdine* (NNRTI) Nelfinavir* (PI) Saquinavir* (PI) **1998** Abacavir (NRTI) Efavirenz (NNRTI) **1999** Amprenavir* (PI)	**2000** Didanosine EC* (NRTI) Kaletra (FDC) Trizivir* (FDC) **2001** Tenofovir DF (NRTI) **2002** Stavudine XR* (NRTI) **2003** Atazanavir (PI) Emtricitabine (NRTI) Enfuvirtide (FI) Fosamprenavir* (PI) **2004** Epzicom* (FDC) Truvada (FDC)	T Ra Et

Drug Class Abbreviations:
AI: Attachment Inhibitor; CA: CCR5 Antagonist; CI: Capsid Inhibitors; FDC: Fixed-Dose Combination; FI: Fusion Inhib
INSTI: Integrase Inhibitor; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; NRTI: Nucleoside Reverse Transcr
Inhibitor; PE: Pharmacokinetic Enhancer; PI: Protease Inhibitor; PAI: Post-Attachment Inhibitor; PrEP: Pre-exposure p



What should an ideal long-acting ART look like?

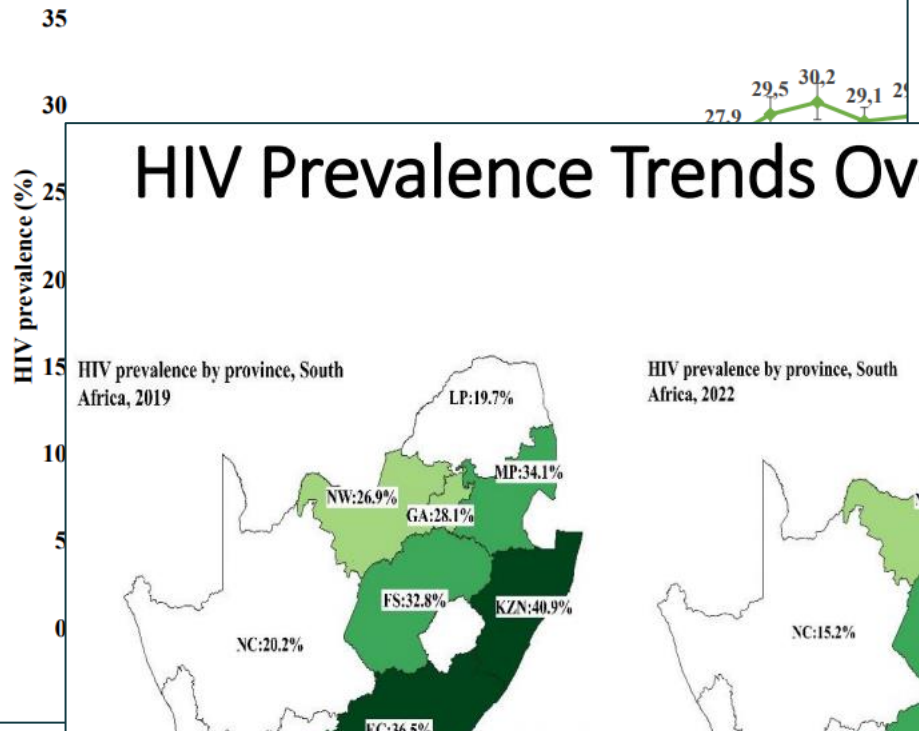
- Discrete, minimizes stigma
- No requirement for daily pill-taking
- Easy to take, palatable
- If pills taken, as few as possible, should be FDC
- Also consider TB prevention e.g., TB vaccine (in future), newer TPT regimens
- Currently cost and access to CAB/RIL treatment are HUGE barriers
- Pre-existing NNRTI resistance is also a challenge
- Refrigeration requirements?
- HCW training

Who would benefit from LA agents?

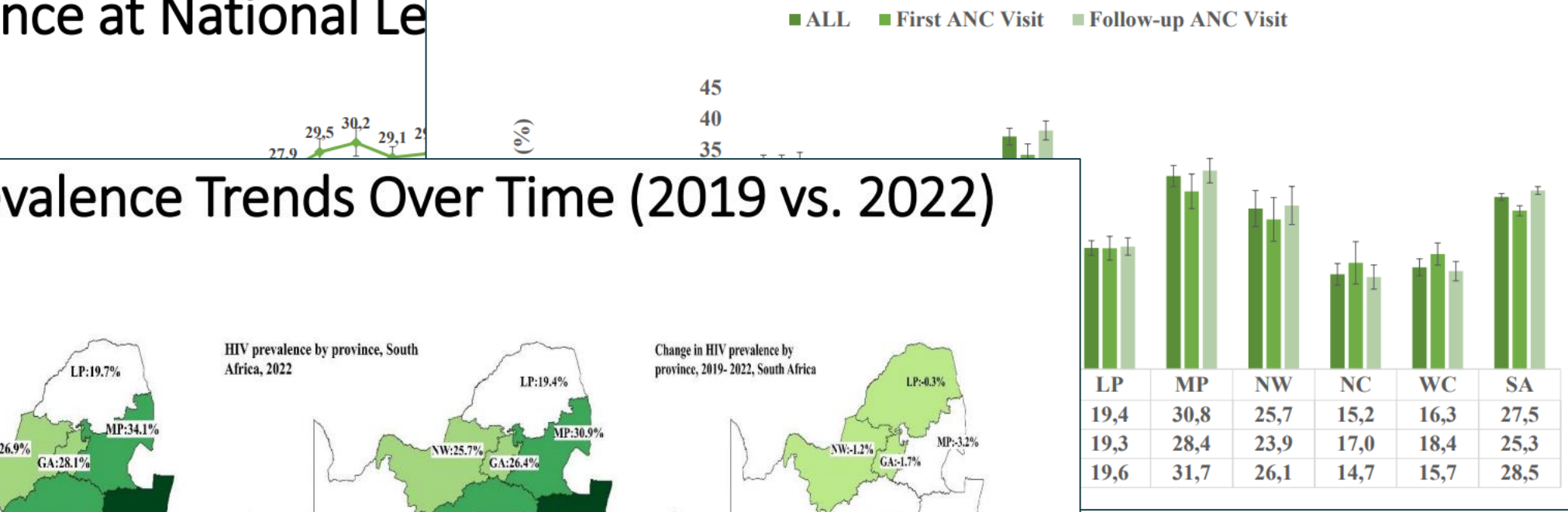
Pregnant and lactating women and people

Although antenatal HIV seroprevalence has eventually declined, it still remains concerningly high (data from 28 Feb-8 April 2022)

HIV Prevalence at National Le

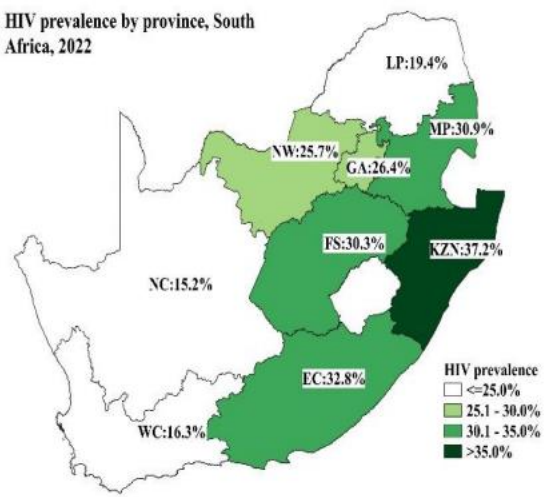


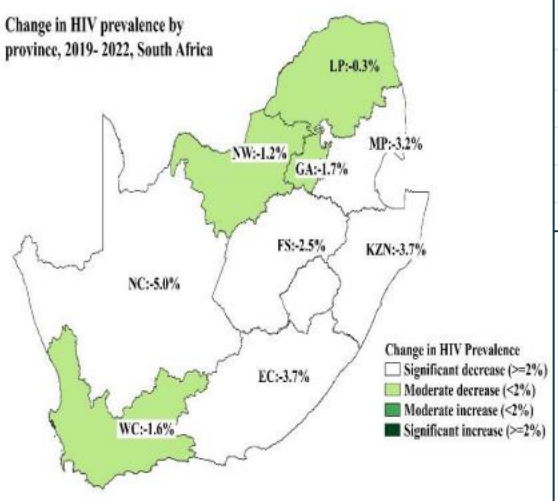
HIV Prevalence by Province and ANC Visit Status



	LP	MP	NW	NC	WC	SA
	19,4	30,8	25,7	15,2	16,3	27,5
	19,3	28,4	23,9	17,0	18,4	25,3
	19,6	31,7	26,1	14,7	15,7	28,5

HIV Prevalence Trends Over Time (2019 vs. 2022)





NICD, 2024

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

health
Department: Health
REPUBLIC OF SOUTH AFRICA

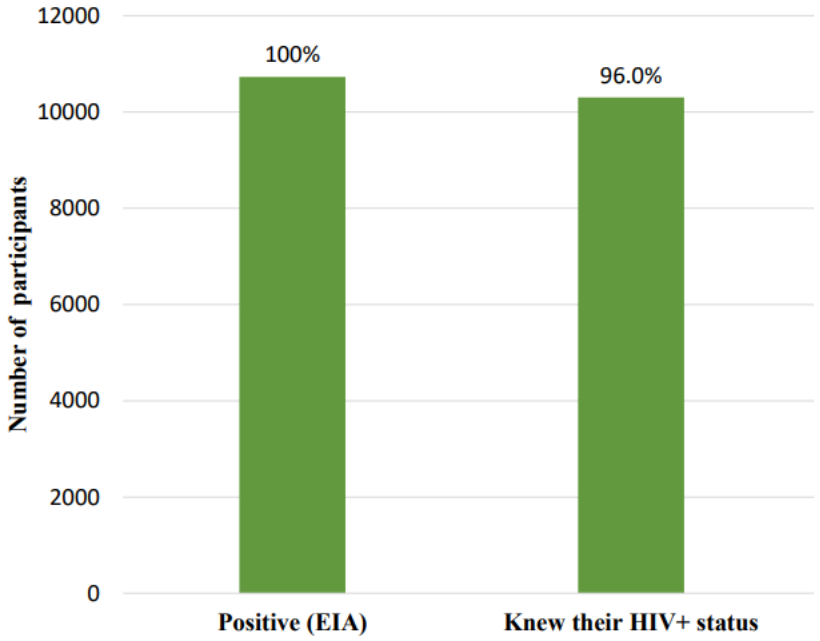
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

The 2022 Antenatal Care HIV Sentinel Surveillance: Key Findings

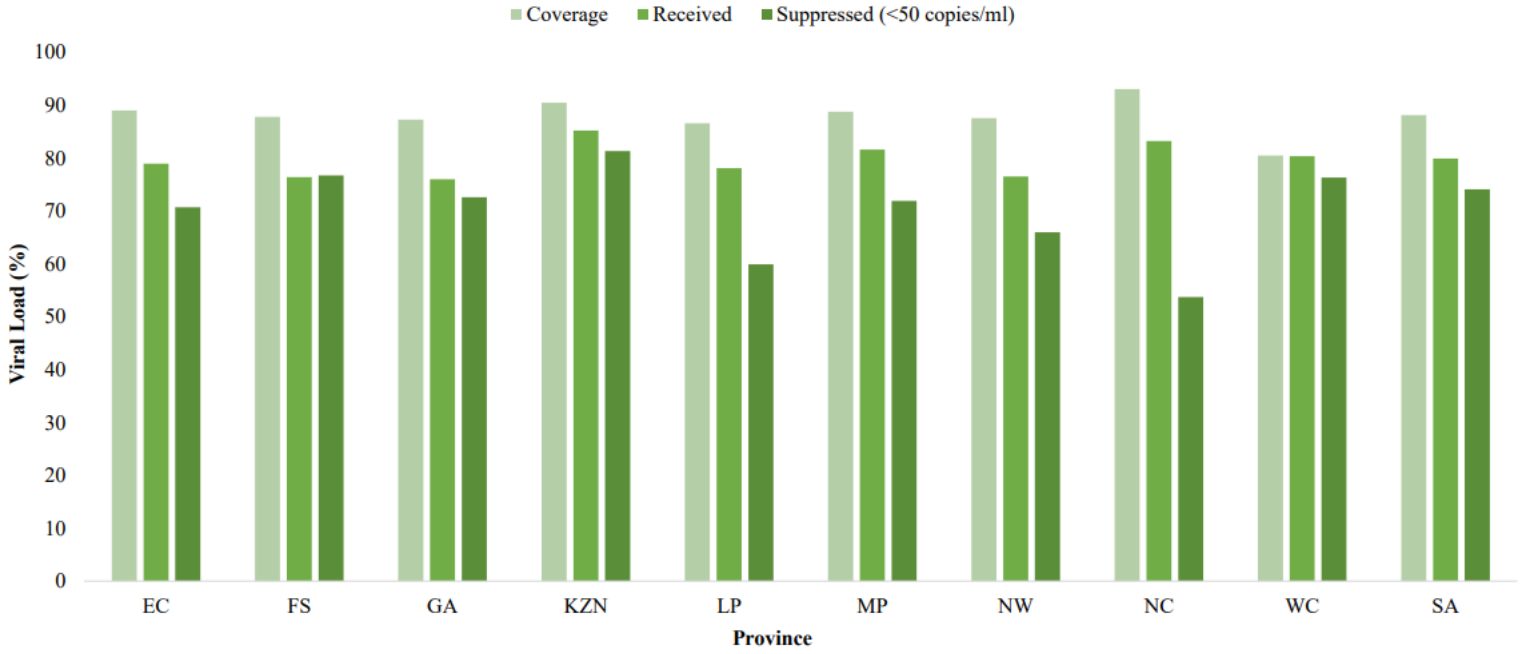
Tendesayi Kufa-Chakezha, MBChB, PhD
Nosipho Shangase, MSPH, PhD
Adrian Puren, MBBCh, PhD

95-95-95 cascade, including viral load coverage, results receipt and suppression are still not optimal

95-95-95 HIV Care Cascade



Viral Load Coverage, Receipt of Results and Suppression (by Record Review and among Eligible)



NICD, 2024

Low VL suppression on EFV

Achieving maternal viral load suppression for elimination of mother-to-child transmission of HIV in South Africa

Faith Moyo[a,b,c], Ahmad Haeri Mazanderani[a,d], Tanya Murray[a,c], Gayle G. Sherman[a,c,e] and Tendesayi Kufa[a,b]

- Among 178 319 pregnant WLHIV, 345 174 VL tests
- First ANC 85 545 (48%) ART experienced
- Proportions of viraemia VL> 50 copies/ml, 39 756 (53.6%) first VL; 14 780 (36.9%) at delivery and 24 328 (33.5%) postpartum.

- Conclusion: Despite high-ART coverage among pregnant women in South Africa, only 63% of WLHIV achieved viral load less than 50 copies/ml at delivery.

Moyo, AIDS, 2021; Moyo, SAMJ, 2021

Maternal HIV viral load testing during pregnancy and postpartum care in Gauteng Province, South Africa

F Moyo,[1,2,3] MSc; A H Mazanderani,[1] PhD; T Kufa,[1,2] PhD; G G Sherman,[1,3,4] PhD

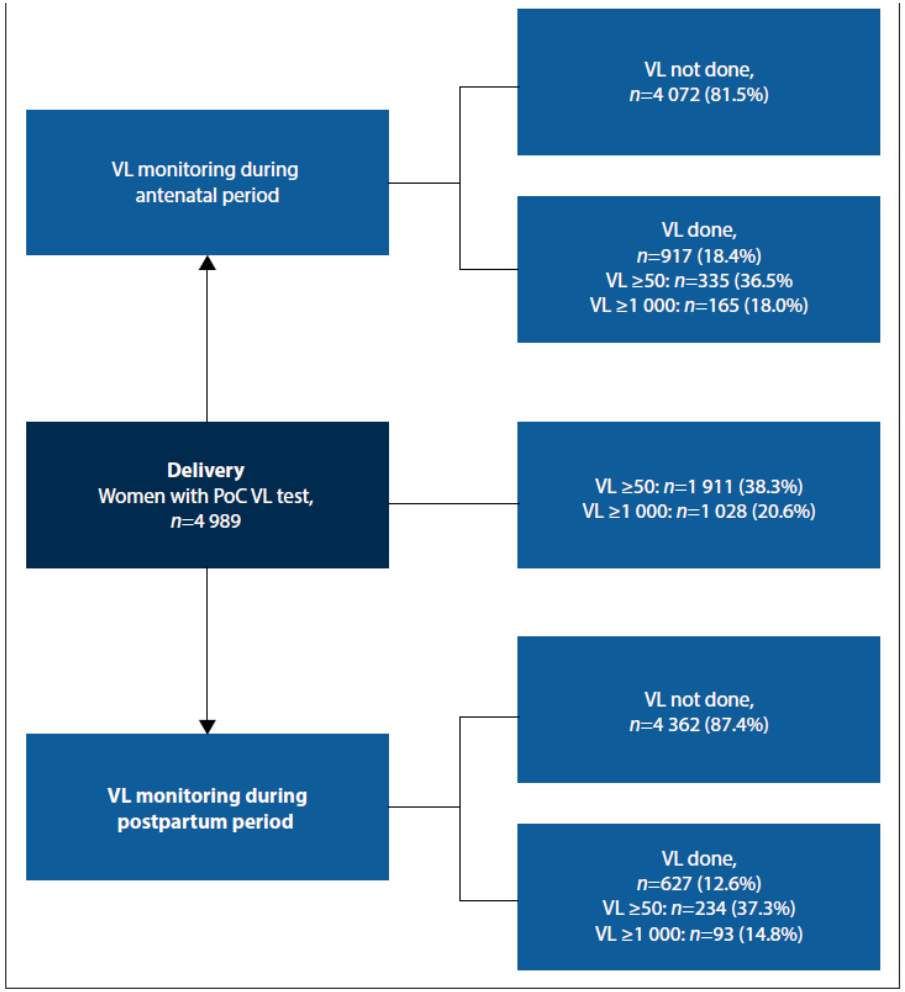


Fig. 1. VL testing compliance and rates of suppression among pregnant and postpartum women living with HIV in the cohort. (VL = viral load (copies/mL); PoC = point-of-care.)

More Frequent HIV Viral Load Testing With Point-Of-Care Tests Detects Elevated Viral Load Earlier in Postpartum HIV-Positive Women in a Randomized Controlled Trial in Two Clinics in Johannesburg, South Africa

Lee Fairlie, MBChB, FCPaeds (SA), MMed (Wits),[a] Shobna Sawry, BSc, MSc,[a] Sherri Pals, PhD,[b] Gayle Sherman, MBBCh, MMed(Haem), DCH, DTM&H, PhD,[c,d] Dhelia Williamson, PhD,[b] Jean Le Roux, MBBCh,[a] Bernadette Ngeno, MBChB, MMED,[b] Leigh Berrie, PhD,[e] Karidia Diallo, MSc, PhD,[e] Mackenzie Hurlston Cox, MSPH,[b] Mary Mogashoa, MBBCh,[e] Matthew Chersich, MBBCh, PhD,[a] and Surbhi Modi, MD, MPH,[b]
For the OPPTIM (Optimised Postpartum PMTCT Testing for Infants and their Mothers) Study Team

TABLE 2. Viral Suppression (VL < 1000 cps/mL and VL < 50) Rates by Time Point and Study Arm

	VL < 1000 cps/mL		VL < 50 cps/mL	
	Arm 1 n (%N)	Arm 2 n (%N)	Arm 1 n (%N)	Arm 2 n (%N)
Observed results				
Baseline	188/200 (94.0)	178/201 (88.6)	154/200 (74.7)	150/201 (74.6)
6 mo	125/131 (95.4)	125/137 (91.2)	101/131 (77.1)	89/137 (65.0)
12 mo	132/140 (94.3)	135/148 (91.2)	87/140 (62.1)	93/148 (62.8)
18 mo	134/142 (94.4)	118/127 (92.9)	92/142 (64.8)	80/127 (63.0)
Multiple imputation results*				
Baseline	2880/3060 (94.1)	2670/3015 (88.6)	2355/3060 (77.0)	2250/3015 (74.6)
6 mo	2790/3060 (91.2)	2600/3015 (86.2)	2323/3060 (75.9)	1927/3015 (63.9)
12 mo	2797/3060 (91.4)	2602/3015 (86.3)	1846/3060 (60.3)	1779/3015 (59.0)
18 mo	2786/3060 (91.1)	2624/3015 (87.0)	1940/3060 (63.4)	1804/3015 (59.8)

P values for the test of study arm difference (pooling across the postbaseline time points and adjusting for baseline viral suppression): observed data VL < 1000 cp/mL, $P = 0.8176$; observed data VL < 50 cp/mL, $P = 0.6282$; multiple imputation VL < 1000 cps/mL, $P = 0.6421$; and multiple imputation VL < 50 cps/mL, $P = 0.3490$.
*Numerators and denominators for multiple imputation results are for 15 separate imputation data sets combined.

Fairlie, JAIDS, 2023

Frequency of Viremic Episodes in HIV-Infected Women Initiating Antiretroviral Therapy During Pregnancy: A Cohort Study

Landon Myer,[1,2] Lorna Dunning,[1] Maia Lesosky,[1] Nei-Yuan Hsiao,[3] Tamsin Phillips,[1,2] Greg Petro,[4] Allison Zerbe,[5] James A. McIntyre,[1,6] and Elaine J. Abrams[5,7]

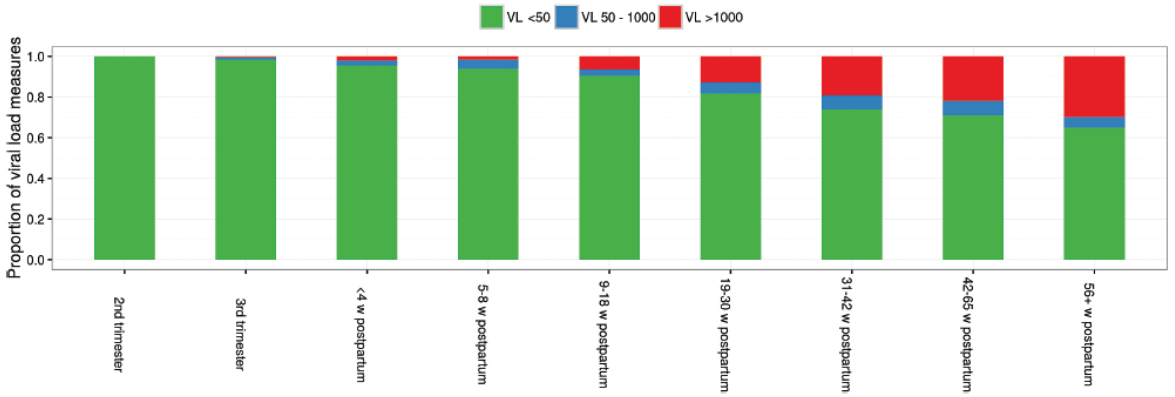


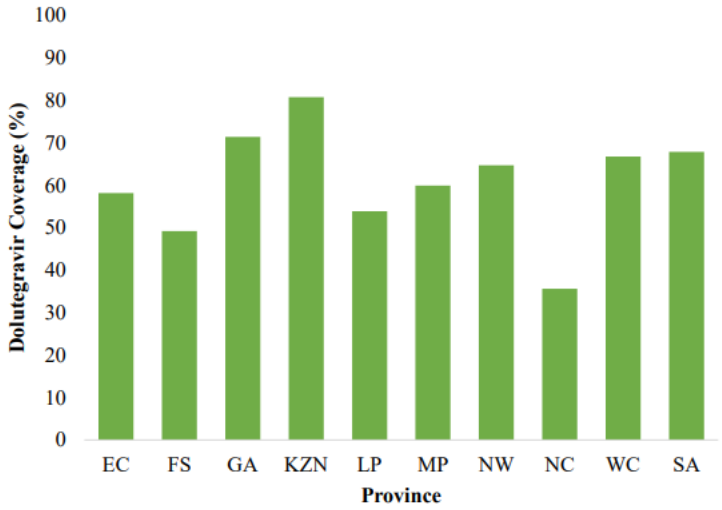
Figure 2. Distribution of viral load (VL) test results during select intervals of time during pregnancy and postpartum; each column shows results for all tests conducted in the cohort during that interval.

Myer, CID, 2016

Dolutegravir coverage has scaled up in the past few years, but VL data on DTG not yet available

DTG Coverage among those on ART Regimen Type Coverage by Province

A



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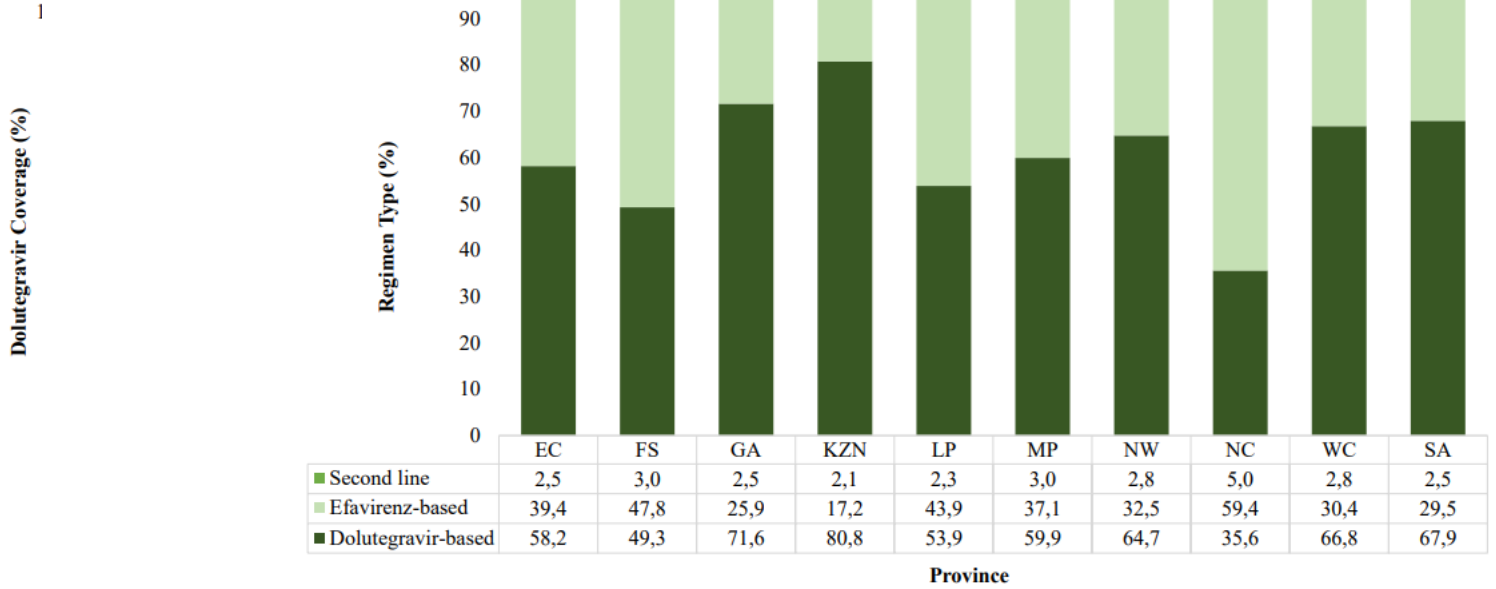


	EC	FS	GA	KZN	LP	MP	NW	NC	WC	SA
Second line	2,5	3,0	2,5	2,1	2,3	3,0	2,8	5,0	2,8	2,5
Efavirenz-based	39,4	47,8	25,9	17,2	43,9	37,1	32,5	59,4	30,4	29,5
Dolutegravir-based	58,2	49,3	71,6	80,8	53,9	59,9	64,7	35,6	66,8	67,9

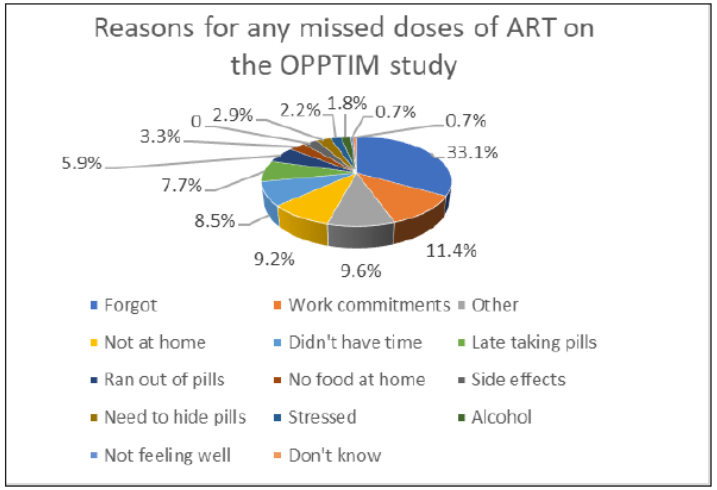
NICD, 2024

Numerous risk factors for suboptimal adherence this group (especially postpartum)

- Myer:
  - Younger age (IRR for 18–22 years of age vs ≥34 years of age, 3.67 [95% CI, 1.78–7.56]),
  - ART initiation during the third trimester (IRR vs first trimester, 2.21 [95% CI, 1.13–4.34])
  - Previous defaulting on ART (IRR, 2.94 [95% CI, 1.29–6.69])
  - Postpartum period- each additional month associated with 11% increase in incidence of viremia (IRR, 1.11 [95% CI, 1.07– 1.15]).
- **Other:**
  - Late ANC booking
  - Elevated VL in pregnancy
  - Fewer number of antenatal visits
  - Alcohol use
  - Stigma
  - IPV
  - Lack of disclosure

HIV treatment adherence challenges in postpartum women living with HIV in the OPPTIM Study, Johannesburg, South Africa

Figure: Reasons for any missed doses of ART on the OPPTIM study



Myer, CID, 2016; Fairlie, JAIDS, 2023; Fairlie, Peds and HIV workshop, 2024

Mixed progress with treatment studies

~~A5425/I3043 (PRACTICAL)~~

Evaluating CAB/RIL postpartum in higher risk WLHIV

Adolescents

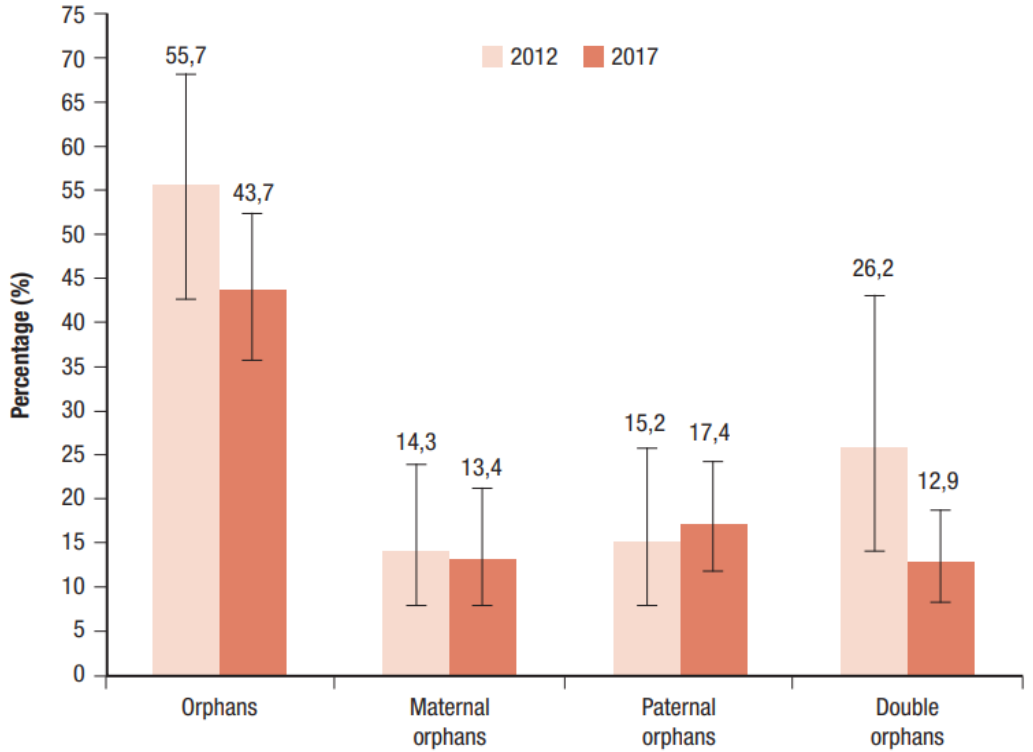
Adolescents are going through many changes and life experiences that make treatment adherence difficult

ALHIV

Unique needs:

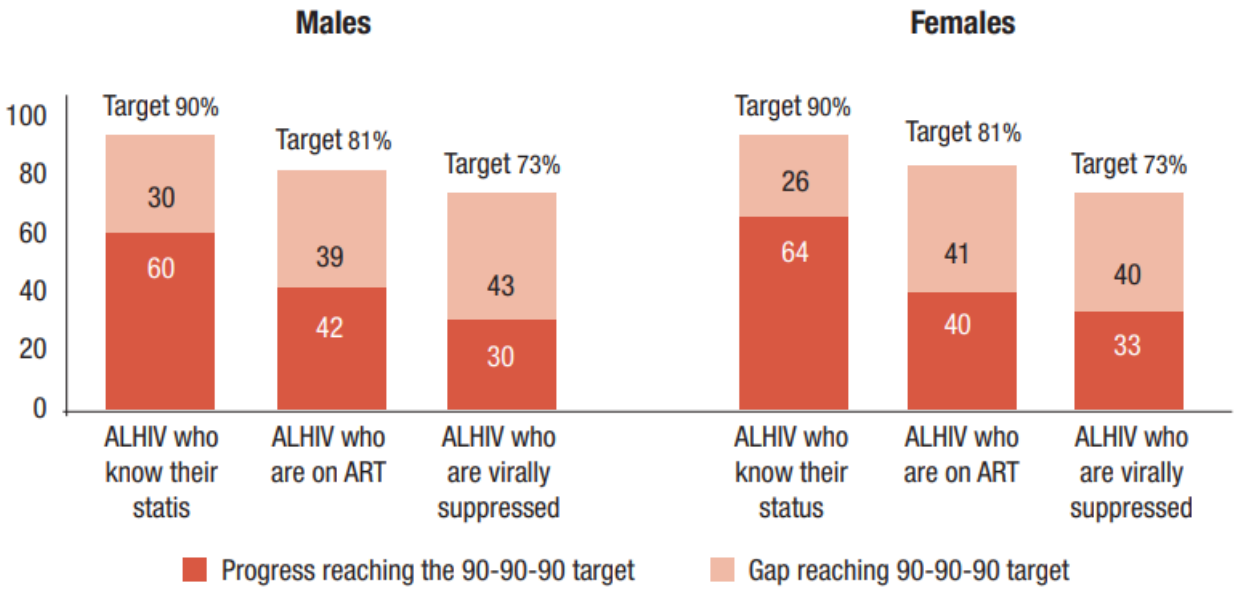
- Vertically HIV infected-highly treatment experienced, may have lost a parent, usual adolescent difficulties may be amplified, chronic illness, growth stunted, delayed puberty compared to peers
- Newly infected adolescents may lack support-might not want to disclose to parents (not required to do so for testing, treatment), might be difficult to disclose to partner/friend or support system

Figure 1: ALHIV aged 15 – 19 by orphanhood type, South Africa, 2012 and 2017



Gaps in achieving 90-90-90 goals

Figure 3: ALHIV progress and gaps in reaching 90-90-90 targets, South Africa, 2017



HSRC, 2021

Table 10: ALHIV with VLS, by sex and age group, South Africa, 2017

	10 to 14 years			15 to 19 years			All 10 – 19 years
	n	%	95% CI	*n*	%	95% CI	*n*
All	95	54.0	41.9 – 65.7	121	45.7	36.5 – 55.3	216
Male	49	67.5	51.9 – 79.9	32	37.4	23.7 – 53.6	81
Female	46	42.8	27.6 – 59.5	89	51.9	41.1 – 62.6	135

Long-Acting Cabotegravir Plus Rilpivirine In Adolescents With HIV: Week 24 Safety/PK

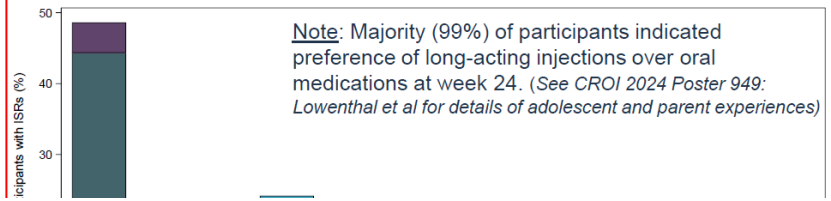
IMPAACT 2017 / More Options for Children and Adolescents (MOCHA) Study

ClinicalTrials.gov ID NCT03497676

Abstract 188
March 6, 2024

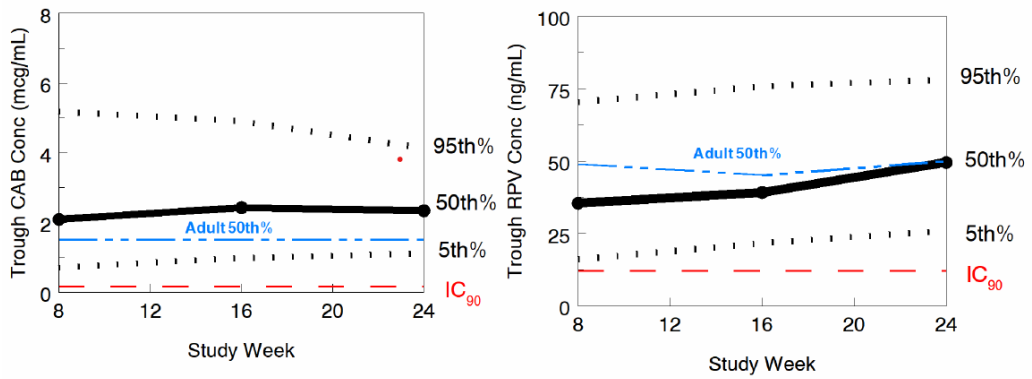
Aditya Gaur*#, Edmund Capparelli, Kristin Baltrusaitis, Mark Marzinke, Conn Harrington, Cindy McCoig, Herta Crauwels, Ellen Townley, John Moye, Sarah Buisson, Avy Violari, Pradthana Ounchanum, Chelsea Krotje, Carolyn Bolton Moore, IMPAACT 2017 Team

Injection Site Reactions (ISR) by study visit



Note: Majority (99%) of participants indicated preference of long-acting injections over oral medications at week 24. (*See CROI 2024 Poster 949: Lowenthal et al for details of adolescent and parent experiences)*

PHARMACOKINETICS

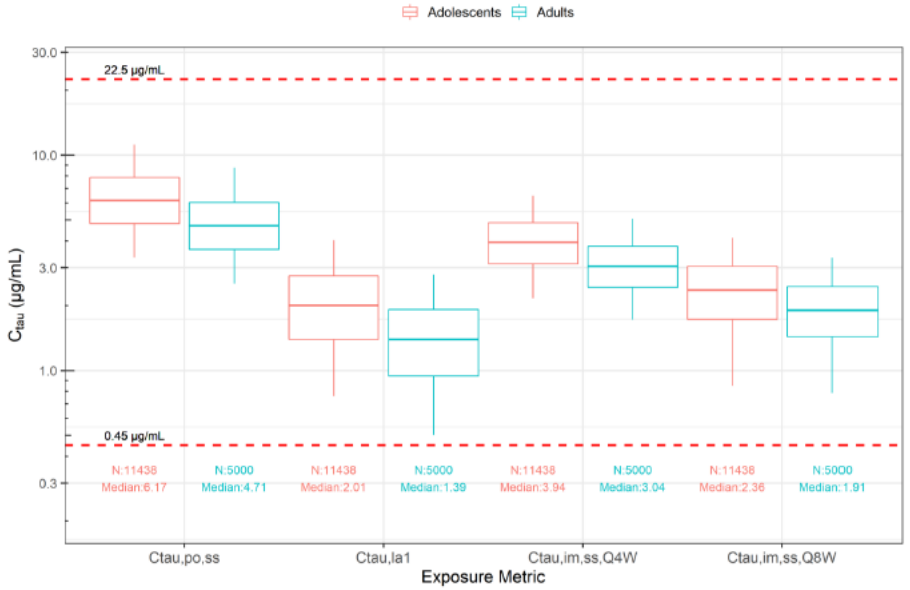


IMPAACT 2017 CAB and RPV troughs (Black lines - medians [solid] with 5th%-95th% [dashed]) compared to adults (Blue lines) from LATTE-2 / ATLAS-2M studies and protein adjusted IC_{90}s (Red lines)

Cabotegravir Population Pharmacokinetic Analysis of Adults & Adolescents Living with HIV or at Risk for HIV Receiving PrEP

Yu-Wei Lin,[1#] S. Y. Amy Cheung,[1#] Isabelle Deprez,[1] Susan Ford,[2] Jon Collins,[3] Cindy McCoig,[4] Conn M. Harrington,[3] Aditya Gaur,[5] Carolyn Bolton,[5] Lynda Stranix-Chibanda,[7] Sybil Hosek,[8] Mark Marzinke,[9] Brookie Best,[10] Edmund Capparelli,[10] for IMPAACT 2017 Team

Figure 4. Box Plot of C_{tau} Following Q4W and Q8W Dosing by Population



Notes: Ctau=plasma concentration at the end of the dosing interval; Ctau,im,ss=Ctau at steady state after the long-acting IM maintenance dose injections; Ctau,la1=Ctau at steady state after the first long-acting IM injection. The horizontal center solid line in each box represents the median value, the box represents the 25th to 75th percentiles, and the whiskers represent the 5th and 95th percentiles.

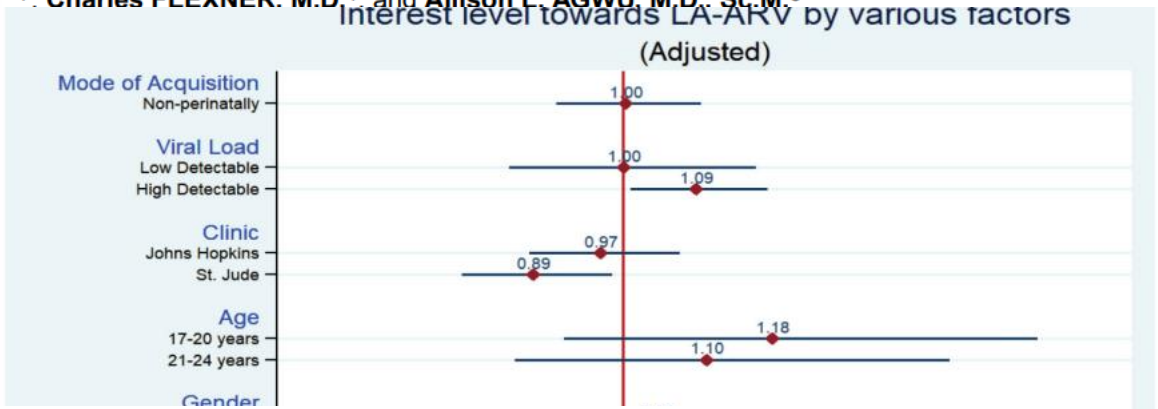
Conclude: "The slightly higher exposure in the adolescent participants is clinically insignificant.

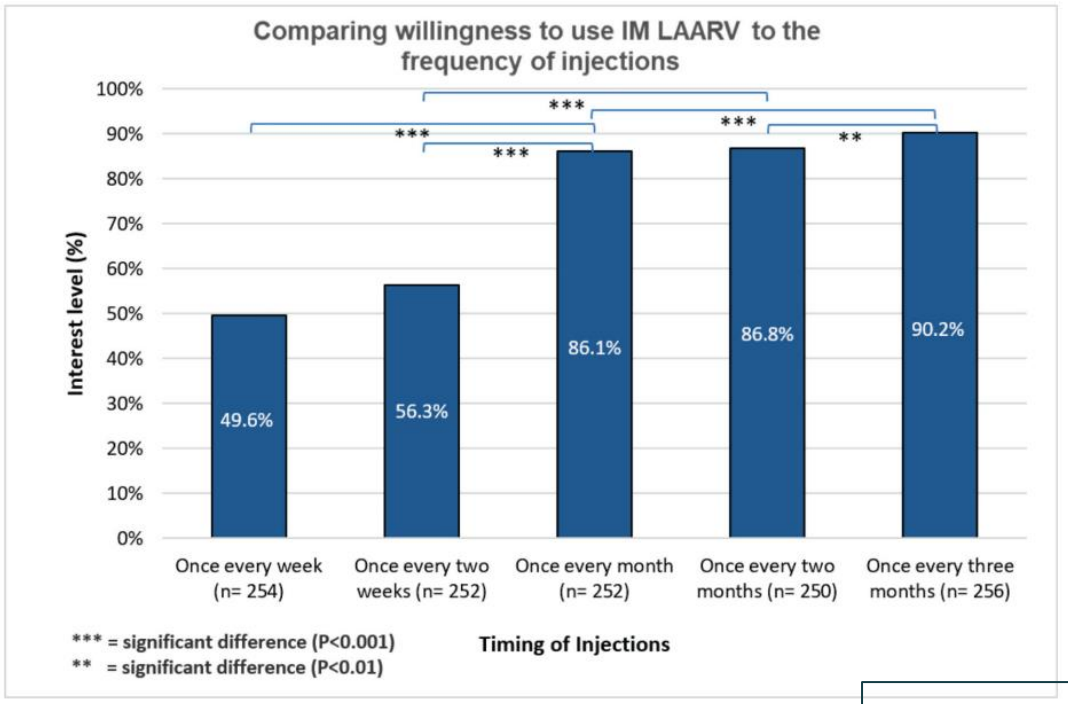
- No dose adjustment is recommended for adolescent participants (12 to <18 years of age) weighing at least 35 kg in accordance with the current label for CAB."

Given the similarity of CAB PK between adolescents and adults, no dose adjustment as compared to the current adult label for CAB is recommended for adolescent participants.

Interest of Youth Living with HIV in Long-Acting Antiretrovirals

Ethel D. WELD, M.D.[1], Md Sohel RANA, M.B.B.S., M.P.H.[2], Ronald H. DALLAS, Ph.D.[3], Andres F. CAMACHO-GONZALEZ, MD, M.P.H.[4,5], Patrick RYSCAVAGE, M.D., M.P.H.[6], Aditya H. GAUR, M.D.[3], Rana CHAKRABORTY, M.D., M.Sc., D.Phil.[4,5], Susan SWINDELLS, M.B.B.S.[7], Charles FLEXNER, M.D.[1], and Allison L. AGWU, M.D., Sc.M.[8]





IMPAACT 2017 Adolescent/Parent Experiences with LA Cabotegravir Plus Rilpivirine for HIV Treatment

Elizabeth D. Lowenthal[1,2], Jennifer Chapman[2], Martina Zapata Vaca[1], Shawn Ward[3], Ryan Milligan[3], Andres Camacho-Gonzalez[4], Gaerolwe Masheto[5], Cindy McCoig[6], Andi Ace[3], Rodica Van Solingen-Ristea[7], Dwight Yin[8], Sarah Buisson[9], Carolyn Bolton Moore[10], Aditya H. Gaur[11], for the IMPAACT 2017 Team

[1]University of Pennsylvania, Philadelphia, PA, USA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, USA, [3]Frontier Science and Technology Research Foundation, Inc, Amherst, NY, USA, [4]Emory University, Atlanta, GA, USA, [5]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana, [6]ViiV Healthcare, Madrid, Spain, [7]Janssen Research and Development, Beerse, Belgium, [8]National Institute of Allergy and Infectious Diseases, Rockville, MD, USA, [9]Fhi 360, Bangkok, Thailand, [10]University of Alabama at Birmingham-Centre for Infectious Disease Research in Zambia, Lusaka, Zambia, [11]St Jude Children's Research Hospital, Memphis, TN, USA

0949

TABLE 1. Characteristics of Cohort

	All Adolescent Participants (N=144)	Interviewed Adolescents (N=8)
Age	Median: 15 Range: 12-17	Median: 16 Range: 12-17
Female Sex	74 (51.4%)	3 (37.5%)
Race Asian Black/African White		
Mode of Infection Perinatal Not Perinatal		
Site Botswana South Africa Thailand Uganda USA	25 (17.4%) 43 (29.9%) 36 (25.0%) 20 (13.9%) 20 (13.9%)	0 0 0 0 8 (100%)

*2 adolescents did not complete week 8 (2 withdrew during oral lead-in); a third did not complete week 24 (pregnancy); a 4th did not complete week 48 (lost to follow-up)

The two most prominent perceived reducers of treatment burden with injectable treatment were: 1) Having the medical team's support and monitoring for adherence to each injection, and 2) Freedom from the daily reminder of HIV diagnosis seen as inherent to oral treatment.

TABLE 2. Reasons for Preferring Injectable Medicines

	Week 8 (N=138)	Week 24 (N=139)	Week 48 (N=140)
Convenience	73 (53%)*	89 (64%)	96
Uninterrupted lifestyle	4 (3%)	8 (6%)	15
No daily treatment	39 (28%)	49 (35%)	47
Burden Reduction	73 (53%)	64 (46%)	65
Anxiety reduction	28 (20%)	21 (15%)	12
Treatment fati			
Adherence			
Privacy			

*totals add up to >1 injectable medicines

Example Coded Data from Preferences Questionnaire:

"It's convenient!" (Convenience without subcode)

"Because I don't have to remember to take my tablets anymore at soccer." (Convenience, uninterrupted lifestyle)

"I don't have to wake up early to take my medicine." (Convenience, uninterrupted lifestyle)

"Because I do not have to take tablets every day." (Convenience, no daily treatment)

tion treatment is not so stressful" (Burden Reduction, anxiety reduction)

d of tablets" (Burden Reduction, treatment fatigue)

s and I would forget to take them" (Burden Reduction, adherence)

tion is more private" (Burden Reduction, Privacy)

on't ask me about the medicine if I get the injection" (Burden Reduction, Privacy)

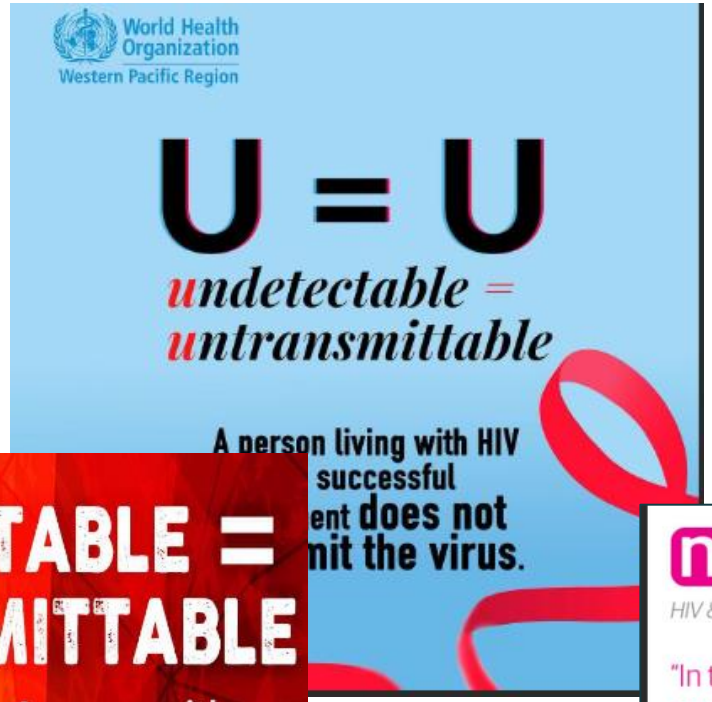
Example IDI Quotes:

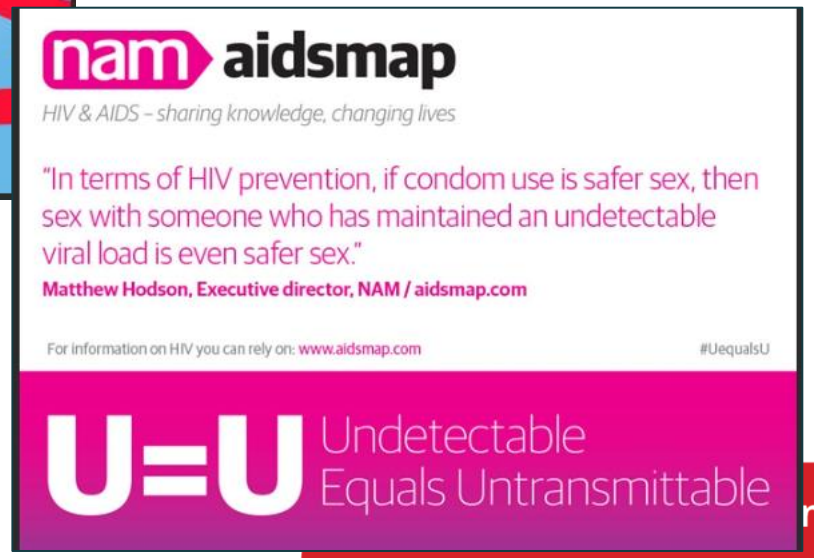
"(having HIV) gave me a whole bunch of worries and stigmas and being open about something like this could have people giving me like a side-eye almost. It feels so freeing. I just feel so lucky. I would much rather have these shots than win the lottery."
-17-year-old male

"And so (LAI) gave me the opportunity to live like a regular human……if someone were over at your house or something, they wouldn't have to see you taking medicine and wonder why."
-12-year-old female

Weld, JAIDS, 2019

U=U as a motivation for good ART adherence, especially in adolescents where disclosure to a partner may be difficult





Treatment as prevention (TASP)


Children

Despite progress towards Prevention of Vertical HIV transmission, around 120 K children still infected in 2023 and children have poor 95-95-95 outcomes

Far fewer children aged 0–14 years are acquiring HIV, a trend that is due largely
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2023.
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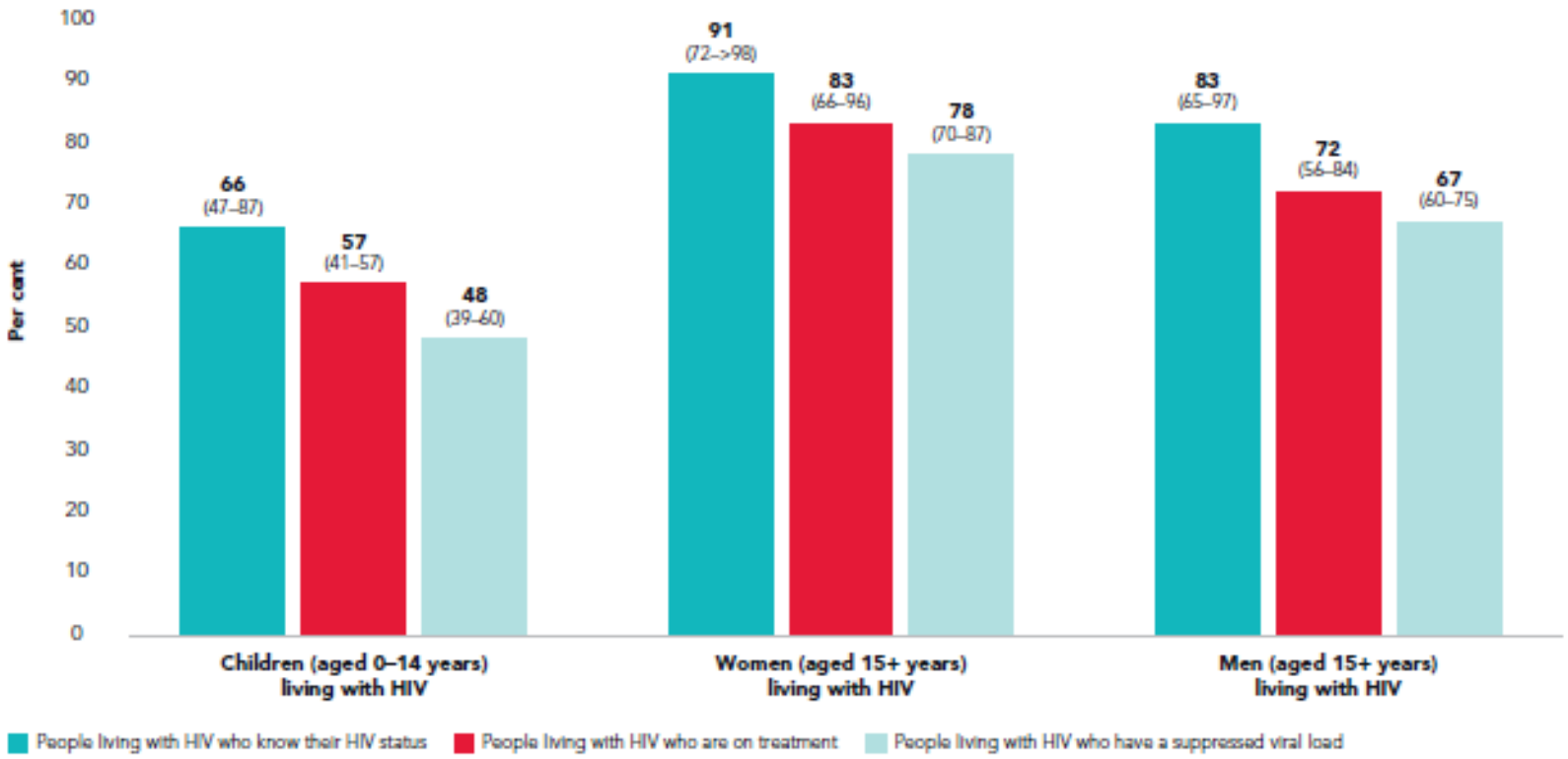
1.4 mi

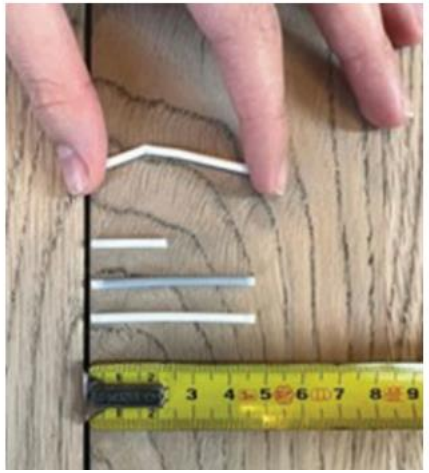
Figure 0.7 Testing and treatment cascade among children, women and men, global, 2023



Source: Further analysis of UNAIDS epidemiological estimates, 2024.

Acceptability of Implants for HIV Treatment in Young Children: Perspectives of Health Care Prov in Johannesburg, South Africa

Fiona Scorgie, PhD,[1,*] Imogen Hawley, MSc,[2,*] Lee Fairlie, MBChB, FCPaeds, MMED,[1] Shenaaz Pahad, MA Psych,[1] Florence Mathebula, BA (Hons),[1] Rebone Mohuba, BA (Hons),[1] Sarah-Jane London, MA,[1] Mackenzie L. Cottrell, PhD,[3] Leah M. Johnson, PhD,[4] and Elizabeth T. Montgomery, PhD[2]



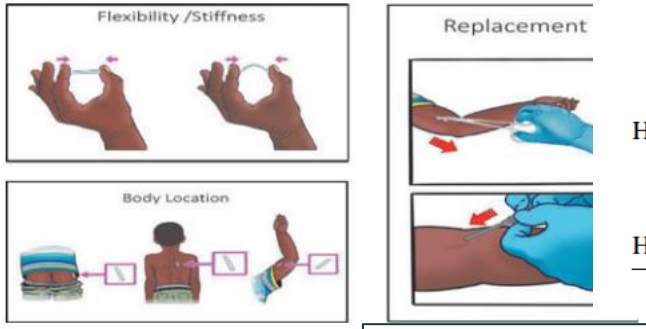


FIG. during implan Photo

FIG. 2. Examples of visual cue explain aspects of pediatric impla

TABLE 1. SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE SAMPLE (N=24)

Variable	n *(%)*
Age, years, median (IQR)	38 (30–44)
Gender	
Female	18 (75)
Male	6 (25)
Ethnicity	
Black	14 (58.3)
Indian/Asian	1 (4.2)
White	8 (33.3)
Other	1 (4.2)
Profession	
Doctor	8 (33.3)
Nurse	7 (29.2)
Counselor	7 (29.2)
Pharmacist/pharmacy assistant	2 (8.3)
Highest level of education	
Secondary school complete	2 (8.3)
Skills training certificate	1 (4.2)
College or university complete	21 (87.5)
Has some experience administering implants	10 (42)

IQR, interquartile range.

Children like to play or play games or watch TV, s... time to take treatment comes, the child starts to h... (Counsellor with 11 years in profession and ... experience).

"It allows them to be kids": perceived benefits of pediatric ART implants

Scorgie, AIDS PATIENT CARE AND STDS, 2022

South African Parents' and Grandparents' Perspectives on the Acceptability of Implant Delivery of Treatment to Young Children with HIV

Authors Imogen Hawley[1*], Alejandro Baez[1], Fiona Scorgie[2], Lee Fairlie[2], Florence Mathebula[2], Mackenzie Leigh Cottrell[3], Leah M. Johnson[4], and Elizabeth T. Montgomery[1,5].

Caregiver perspectives:

Current treatment options often involve adherence challenges, impact the lives of children, their caregivers, and their interactions within broader social settings. Caregivers felt that implants as a long-acting approach to HIV treatment may offer distinct advantages compared to the current treatment options. However, caregivers also cited some apprehensions about the hypothetical implant that they felt would limit acceptability if not addressed during its development.

Generally:

- Current treatment challenges
- Perceived advantages of the implant
- Uncertainties and potential disadvantages

"Lord, let there be at least a way [of administering HIV treatment] for children that is simpler. Because I have seen with my child... because no child asks for this [HIV positive status]."

I know personally it was painful as my hand was painful for two weeks [after insertion of the contraceptive implant]. So, like, in terms of pain, how do you overcome it as doctors and all that?"

Hawley, AIDS and Behaviour, 2024 (in press)

There are a few paediatric LAI studies ongoing..

IMPAACT 2036

Phase I/II Study of the Safety, Tolerability, Acceptability, and Pharmacokinetics of Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in Virologically Suppressed Children Living with HIV-1, Two to Less Than 12 Years of Age

CRAYON
IMPAACT 2036
Cabotegravir and Rilpivirine Long-Acting Injections in Young Children

GILEAD

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Study Title: A Phase 2, Open-label, Single-Arm Study to Evaluate the Pharmacokinetics, Safety, Tolerability, and Antiviral Activity of Long-Acting Lenacapavir in Combination With an Optimized Background Regimen in Treatment-experienced Adolescents and Children With HIV-1

Issues for LAI and treatment

Pros

- Improved adherence in chaotic periods
- Easier to administer
- Possibly fewer visits
- Decreased VL=decreased risk of vertical/horizontal transmission

Cons

- Resistance (esp with background high NNRTI resistance, increased risk of failure if VL increased)
- Increased staff capacity
- Painful and tricky to administer (z-track, RIL very viscous=painful

LAI as treatment-who should get it?

The potential role of long-acting injectable cabotegravir–rilpivirine in the treatment of HIV in sub-Saharan Africa: a modelling analysis

Andrew N Phillips, Loveleen Bansi-Matharu, Valentina Cambiano, Peter Ehrenkranz, Celicia Serenata, Francois Venter, Sarah Pett, Charles Flexner, Andreas Jahn, Paul Revill, Geoff P Garnett

Will result in increased numbers of PLHIV on ART
Decreased morbidity and mortality secondary to AIDS-related deaths
Less benefit in people with VL < 1000 copies/ml
Increased risks of INSTI resistance and NNRTI resistance
In people with VL < 1000 cps/ml, more adherent and therefore less risk of resistance compared to those with VL > 1000 cps/ml
Cost-effective if cost $120 per year and used in PLHIV with VL > 1000 cps/ml = suboptimal adherence

Increased implementation complexity:

- Including cold chain
- Syringes, mechanism (z-track)
- Co-administration of two separate products
- Possible need for an oral CAB–RPV dose lead-in dose (evaluate toxicity)
- Rule out hepatitis B before stopping tenofovir
- Treatment for active tuberculosis
- 1/2-monthly clinic visits, and time required at clinic

Phillips, Lancet Global Health, 2021

Long-acting agents in HIV prevention in niche populations

Increased risk of HIV acquisition in pregnancy and postpartum

Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners

Kerry A. Thomson,[1] James Hughes,[2] Jared M. Baeten,[1,3,4] Grace John-Stewart,[1,3,4,5] Connie Celum,[1,3,4,5] Craig R. Cohen,[6] Kenneth Ngure,[3,7] James Kiarie,[3] Nelly Mugo,[3,8] and Renee Heffron,[1,3]; for the Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study Teams[a]

Table 5. HIV Acquisition Probability and Relative Risk (RR) of HIV Acquisition Among 2751 African Women With HIV-Infected M Reproductive Stage

	Base Model[a]			Adjusted Model[b]	
Reproductive Stage	Probability[c] of HIV Acquisition per Condomless Sex Act (95% CI)	RR[d] for per-Act Probability of HIV Acquisition (95% CI)	*P*	Probability[c] of HIV Acquisition per Condomless Sex Act (95% CI)	RR[d] for pe Probability Acquisition (9
Early pregnancy through postpartum period	0.0027 (0.0009, 0.0074)	4.97 (2.95, 8.38)	<.001	0.0029 (0.004, 0.0093)	2.76 (1.58, 4.
Early pregnancy	0.0018 (0.0003, 0.0070)	3.20 (1.24, 8.25)	.02	0.0022 (0.0004, 0.0093)	2.07 (0.78, 5.
Late pregnancy	0.0031 (0.0008, 0.0102)	5.54 (2.62, 11.69)	<.001	0.0030 (0.0007, 0.0108)	2.82 (1.29, 6.
Postpartum period	0.0044 (0.0008, 0.0167)	7.80 (3.04, 20.02)	<.001	0.0042 (0.0007, 0.0177)	3.97 (1.50, 10
Nonpregnant/nonpostpartum periods	0.0005 (0.0003, 0.0009)	1.00	…	0.0011 (0.005, 0.0019)	1.00

Early pregnancy was defined as the interval from the start of pregnancy (typically the time of the last menstrual period) to gestation week 13. Late pregnancy was defined as the interval from gestation week 14 to the end of pregnancy. The postpartum period was defined as the interval from the end of pregnancy to month 6 after delivery (for women with live births), week 6 after pregnancy loss (for women with pregnancy loss at gestation week ≥20 or newborn death), or week 4 after pregnancy loss (for women with pregnancy loss during gestation weeks 6–19).

Abbreviations: CI, confidence interval; PrEP, preexposure prophylaxis.

[a]Adjusted for condom use and reproductive stage.

[b]Adjusted for condom use, reproductive stage, male partner viral load, female partner age, and active PrEP for women randomly assigned to receive and dispensed active PrEP in the Partners PrEP study.

[c]Adjusted absolute HIV acquisition probabilities among female partners represent infectivity estimates per condomless sex act with an HIV-infected partner with a viral load of 10 000 copies/mL for a 25-year-old female partner not taking PrEP.

[d]The reference group for the adjusted model represents a condomless sex act with an HIV-infected partner with a viral load of 10 000 copies/mL for a 25-year-old female not taking PrEP occurring while the woman is not pregnant or is in the postpartum period.

Thomson, JID, 2018

Incident HIV during Pregnancy and Postpartum and Risk of Mother-to-Child HIV Transmission: A Systematic Review and Meta-Analysis

Alison L. Drake[1]*, Anjuli Wagner[2], Barbra Richardson[1,3,4], Grace John-Stewart[1,2,5,6]

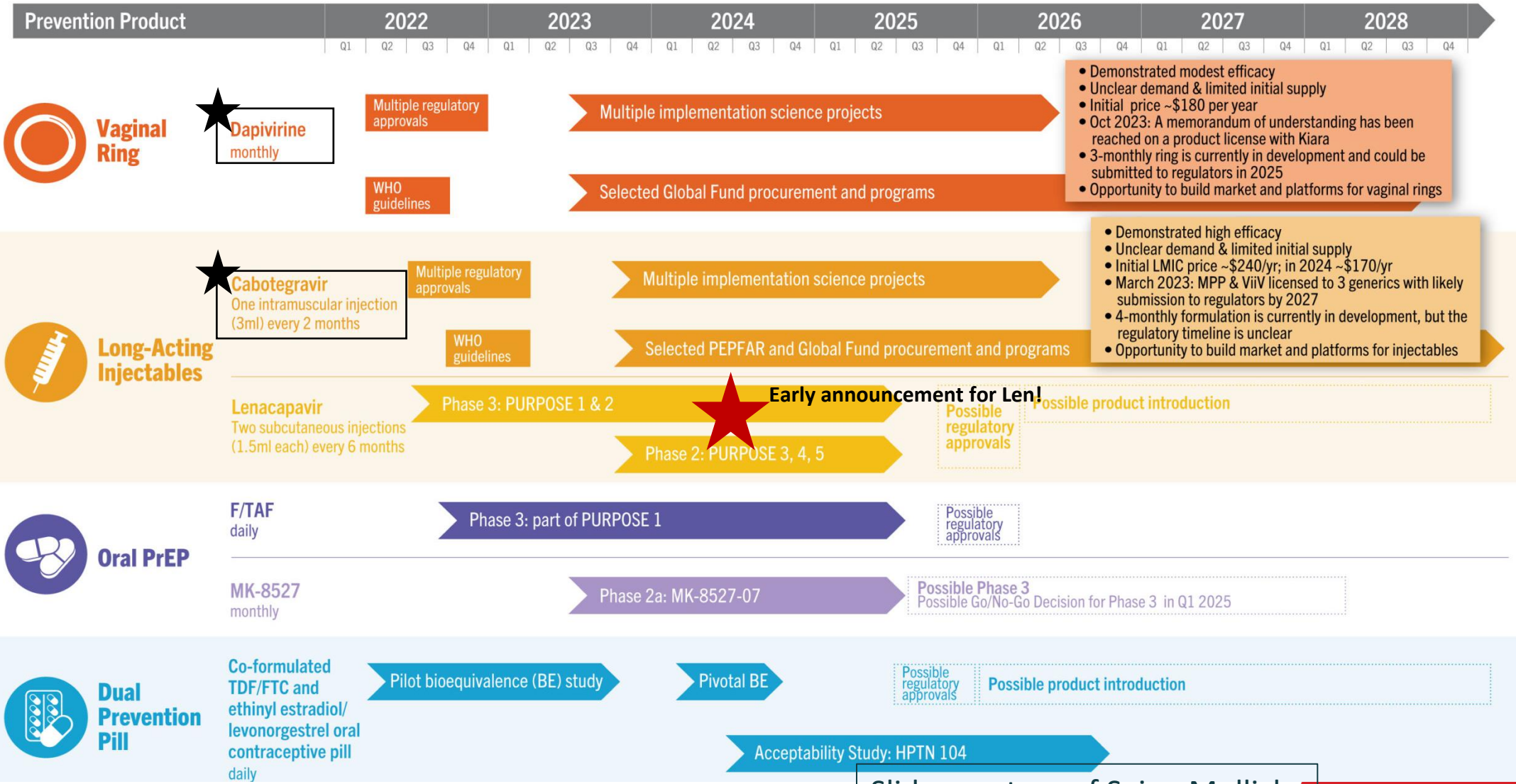
Methods and Findings: We searched PubMed, Embase, and AIDS-related conference abstracts between January 1, 1980, and October 31, 2013, for articles and abstracts describing HIV acquisition during pregnancy/postpartum. The inclusion criterion was studies with data on recent HIV during pregnancy/postpartum. Random effects models were constructed to pool HIV incidence rates, cumulative HIV incidence, hazard ratios (HRs), or odds ratios (ORs) summarizing the association between pregnancy/postpartum status and HIV incidence, and MTCT risk and rates. Overall, 1,176 studies met the search criteria, of which 78 met the inclusion criterion, and 47 contributed data. Using data from 19 cohorts representing 22,803 total person-years, the pooled HIV incidence rate during pregnancy/postpartum was 3.8/100 person-years (95% CI 3.0–4.6): 4.7/100 person-years during pregnancy and 2.9/100 person-years postpartum ($p = 0.18$). Pooled cumulative HIV incidence was significantly higher in African than non-African countries (3.6% versus 0.3%, respectively; $p<0.001$). Risk of HIV was not significantly higher among pregnant (HR 1.3, 95% CI 0.5–2.1) or postpartum women (HR 1.1, 95% CI 0.6–1.6) than among non-pregnant/non-postpartum women in five studies with available data. In African cohorts, MTCT risk was significantly higher among women with incident versus chronic HIV infection in the postpartum period (OR 2.9, 95% CI 2.2–3.9) or in pregnancy/postpartum periods combined (OR 2.3, 95% CI 1.2–4.4). However, the small number of studies limited power to detect associations and sources of heterogeneity.

Pooled vertical transmission rate 22.7%
2-3 times higher risk of vertical transmission with incident compared to chronic HIV infection

Drake, PLOS Med, 2014

We have two new approved products.....and a new product on the horizon

Time to Market



Does not include the 3-monthly ring or 4-monthly CAB-LA: regulatory pathway and timeline unclear.

★ Current products available through IS studies

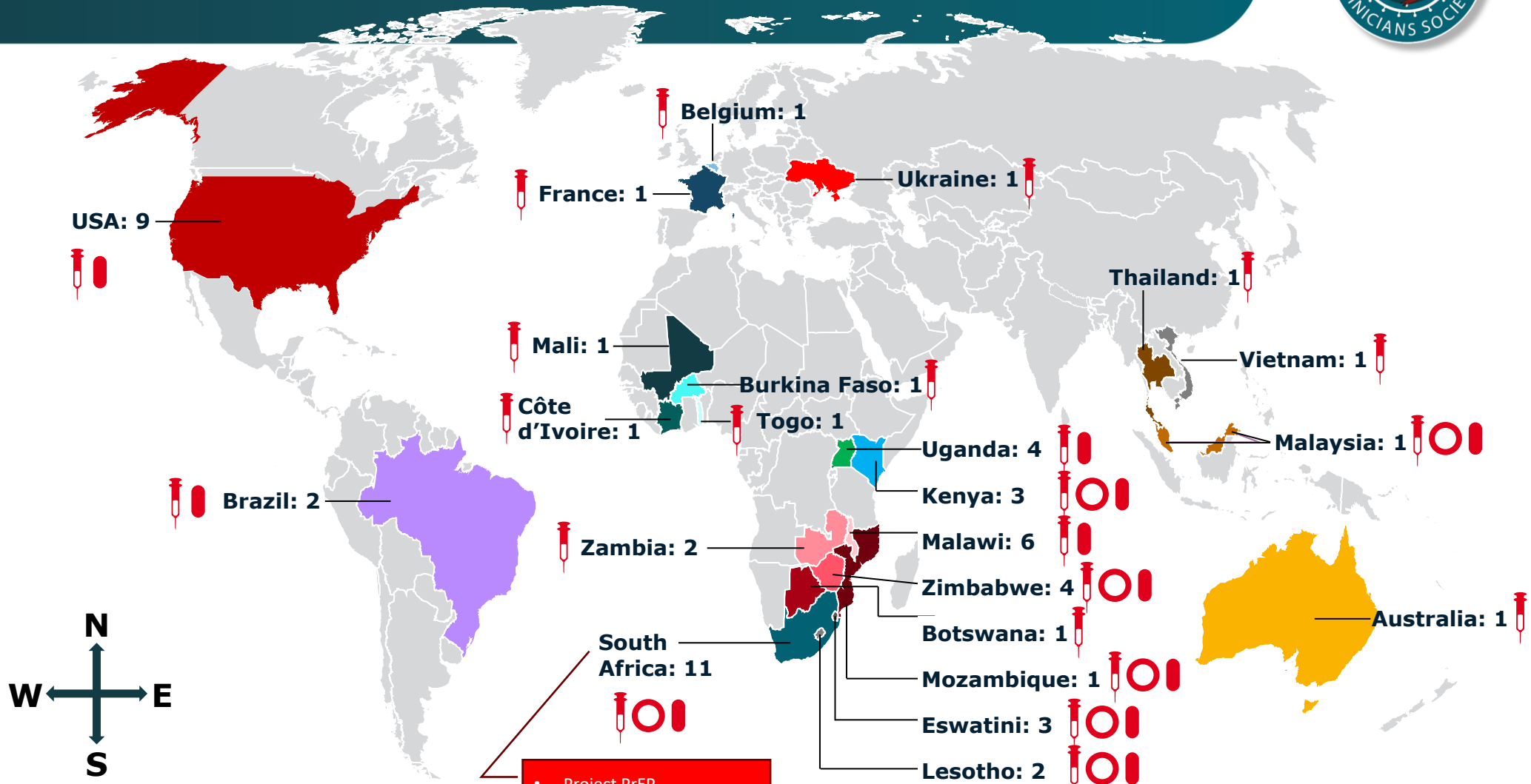
Slide courtesy of Saiqa Mullick

PrEParing for New Products: Geographically

44

CAB for PrEP and DVR *Implementation Science* studies across the globe:

Some studies are happening in more than one country, with a total of 44 studies in 23 countries



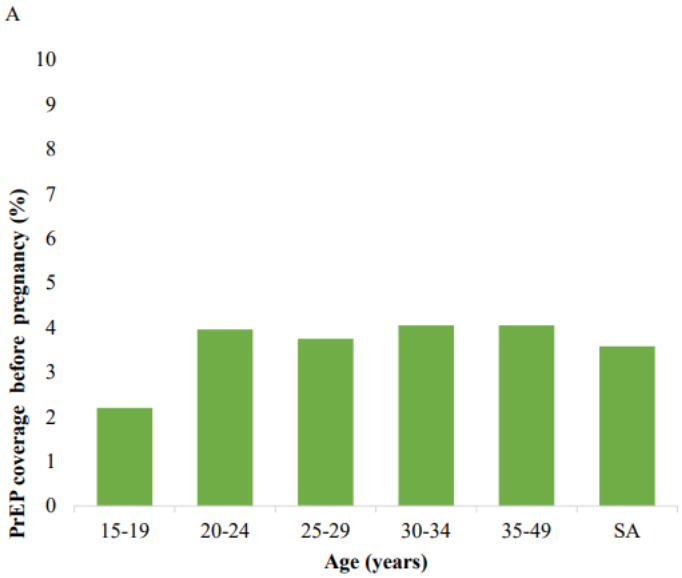
Currently no demonstration studies on Lenacapavir.

Slide courtesy of Saiqa Mullick

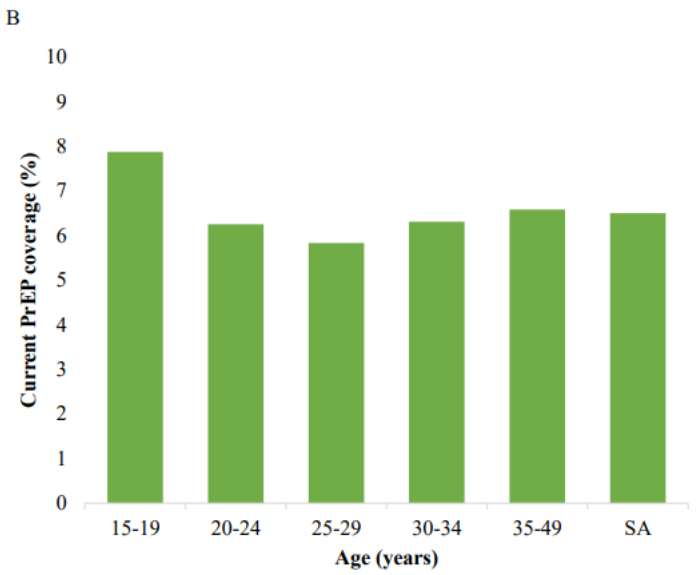
BioPIC Implementation Study Tracker

PrEP coverage remains low in routine services

PrEP Coverage Before/During Pregnancy by Age



The denominator for PrEP coverage before pregnancy was the number of HIV-negative women who met the PrEP eligibility criteria. Missing data excluded.



The denominator for PrEP coverage during current pregnancy was the number of HIV-negative women who met the PrEP eligibility criteria. Missing data excluded.

NICD, 2024

Increasing data available on LAI, specifically CAB-LA

HPTN 084

Long-acting Injectable For the Epidemic

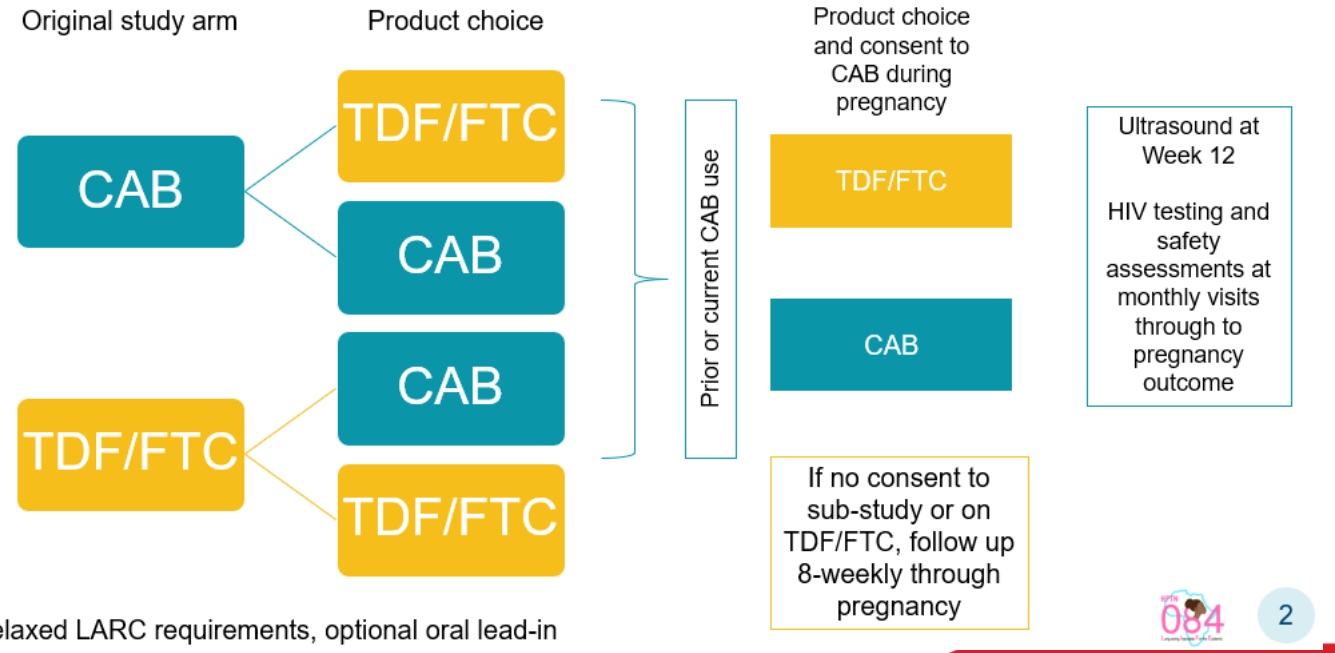
HPTN HIV Prevention Trials Network

Initial evaluation of injectable cabotegravir (CAB-LA) safety during preg
084 open-la

S Delany-Moretlwe, Bhondai-Mhuri, P Mpendo, P Nahirya Bock, C Mathev Nuwagaba-Birib Mudhune, J Farrior Soto-Torres, S Zwe Hosseinipour on

OLE Study design

HPTN HIV Prevention Trials Network



Relaxed LARC requirements, optional oral lead-in

Slide courtesy of Sinead Delany-Moretlwe

OLE participant disposition

From start of OLE until 31 DEC 2023

2472 participants
joined the OLE

410 participants
had ≥ 1 pregnancy recorded

312 participants
had ≥1 pregnancy with a recor

325 pregnancies with record
(n=64 pregnancies at time of OLE s

320 pregnancies with
5 pregnancies with 2 c

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			
Total no. CAB injections pre-pregnanc			
None			
1 to 3			
> 3			
Median interval between last injection positive pregnancy test (weeks)			
Median no. CAB injections during pre			

OLE maternal adverse events, by exposure

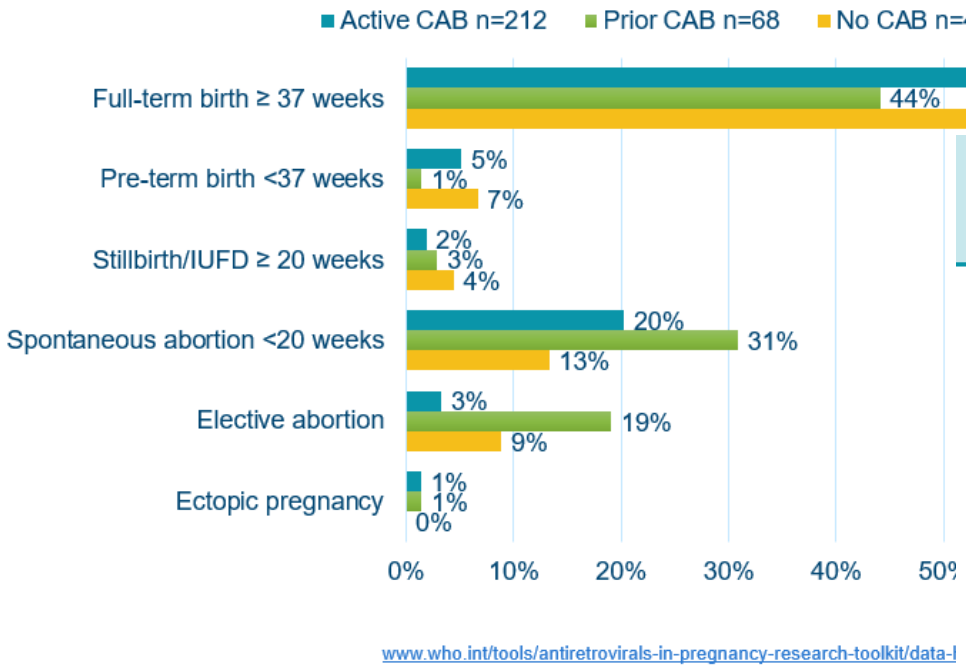
	Active CAB-LA n (95% CI)	Prior CAB-LA n (95% CI)	No CAB-LA n (95% CI)
Any Grade 2+ AE incidence rate*	376 (337-417)	282 (208-374)	238 (168-326)
Pregnancy-related Grade 2+ AE incidence rate*	38 (27-53)	47 (20-93)	31 (10-73)
Gestational hypertension	9 (4-17)	6 (<1-33)	6 (<1-35)
Hyperemesis gravidarum	6 (2-14)	12 (1-42)	0 (0-23)
Afterbirth pain	6 (2-14)	6 (<1-33)	0 (0-23)
Pre-eclampsia	3 (1-9)	0 (0-22)	6 (<1-35)
Meconium-stained amniotic fluid	2 (<1-8)	0 (0-22)	0 (0-23)
Premature labour	1 (<1-6)	0 (0-22)	6 (<1-35)
Foetal distress	1 (<1-6)	6 (<1-33)	0 (0-23)
Post-partum haemorrhage	1 (<1-6)	6 (<1-33)	0 (0-23)
Cephalo-pelvic disproportion	0 (0-4)	6 (<1-33)	13 (2-45)

** Per 100 person-years*

No difference in weight gain during pregnancy across exposure groups
No difference in modes of delivery across exposure groups

Slide courtesy of Sinead Delany-Moretlwe

OLE pregnancy outcomes, by exposure



www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit/data-l

Similar composite birth outcomes, although high rates of spontaneous and elective abortions in the prior CAB group
No difference in infant growth parameters per exposure group

Conclusions

- Maternal, pregnancy and infant 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
- Initial data provide reassurance regarding use of CAB in pregnancy in populations where pregnancy and HIV incidence are high.
  - High pregnancy incidence allows for ongoing accrual of safety information

Slide courtesy of Sinead Delany-Moretlwe

HPTN 084 Long-acting Injectable For the Epidemic

Evaluation of Long-Acting Cabotegravir (CAB-LA) Pharmacokinetics During Pregnancy: A Sub-Study Analysis of the HPTN 084 Open Label Extension Study

Marzinke MA, Voldal E, Hanscom BS, Guo X, Piwowar-Manning E, Agyei Y, Farrior J, Stranix-Chibanda L, Nakabiito C, Saidi F, Ford SL, Rinehart AR, Rooney J, Soto-Torres L, Cohen MS, Hosseinipour M, Delany-Moretlwe S, HPTN 084 Study Team

AIDS 2024
Session: Use of long-acting injectable cabotegravir in pregnant and lactating people

HPTN HIV Prevention Trials Network

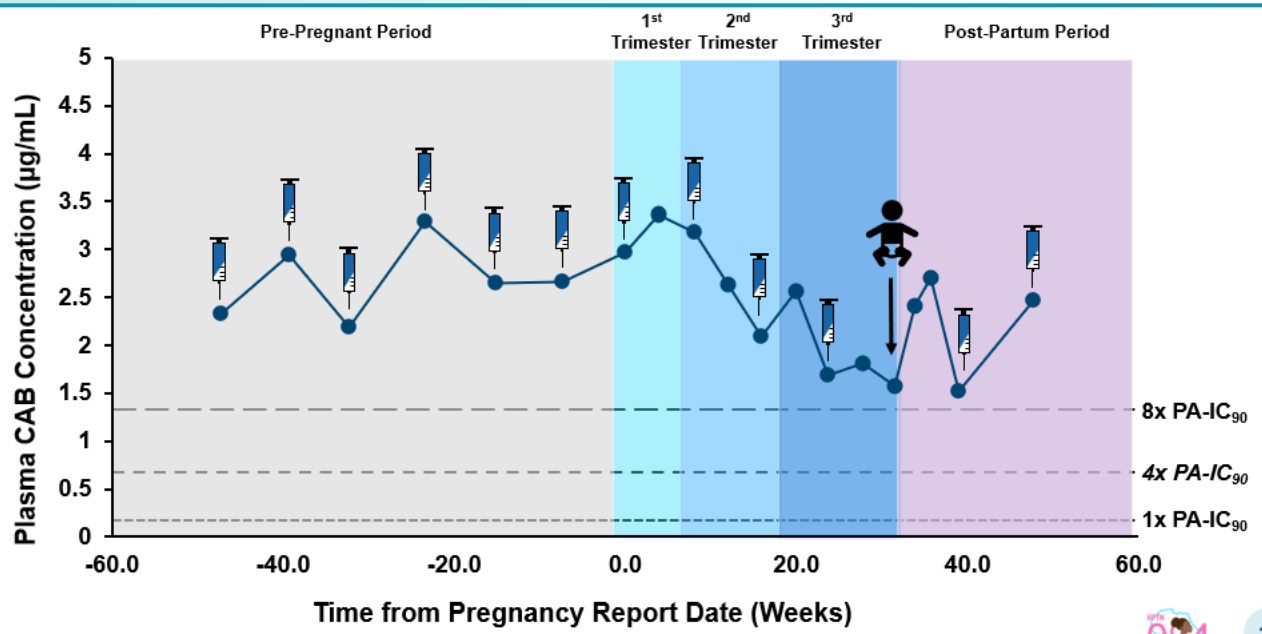
CAB-LA C_{trough} Ratios Betwe Pregnant and Pregnant Peric

	Pregnancy/ Total Pre-Pregnancy	1st Trimester/ Total Pre-Pregnancy	
CAB-LA C_{trough} Ratio*			
Median (Q1, Q3)	0.9 (0.7, 1.5)	1.3 (1.0, 1.9)	0.9 (0
95% CI for median	0.9, 1.1	1.1, 1.7	0.8

*A ratio of 1.0 means no difference between pre-pregnancy and pregnancy

- Ratios of C_{trough} CAB concentrations between pre- pregnant periods were calculated for each particip summarized across the cohort
- CAB-LA C_{trough} ratios decline from the 1st through and are lowest during the 3rd trimester

Example CAB-LA Concentration Time Profile



HPTN HIV Prevention Trials Network

- 100% of participants evaluated in 1st and 2nd trimesters and 98% of participants evaluated in the 3rd trimester yielded average C_{trough} concentrations above the protocol-specified threshold for CAB-LA 600 mg (4x $PA\text{-}IC_{90}$)
- While dose modifications are unlikely for those who continue CAB-LA during pregnancy, additional analyses are required
  - Analysis of additional 25 participants who continued to receive CAB-LA injections during pregnancy
  - Contribution of weight, BMI, and protein concentrations on CAB-LA pharmacokinetics during pregnancy
  - Determination of unbound CAB-LA concentrations

Slide courtesy of Sinead Delany-Moretlwe

PrEP and special populations

Journal of Adolescent Health 73 (2023) S4–S7

JOURNAL OF ADOLESCENT HEALTH

Commentary

Implementing Differentiated and Integrated PrEP Services for Adolescent Key Populations: What Works and What Is the Way Forward?

Inês Dourado, M.D., Ph.D., M.P.H. [a,*], Saiqa Mullick, M.D., Ph.D. [b], Laio Magno, Ph.D., M.Sc. [c], Alexandre Grangeiro [d]

[a] Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, Bahia, Brazil
[b] Wits RHI, University of the Witwatersrand, Johannesburg, South Africa

Clinical Trial > AIDS Behav. 2023 Dec;27(12):4114-4123. doi: 10.1007/s10461-023-04125-w. Epub 2023 Jul 11.

Acceptability and Use of the Dapivirine Vaginal Ring and Daily Oral Pre-exposure Prophylaxis (PrEP) During Breastfeeding in South Africa, Malawi, Zimbabwe, and Uganda

Marie C D Stoner [1], Imogen Hawley [2], Florence Mathebula [3], Elizea Horne [3], Juliane Etima [4], Doreen Kemigisha [4], Prisca Mutero [5], Adlight Dandadzi [5], Linly Seyama [6], Zayithwa Fabiano [6], Rachel Scheckter [7], Lisa Noguchi [8], Elizabeth T Montgomery [2]

Affiliations + expand

PMID: 37432541 PMCID: PMC1061

DOI: 10.1007/s10461-023-04125-w

PLOS ONE

RESEARCH ARTICLE

A randomized trial of safety, acceptability and adherence of three rectal microbicide placebo formulations among young sexual and gender minorities who engage in receptive anal intercourse (MTN-035)

Jose A. Bauermeister[1]*, Clara Dominguez Islas[2,3], Yuqing Jiao[2,3], Ryan Tingler[1], Elizabeth Brown[2], Jillian Zemanek[2], Rebecca Giguere[4], Ivan Balan[4], Sherri Johnson[5], Nicole Macagna[5], Jonathan Lucas[5], Matthew Rose[5], Cindy Jacobson[6], Clare Collins[6], Edward Livant[6], Devika Singh[6], Ken Ho[7], Craig Hoesley[8], Albert Liu[9], Noel Kayange[10], Thesla Palanee-Phillips[11,12], Suwat Chariyalertsak[13], Pedro Gonzales[14], Jeanna Piper[15], on Behalf of the MTN-035 Protocol Team[¶]

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Check for updates

OPEN ACCESS

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RECEIVED 17 May 2023

Evaluating the use of oral pre-exposure prophylaxis an pregnant and postpartum adolescent girls and young women in Cape Town, South Africa

Nehaa Khadka[1]*, Pamina M. Gorbach[1], Dorothy C. Nyemba[2,3], Rufaro Mvududu[2], Nyiko Mashele[2], Marjan Javanbakht[1], Roch A. Nianogo[1], Grace M. Aldrovandi[4], Linda-Gail Bekker[5],

White RR et al. Journal of the International AIDS Society 2023, 26(S2):e26120
http://onlinelibrary.wiley.com/doi/10.1002/jia2.26120/full | https://doi.org/10.1002/jia2.26120

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

NT

pregnant and breastfeeding people in trials of novel P agents: perspectives from sub-Saharan Africa y stakeholders

[1,8], Molly C. Dyer[1], Mina C. Hosseinipour[2] and Sinead Delany-Moretlwe[3]

Rhonda Renee White, 1742 McLaurin Lane, Fuquay Varina, NC 27526, USA. Tel: 1-919-321-3598. (rwhite@fhi360.org)

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deliver

A Safety Study of a Dapivirine Vaginal Ring and Oral PrEP for the Prevention of HIV During Pregnancy

Bunge*, Balkus, Mhlanga, Mayo, Fairlie, Nakabiito, Gadama, Chappell, Piper, Chakhtoura, Szydlo, Richardson and Hillier
*University of Pittsburgh

Dr. Hillier receives support for her institution and herself from Merck
Dr. Chappell receives research funding and served as a consultant to Gilead Sciences

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Author man
AIDS Behav.

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Correlates of Dapivirine Vaginal Ring Acceptance among Women Participating in an Open Label Extension Trial

Brenda Gati Mirembe[1,16,17], Maria Valdez Cabrera[2], Ariane van der Straten[3,4], Rita Nakalega[1], Mandy Cobbing[5], Nyaradzo M. Mgodi[6], Thesla Palanee-Phillips[7], Ashley J. Mayo[8], Sufia Dadabhai[9], Leila E. Mansoor[10], Samantha Siva[5], Gonasagrie Nair[11], Lameck Chinula[12], Carolyne A. Akello[1], Clemensia Nakabiito[1], Lydia E. Soto-Torres[13], Jared M. Baeten[14,15], Elizabeth R. Brown[2,16]

frontiers | Frontiers in Reproductive Health

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Safety surveillance for PrEP in pregnant and breastfeeding women

Lee Fairlie[1]*, Diane Lavies[2], Emma Kalk[2], Otty Mhlongo[1], Faeezah Patel[1], Karl-Günter Technau[4], Sana Mahtab[3], Dhayendre Moodley[5], Hasina Subedar[7], Saiqa Mullick[1], Shobna Sawry[1] and Ushma Mehta[2]

MTN

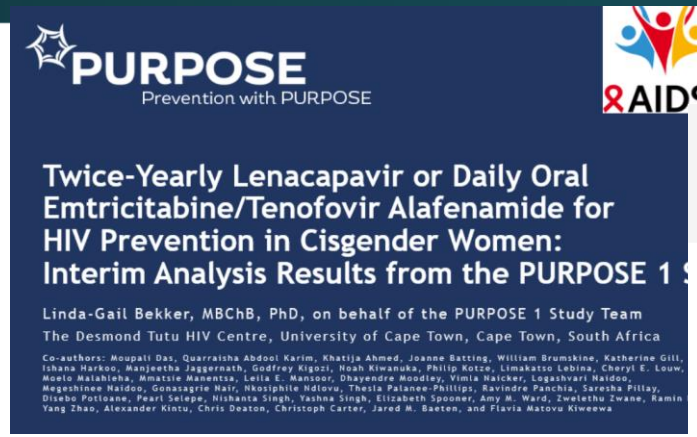
deliver

Safety Outcomes Among Infants Whose Mothers Used Dapivirine Vaginal Ring or Oral PrEP During pregnancy (MTN-042/DELIVER)

Lee Fairlie, Daniel W Szydlo, Ashley J Mayo, Katie Bunge, Felix Mhlanga, Jeanna Piper, Sufia Dadabhai, Vanessa M Gatsi, Elizea Horne, Phionah Kibalama Ssemambo, Vitumbiko D Mandiwa, Nyaradzo M Mgodi, Maxensia Owor, Rachel Scheckter, Catherine Chappell, Sharon L Hillier
For the MTN-042 team

Slide courtesy of Saiqa Mullick

PURPOSE 1 Study



Adherence to Lenacapavir was excellent, to F/TDF and F/TAF poor
No safety concerns
Injection pain improved with each dose

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

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Baseline Characteristics

Characteristic	LEN, n = 2138	F/TAF, n = 2137	F/TDF, n = 1070
Age, years, median (range)	21 (16-25)	21 (16-26)[a]	21 (16-25)
Age 16 to <18, years, n (%)	56 (2.6)	45 (2.1)	23 (2.1)
Black race,[b] n (%)	2135 (99.9)	2136 (100)	1068 (99.8)
Highest education level college/university,[c] n (%)	183 (8.6)	198 (9.3)	109 (10.2)
Marital status, n (%)			
Married	26 (1.2)	30 (1.4)	17 (1.6)
Living with primary partner	148 (6.9)	132 (6.2)	73 (6.8)
STIs, n (%)			
Chlamydia trachomatis	520 (24.3)	562 (26.3)	263 (24.6)
Neisseria gonorrhoeae	197 (9.2)	178 (8.3)	90 (8.4)
Trichomonas vaginalis	154 (7.2)	165 (7.7)	82 (7.7)
Syphilis	57 (2.7)	63 (2.9)	29 (2.7)
Any prior use of PrEP, n (%)	143 (6.7)	121 (5.7)	71 (6.6)
Any prior HIV testing, n (%)	1713 (80.1)	1731 (81.0)	860 (80.4)
Median time since last HIV test, months (Q1, Q3)	6.8 (4.7, 11.5)	6.6 (4.8, 11.0)	6.5 (4.6, 11.0)

Participants

84.3%
South Africa

15.7%
Uganda

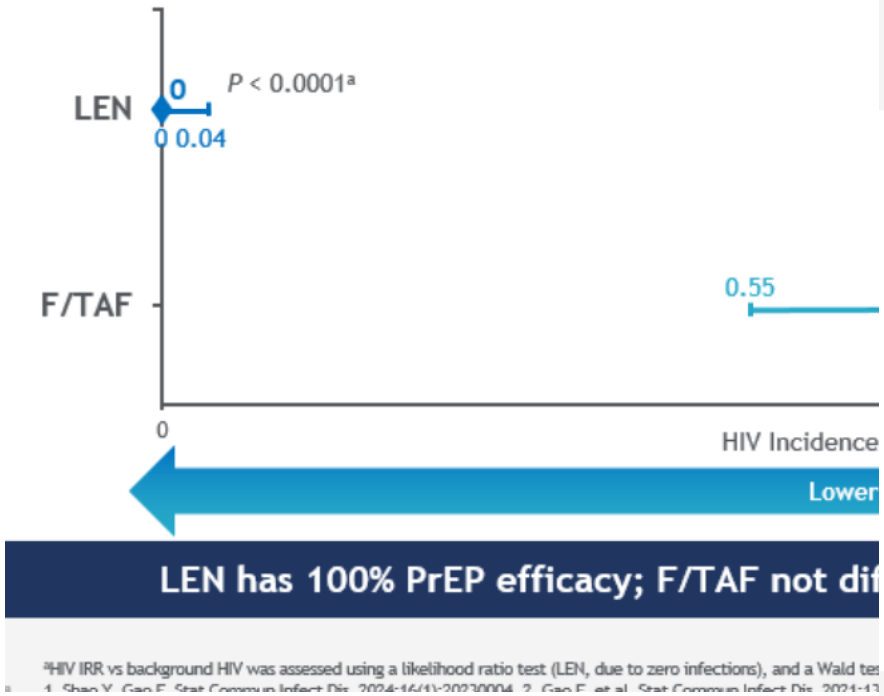
Baseline demographics and clinical characteristics were balanced across randomized groups

Seven participants were subsequently determined to have had HIV infection at the time of randomization, and thus 5338 were included in the modified intention-to-treat efficacy analysis. [a]One participant was aged 25 years at screening but turned 26 by randomization—this was not a violation of eligibility criteria. [b]All non-Black participants were multiracial; [c]Sample size LEN: 2136; F/TAF: 2134; F/TDF: 1069
Q, quartile; STI, sexually transmitted infection.

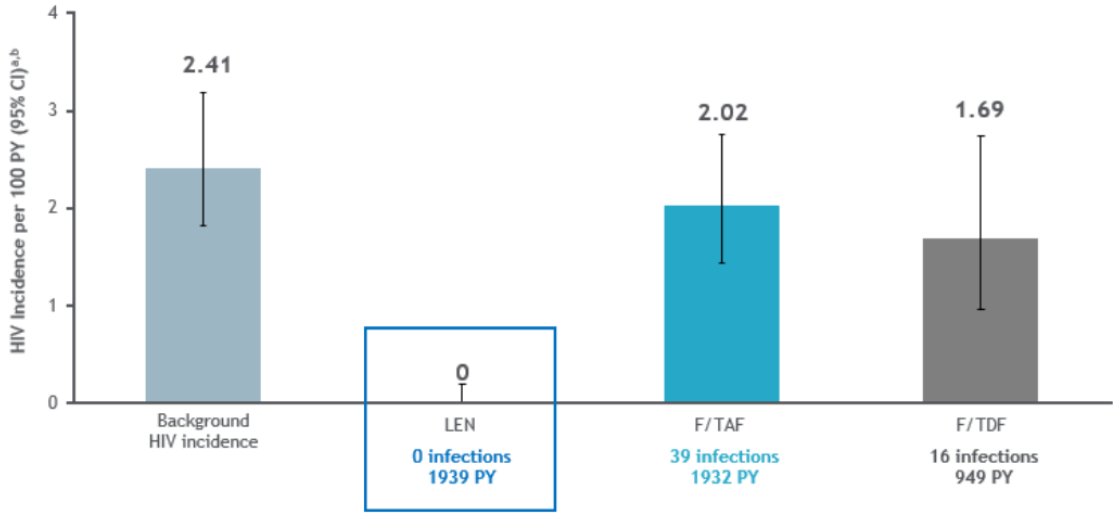
Bekker, AIDS 2024, Bekker, NEJM, 2024

Of particular concern is the low adherence to oral TAF or TDF

Primary Analysis: LEN has 100% Efficacy for PrEP



Zero HIV Infections in Cisgender Women receiving LEN



[a]Overall n: background HIV incidence group 8094; LEN, 2134; F/TAF, 2136; F/TDF, 1068. [b]95% CIs: background HIV incidence group 1.82, 3.19, LEN 0, 0.19, F/TAF 1.44, 2.76. F/TDF 0.96, 2.74.
CI, confidence interval; PY, person-years.

Bekker, AIDS 2024, Bekker, NEJM, 2024

HIV prevention and cure/optimization in children

bNAbs hold promise for treatment (cure, viral control) and prevention

Safety, Tolerability, and Pharmacokinetics of the Broadly Neutralizing Human Immunodeficiency Virus (HIV)-1 Monoclonal Antibody VRC01 in HIV-Exposed Newborn Infants

Coleen K. Cunningham,[1] Elizabeth J. McFarland,[2] R. Leavitt Morrison,[3] Edmund V. Capparelli,[4] Jeffrey T. Safrit,[5,a] Lynne M. Mofenson,[5] Bonnie Mathieson,[6,b] Megan E. Valentine,[7] Charlotte Perlowski,[7] Betsy Smith,[8] Rohan Hazra,[9] Lynette Purdue,[10] Petronella Muresan,[3,11] Paul A. Harding,[2] Tapiwa Mbengeranwa,[12] Lisa-Gaye Robinson,[13] Andrew Wiznia,[14] Gerhard Theron,[15] Bob Lin,[16] Robert T. Bailer,[16] John R. Mascola,[16] and Barney S. Graham[16]; for the IMPAACT P1112 team

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

NIH National Institute of Allergy and Infectious Diseases

Red HIV/AIDS awareness ribbons and red antibodies on a blue and white background.

Credit: NIAID

Researchers are also evaluating bNAb-based HIV cure strategies in children through the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network. The IMPAACT P1115 study has examined very early HIV treatment strategies in infants who were exposed to or acquired HIV before birth. The study is assessing VRC01 and VRC07-523LS to see whether these bNAbs, when given with ART early in life, may enable ART-free remission in children. Another study, IMPAACT 2042, will evaluate the use of three bNAbs, VRC07-523LS, PGDM1400LS, and PGT121.414.LS, in c[illegible] ages of 2 and 25 to determine whether the bNAbs can be part[illegible] from the body.

PedMAb

The 3 steps are summarized below.

Step 1 : single bNab		Step 2 : combined bNabs	Step 3 : combined bNabs multiple administrations
Group 1 : CAP256V2LS (@96h) Arm 1: Dose 5 Arm 2: Dose 10 Arm 3: Dose 20	Group 2: VRC07-523LS (@<96h) Arm 4: Dose 20 Arm 5: Dose 30	Group 3: CAP256V2LS + VRC07-523LS (@<96h) Arm 6: 60 + 90	Group 3 continued: CAP256V2LS + VRC07-523 LS (@ 3 months) Arm 6b: 120 + 120

NIAID, 2024; Cunningham, JID, 2020

Potential for LAI in infant prophylaxis

- CAB LA
- Lenacapavir
- bNAbs
- Potential gamechanger especially where difficulties with maternal ART adherence during breastfeeding

Benefits of LAI Drugs in African Context

- Improved Adherence:
  - Many patients struggle with daily oral medications due to stigma, forgetfulness
  - This may occur more frequently during “chaotic” life periods
  - LAI drugs administered every few weeks or months ensure steady exposures, VL suppression
- Reduced Stigma:
  - Monthly or quarterly injections are discrete, reducing stigma associated with daily oral medication.
- Lower Healthcare Resource Burden:
  - Fewer clinic visits required, relieving pressure on overburdened healthcare systems (but skill required)
- PrEP:
  - LAI PrEP can significantly reduce the transmission of HIV among high-risk populations
  - Cabotegravir, lenacapavir extremely promising
- Treatment for PLHIV:
  - LAI antiretroviral therapy (ART) may benefit those with adherence issues, reducing treatment failure and resistance.

Challenges and Considerations

- **Infrastructure and availability:**
  - Rural areas may lack facilities to administer LAI drugs consistently
  - Solutions include mobile health clinics or integrating LAI into existing health programs like maternal and child health
  - Capacity building of healthcare workers on preparation and administration of LAI
- **Cold Chain Requirements:**
  - Some LAI formulations require refrigeration, challenging in areas with unreliable electricity
- **Cultural and Perception Barriers:**
  - Local populations may prefer oral treatments or traditional remedies, necessitating community education and awareness campaigns
- **Cost: (THIS IS A HUGE ISSUE)**
  - LAI drugs are more expensive than oral alternatives.
  - Long-term savings through reduced clinic visits, improved outcomes may offset costs
- **ACCESS is also a HUGE issue, unclear registration paths etc**

Conclusion

- **LA Drugs as a Game-Changer**:
  - For Africa, especially niche populations, LAI drugs may have a huge impact on HIV treatment and prevention
  - For PLHIV, reduce vertical and horizontal transmission
  - Increase choice for HIV prevention
  - However, success hinges on overcoming logistical, economic, and cultural challenges
- **Unfortunately, not a silver bullet (Especially for treatment)**

  - Resistance
  - Oral lead-in
  - Cost
  - Availability
  - Accessibility
- Will require **advocacy** and **commitment** from HCW and patients

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