Cabotegravir as PrEP: Lessons from HPTN 083 and HPTN 084

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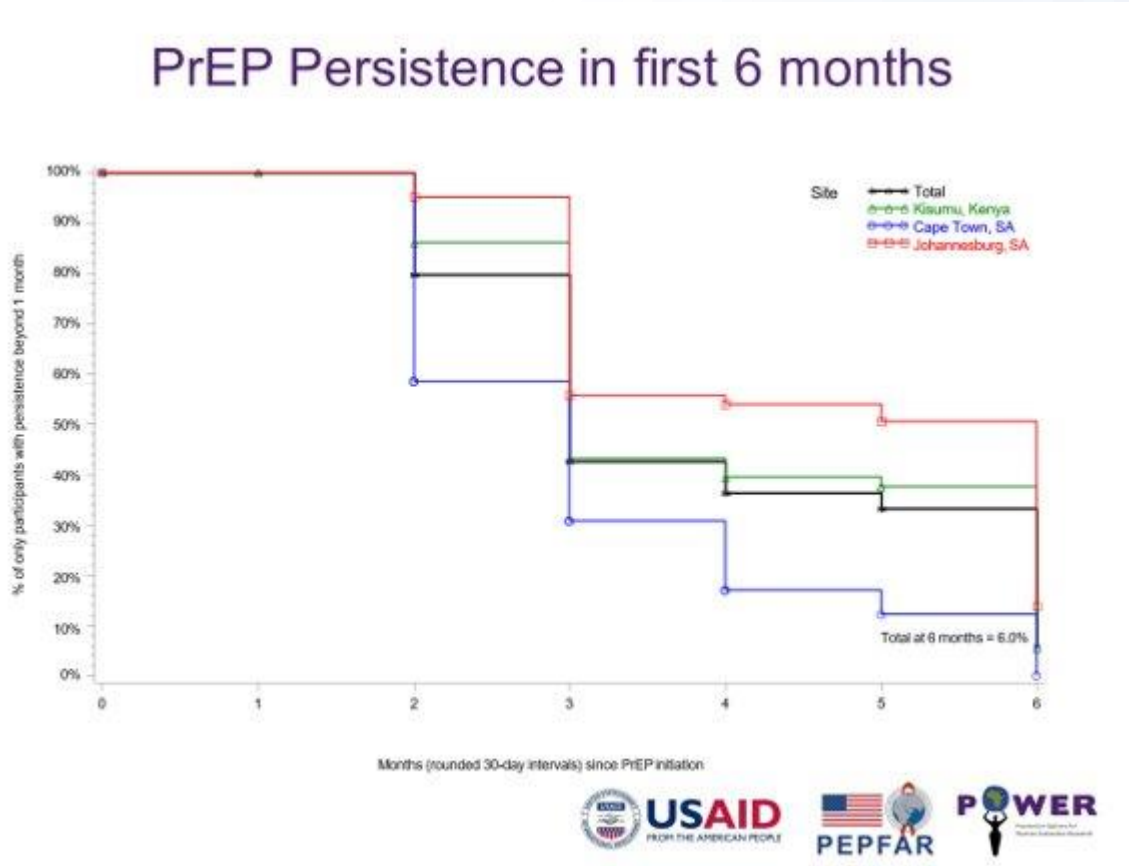
The Future of Antiretrovirals in Africa: Long-acting agents and beyond Conference, 2022

Current challenges to oral PrEP



- Side effects
- Pill size
- Pill burden
- Cost
- Access
- Visit burden
- Stigma and discrimination
- Violence
- Substance use
- Poor mental health
- .. COVID19 pandemic

- ***Need a range of PrEP options…***

Celum, PLoS Med, 2022


OPTIONS AHEAD

CAB-LA is generally safe and effective as PrEP

HPTN 083

- Cisgender men and transgender women who have sex with men
- 4,566 participants
- Argentina, Brazil, Peru, US, South Africa, Thailand, Vietnam (43 sites)

Results: **66% reduction in HIV infections** in CAB-LA arm compared to TDF/FTC.

HPTN 084

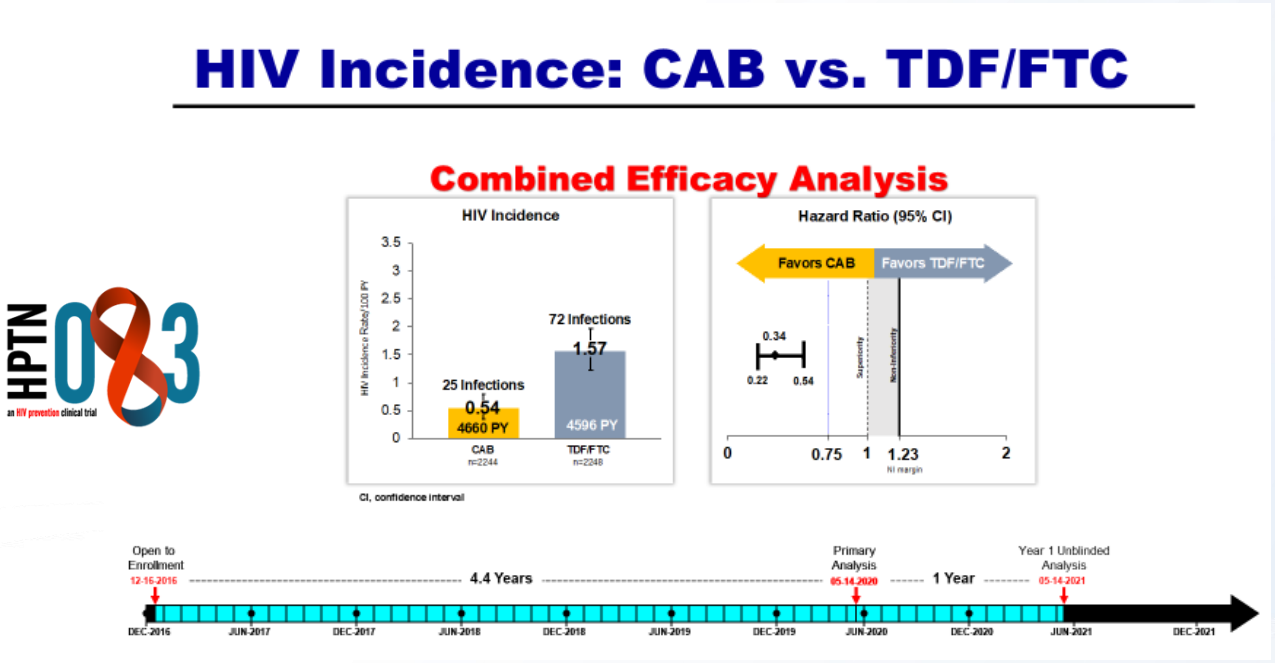
- Cisgender women 18 to 45 years
- 3,224 participants
- Uganda, Kenya, Malawi, Zimbabwe, Eswatini, South Africa, Botswana (20 sites)

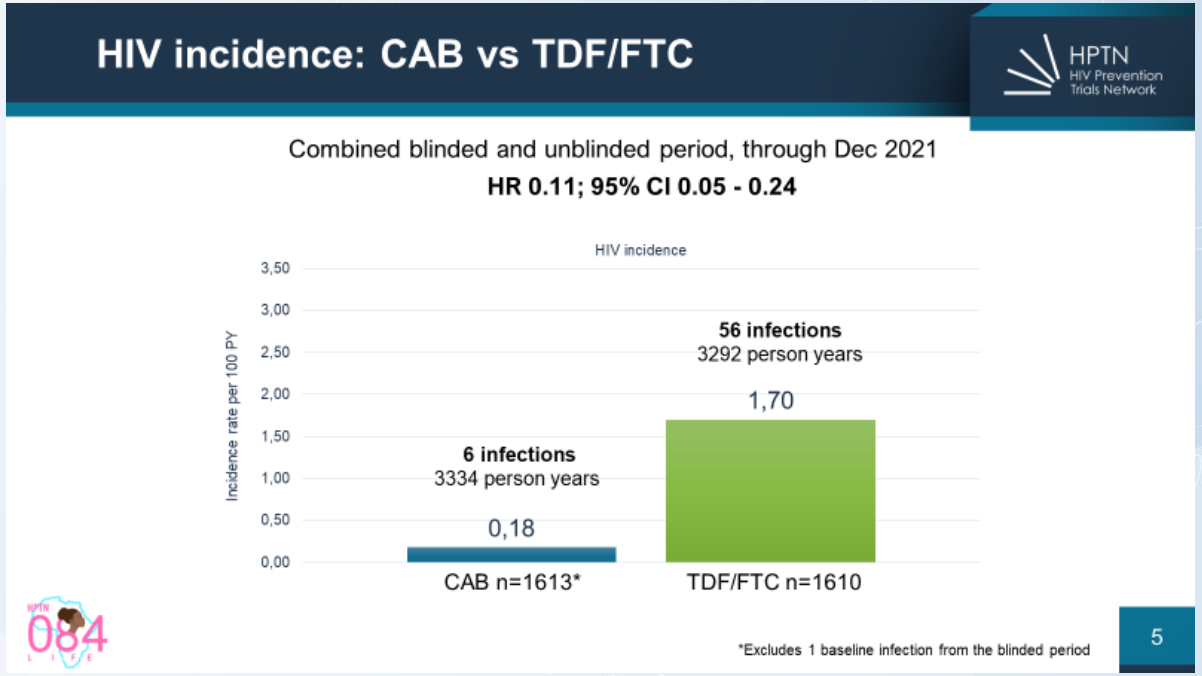
Results: **88% reduction in HIV infections** in CAB-LA arm compared to TDF/FTC.

Both trials were unblinded early in 2020 as CAB-LA demonstrated to be effective in preventing HIV compared to daily oral PrEP. CAB-LA likely confers an adherence advantage

Landovitz, NEJM 2021; Delany-Moretlwe, Lancet 2022

Protective effect of CAB-LA sustained





HPTN 083 66% risk reduction for CAB-LA vs. TDF/FTC in Year 1 unblinded phase

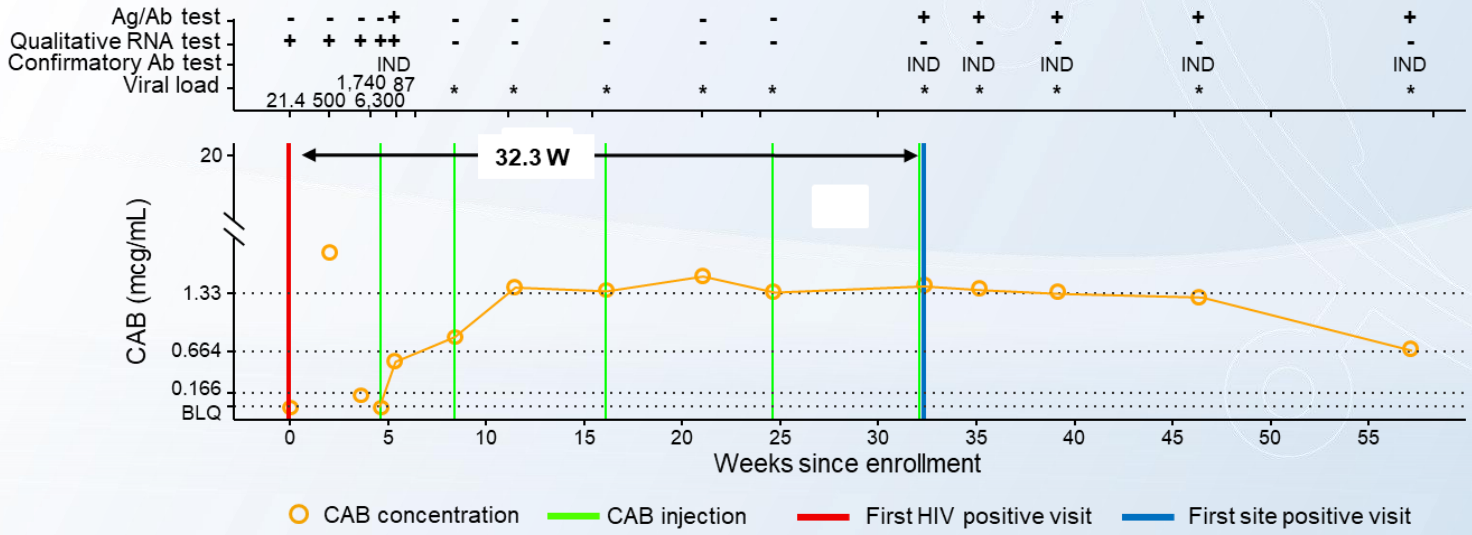
- HR=0.34 95% CI 0.17-0.67
- Majority of CAB infections d/t injection delays or ≥ 6 months off-CAB-LA

HPTN 084 89% risk reduction for CAB-LA vs. TDF/FTC in Y1 unblinded phase

- HIV infections associated with poor/absent CAB-LA use
- No on-injection breakthrough infections

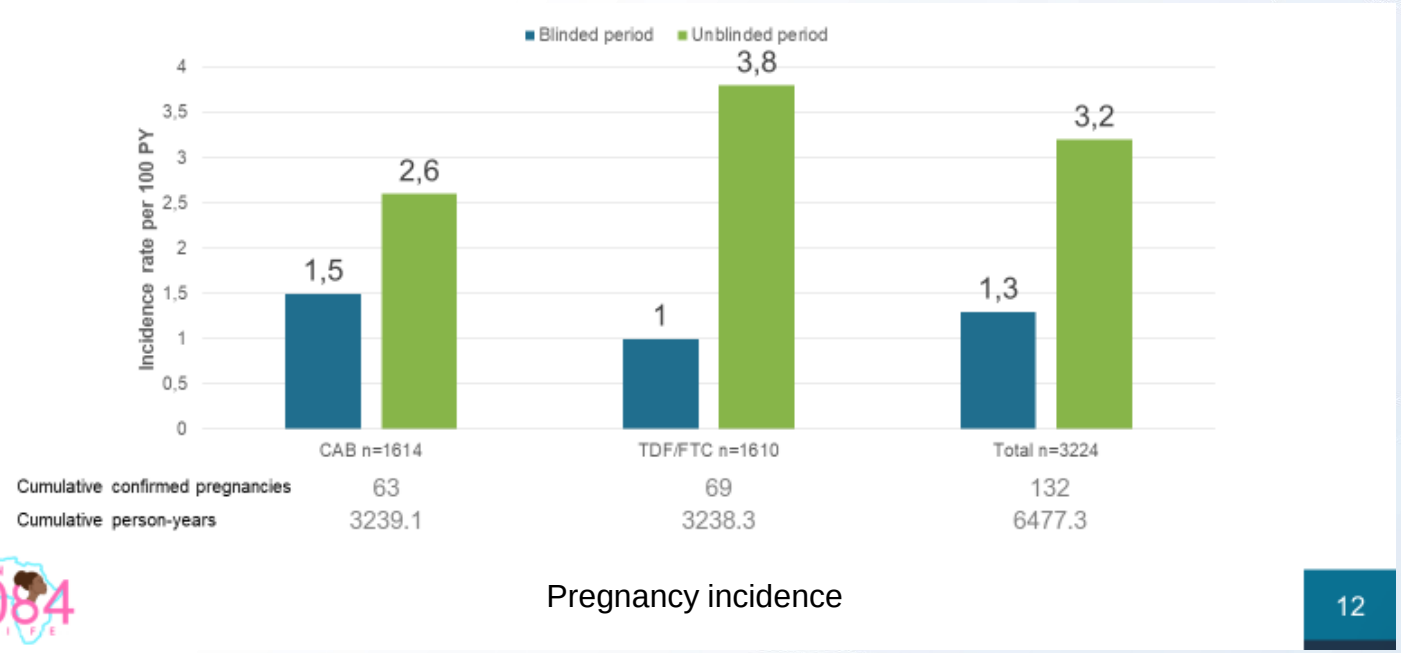
CAB-LA: delayed detection of HIV

- CAB-LA delayed detection of HIV with conventional diagnostics
  - CAB-LA suppresses viral replication and delays antibody production
  - Prolonged monotherapy may lead to INSTI resistance in rare cases
  - Resistance can be overcome by other (non-INSTI) HAART regimens
  - Use of a sensitive HIV RNA assay may detect early infection and prevent INSTI resistance



Landovitz, CROI 2022; Marzinke, JID 2021; Eshleman, JID 2022; Eshleman, CROI 2022; Delany-Moretlwe, IAS 2022

CAB-LA: Pregnant and breastfeeding women



Pregnancy incidence

12

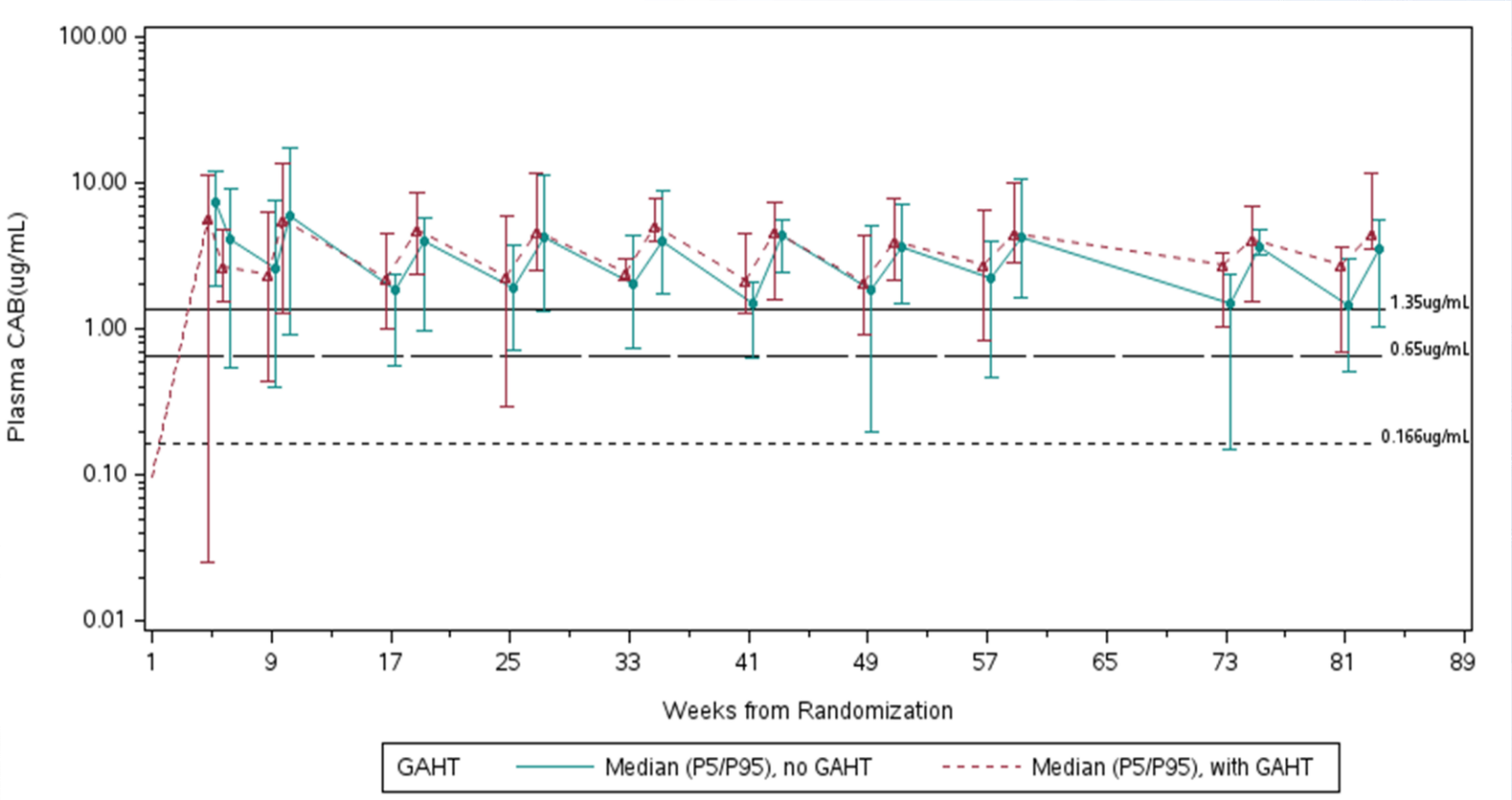
Women wish to conceive safely without fear of HIV infection

Confirms importance of ongoing evaluation of CAB safety and pharmacology in pregnancy during the HPTN 084 open-label extension

- In pregnant women who received CAB-LA up until pregnancy diagnosis
  - No congenital anomalies
  - Residual CAB-LA generally well tolerated during pregnancy
  - Drug concentrations comparable in pregnant vs non-pregnant women

Delany-Moretlwe, CROI 2022; Delany-Moretlwe IAS, 2022

CAB-LA: interactions with hormone therapy



- HPTN 083: 12% TGW, 58% reported GAHT use
- Most common estradiol valerate
- CAB drug concentrations were comparable between the two groups, suggesting the lack of a GAHT effect on CAB PK

- *Analysis of CAB-LA PK and contraceptive levels for DMPA, NET-EN and etonorgestrel pending; significant interactions not expected*
- *Limited data on interactions with testosterone therapy*

HIV Prevention Trials Network (HPTN) – ongoing open-label trials of CAB-LA PrEP

- Protocol amendment to offer open-label CAB LA
  - includes participants from adolescent (<18 years population) in adolescent sub-study
  - Includes optional oral lead in
  - Includes HIV RNA testing as part of HIV testing algorithm
  - Includes relaxed contraceptive requirements and option to consent for active dosing through pregnancy with additional data collection on safety and PK in pregnancy and lactation

- Additional activities to support implementation decisions
  - Extended interval dosing 8 vs 12 weeks in women
  - Evaluation of performance of current HIV diagnostic algorithm
  - Evaluation of VL platforms for future use for VL testing, incl. POC or near POC
  - Drug levels associated with protection analysis

HPTN 083 an HIV prevention clinical trial

HPTN 084 Long-acting Injectable For the Epidemic

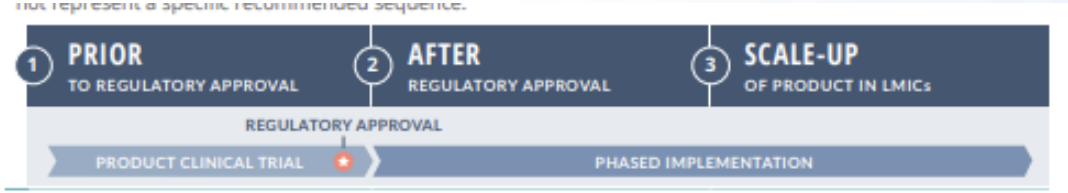
BioPIC
Biomedical Prevention Implementation Collaborative

CLINTON HEALTH ACCESS INITIATIVE

HIV Prevention Market Manager
Accelerating Product Introduction, Informing Product Development, Reducing Time to Impact
AVAC
CLINTON HEALTH ACCESS INITIATIVE
Supported by the Bill & Melinda Gates Foundation

BIOMEDICAL HIV PREVENTION

Adaptable Product Introduction Framework



Critical Pathway Activities for Biomedical HIV Prevention Products

NDA reviews in progress WHO guidelines

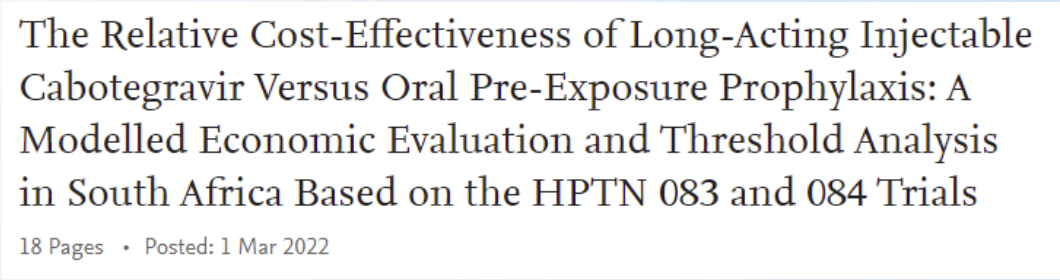
Costs, cost-effectiveness, pricing and access

Annals of Internal Medicine ORIGINAL RESEARCH

Cost-Effectiveness of Long-Acting Injectable HIV Preexposure Prophylaxis in the United States

A Cost-Effectiveness Analysis

Anne M. Neilan, MD, MPH; Raphael J. Landovitz, MD, MSc; Mylinh H. Le, BA; Beatriz Grinsztejn, MD, PhD; Kenneth A. Freedberg, MD, MSc; Marybeth McCauley, MPH; Nattanicha Wattananimitgul, BA; Myron S. Cohen, MD; Andrea L. Ciaranello, MD, MPH; Meredith E. Clement, MD; Krishna P. Reddy, MD, MS; Emily P. Hyle, MD, MSc; A. David Paltiel, PhD; and Rochelle P. Walensky, MD, MPH



The Relative Cost-Effectiveness of Long-Acting Injectable Cabotegravir Versus Oral Pre-Exposure Prophylaxis: A Modelled Economic Evaluation and Threshold Analysis in South Africa Based on the HPTN 083 and 084 Trials

18 Pages • Posted: 1 Mar 2022

- Concerns that prices may limit access despite effectiveness
- Cost-effectiveness analyses highlight that incremental benefits may not justify large price differential

Neilan, 2022 (USA)	Jamieson, in press 2020
– CAB-LA would be value for money if annual price <$6600 higher than generic F/TDF – i.e. <branded F/TDF or F/TAF and < half current CAB-LA/RPV price	– CAB-LA could avert 3x more HIV infections and save 3x more life years – Cost per CAB injection should be < 2x cost of 2-month supply of TDF/FTC to be cost-effective – Acceptable range cost per injection range of cost per injection $9 -$15

Costs, cost-effectiveness, pricing and access

- Access will be constrained unless there is tiered pricing for LMIC

- Coalition for Preparing for Access to CAB-LA Together via Voluntary Licensing (PrEP-ACT VL Coalition) will support coordinated work towards the goal of broad access to CAB-LA for PrEP in LMICs.
  - Led by MPP with ViiV Healthcare
  - Recent announcements confirm agreements around voluntary licensing with MPP

NON-PROFIT PRICE ESTIMATES

We are assuming two phases to access:

1. **Initial procurement phase:**
   - Implementation science studies drive majority of demand
   - Limited country-initiated procurement following national regulatory approval
2. **Scale-up phase:**
   - Conditional on successful implementation science outcomes
   - Assumes broader adoption and volume increase

The estimated non-profit price of a vial of CAB LA for PrEP is:

1. **2022/23 non-profit price:** £30-35 per dose
2. **Scale-up phase:** working to reduce price over time with a target of 20-50% lower

Please see the important notice and disclaimer on slide 2, which states, among other things, that the above is affected by multiple factors (such as manufacturing assumptions, inflationary pressures and demand volumes) and is subject to change at any time.

CAB-LA: implementation considerations

- Populations and approaches
  - How to deliver for specific focus populations
    - **Key populations**: more experience needed delivering to KP,
    - **Transgender women**: alternative injection sites for people with buttock implants or fillers
    - Adolescents
    - Pregnant and breastfeeding women
- Models of delivery
  - Add on to existing PrEP programmes?
  - Within KP services
  - Within SRH services
  - Approaches to offer choice
- Supporting product choice
  - HIV prevention has limited experience with offering options unlike contraception
  - Options vary quite differently for a range of attributes
- HIV testing
  - optimal testing strategies to minimize emergence of resistance
- ***Need an implementation science agenda***

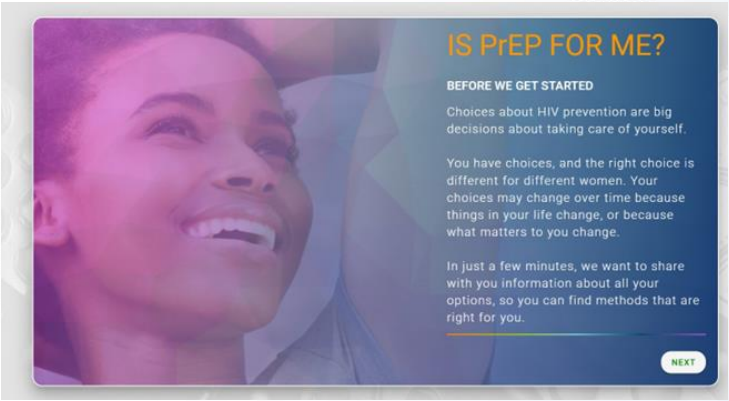
Funded PrEP introduction studies that include CAB-LA for PrEP

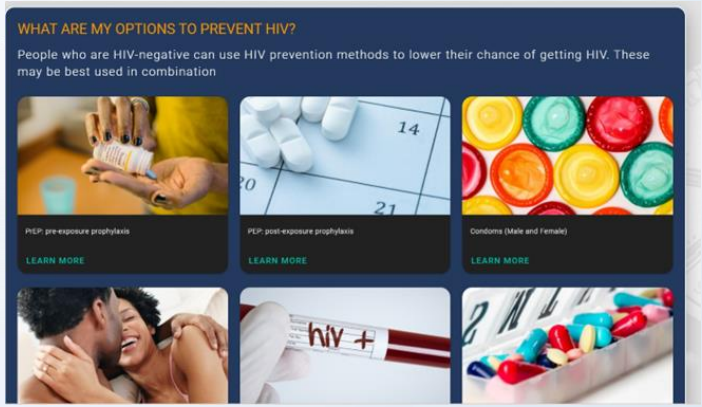
Funder/project	Location	Population	Sample size	status
CATALYST/MOSAIC (USAID)	Lesotho, Kenya, SA, Uganda, Zimbabwe	AFAB, TGW	4225 CAB	Funded 2022-5
Project PrEP (Unitaid)	South Africa	AGYW 18-24+ years	2609 CAB	Funded 2022-4
imPrEP/CAB-Brasil (Unitaid)	Brazil	MSM, TGW, non-binary	1200 CAB	Funded 2022-4
PrEP 1519 (Unitaid)	Brazil	Adolescent 15-19 years MSM, TGW, non-binary	340 CAB	Funded 2022-4
DTHF/Ezintsha/AHRI (BMGF)	South Africa	Various populations	TBD	Funded
PEPFAR	Thailand	KP-led services	TBD	Under consideration
SEARCH (NIH)	Kenya, Uganda	Population-level	TBD	Under consideration
Kirby institute (ViiV)	Australia	MSM, ?other	TBD	Under consideration
Prevenir/CohMSM (ANRS)	France, West Africa	MSM	400/400	Under consideration

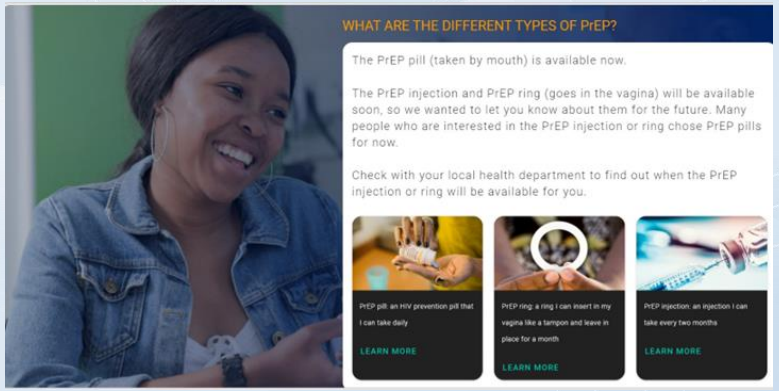
For more details see AVAC CAB for PrEP implementation study tracker wwww.prepwatch.org

Supporting product choice

- Decision support tools (DST) have been used successfully in health care settings to improve client knowledge, values-congruent choices and risk perception.
- A PrEP DST could overcome multiple client and provider barriers to PrEP delivery, particularly in resource-constrained settings where time constraints, lack of provider training and skills, and provider-client power disparities may be barriers to shared decision-making.
- Version 1.0 evaluated in an RCT demonstrated 2-fold higher PrEP continuation at M1
- Version 2.0 updated to include DVR and CAB; pending additional evaluation







Summary and conclusions

- Long-acting PrEP agents may overcome current PrEP persistence challenges
- CAB-LA approved by FDA, TGA - additional approvals anticipated
- Additional questions about safety and effectiveness in adolescents, pregnant and breastfeeding women are essential to future implementation
- WHO has issued guidance and CAB LA will be included in several funded demonstration projects once country approvals in place
- Coverage estimates will be critical for informing price, cost-effectiveness and ensuring access
- Particular consideration may need to be given to HIV testing approaches of long-acting systemic agents
- Decision support tools and other job aids will be importing for supporting health care providers to offer PrEP clients choice

Acknowledgements

- HPTN 083/04 participants, communities and study teams
- Sinead Delany-Moretlwe, Wits RHI
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