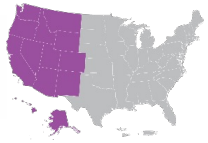
Injectable PrEP: What the science and users have to say about it

Hyman Scott, MD, MPH, SFDPH

Hosted by getSFcba, Center for Learning & Innovation, SFDPH

getSFcba



POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

Welcome!

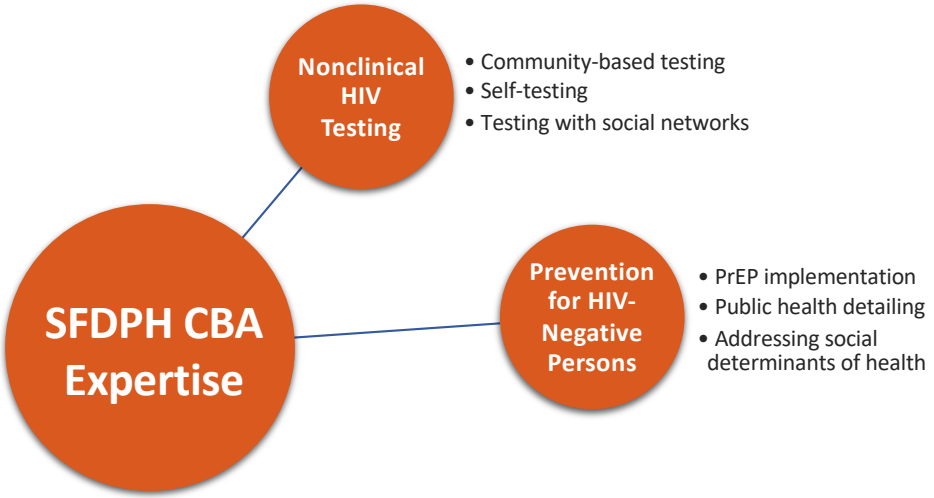
Jessica Bloome, MD, MPH (she/her/hers)
Assistant Clinical Professor, UCSF
Deputy Director, getSFcba
San Francisco Department of Public Health

Frank Sidders, MPH (he/him/his)
CBA Manager, getSFcba
San Francisco Department of Public Health

getSFcba

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

SFDPH CBA Program



Capacity Building Initiatives
SFDPH, Center for Learning & Innovation

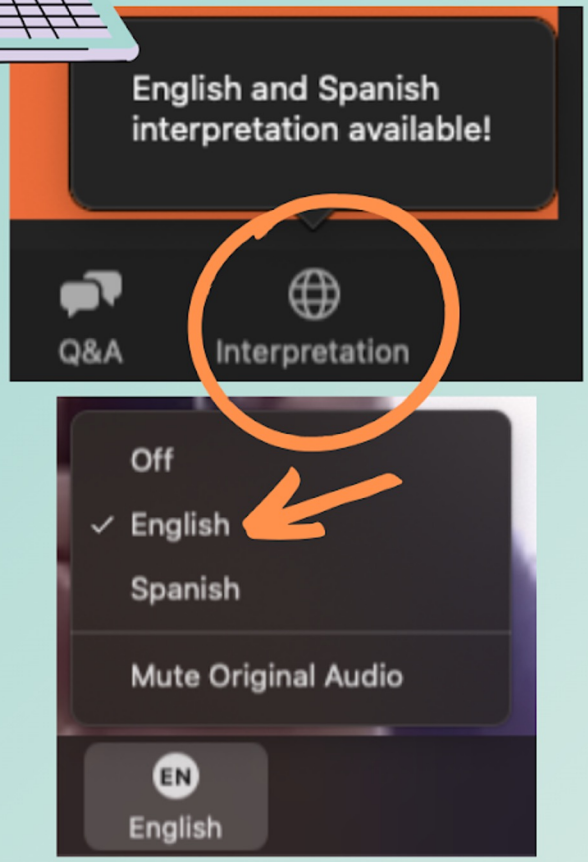
Visit: **www.getSFcba.org**
Email: **get.SFcba@sfdph.org**

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

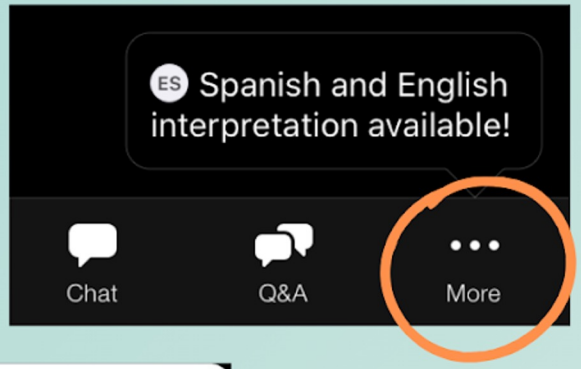
getSFcba

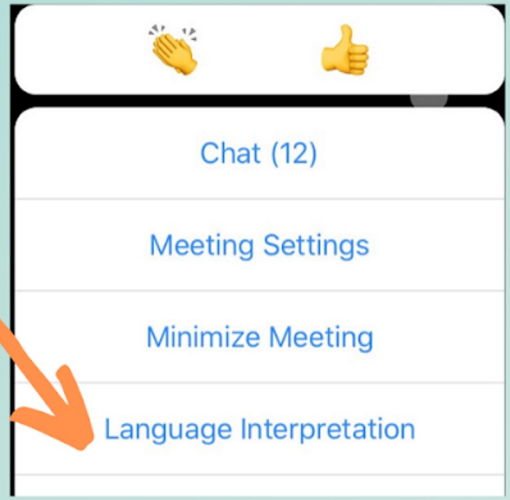
TO ACCESS INTERPRETATION

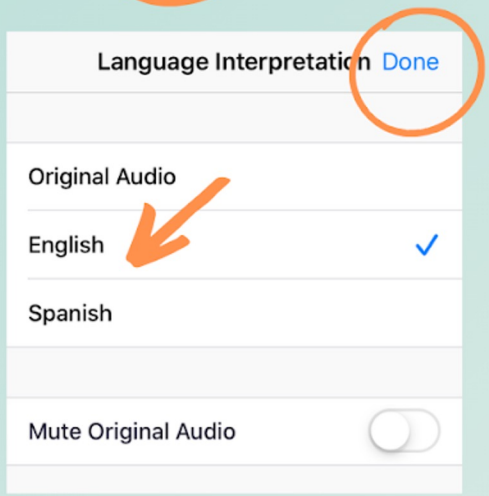
Via computer



Via smartphone







PARA ACCEDER A LA INTERPRETACIÓN

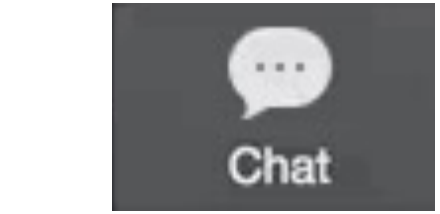
Por computador

Por teléfono inteligente

Gentle encouragements

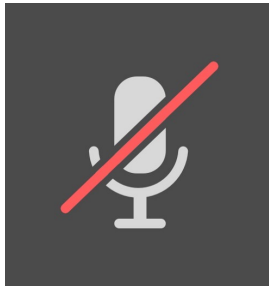
We'd love to see you!

Please turn on your camera when possible.



What's on your mind?

Use chat function, raise your hand, or send a reaction.



Shhh!

Don't forget to mute your audio when you're listening.

Getting to Know You

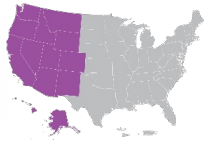
What type of organization do you work for?

Please complete the Zoom poll.

Learning Objectives

1. Describe the efficacy of injectable PrEP.
2. Review criteria for identifying who may benefit from injectable PrEP.
3. Identify implementation challenges and opportunities for injectable PrEP.

getSFcba



POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

Agenda

- The Science of Injectable PrEP
  - Dr. Hyman Scott (he/him), SFDPH
- Injectable PrEP Users Panel

getSFcba

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

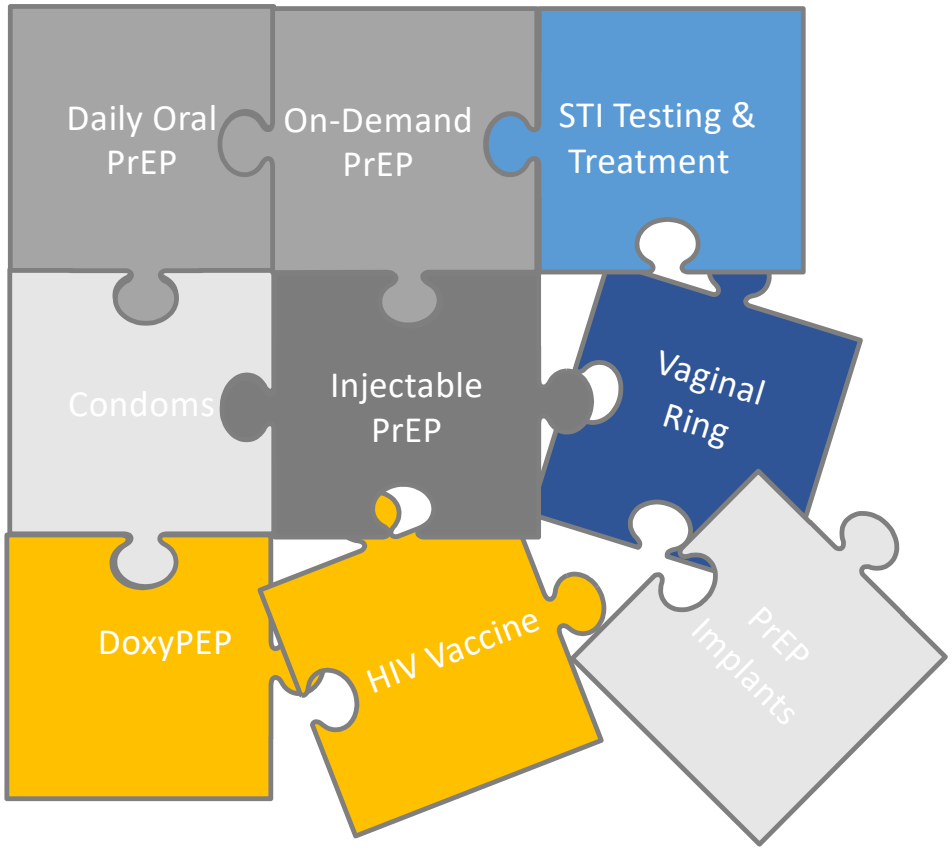
Injectable PrEP: What the science and users have to say about it

Hyman Scott, MD, MPH

Bridge HIV, San Francisco Department of Public Health

Assistant Clinical Professor, University of California, San Francisco

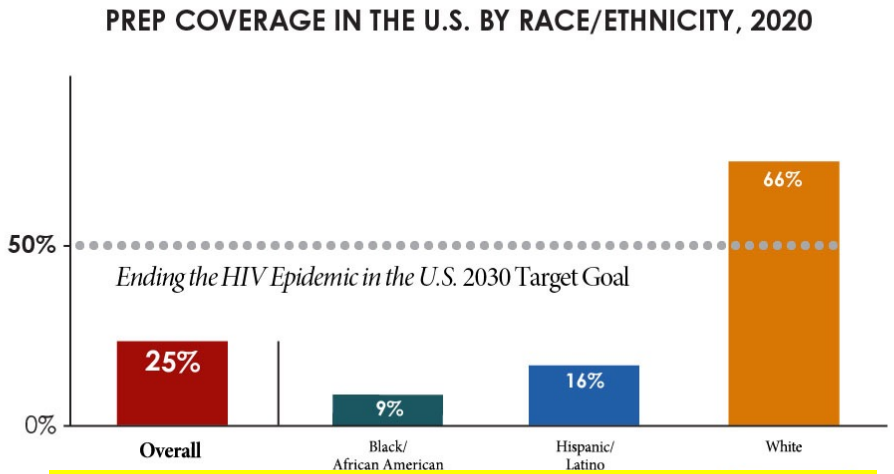
Filling in the Biomedical HIV Prevention Mosaic



Scott Lancet HIV 2019; Haynes Curr Opinion in Imm 2015; Landovitz Curr Opinion HIV 2016; Green AIBE 2017

Inequitable Oral PrEP Uptake in the US

WHILE 25% OF PEOPLE ELIGIBLE FOR PREP WERE PRESCRIBED IT IN 2020, COVERAGE IS NOT EQUAL



25% PrEP Use:
28% among men, 10% among women

CDC HIV Surveillance Data Tables 2021;2(No. 5)

Universal PrEP Discussion Recommendation in US

All sexually active adults and adolescents should have PrEP discussed/considered as an option

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE

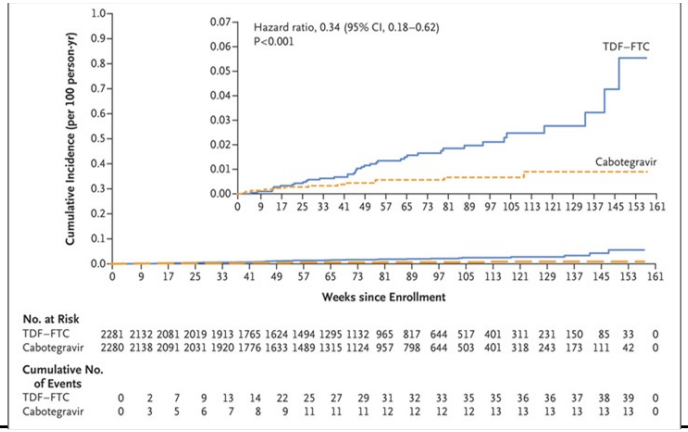
A CLINICAL PRACTICE GUIDELINE

	Daily Oral TDF/FTC	Daily Oral TAF/FTC	2-1-1 Oral TDF/FTC	CAB-LA
Cis Men	√	√	√	√
Cis Women	√			√
Trans women	√	√	(√)	√
Trans men	√			√
PWID	√			
Renal dz (↓CrCl)		√		√

CAB-LA is superior to TDF/FTC

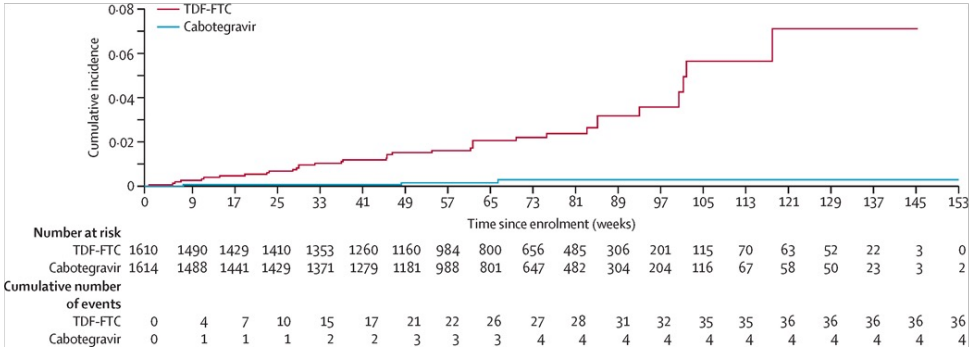
Efficacy: 66%

Landovitz et al NEJM 2021



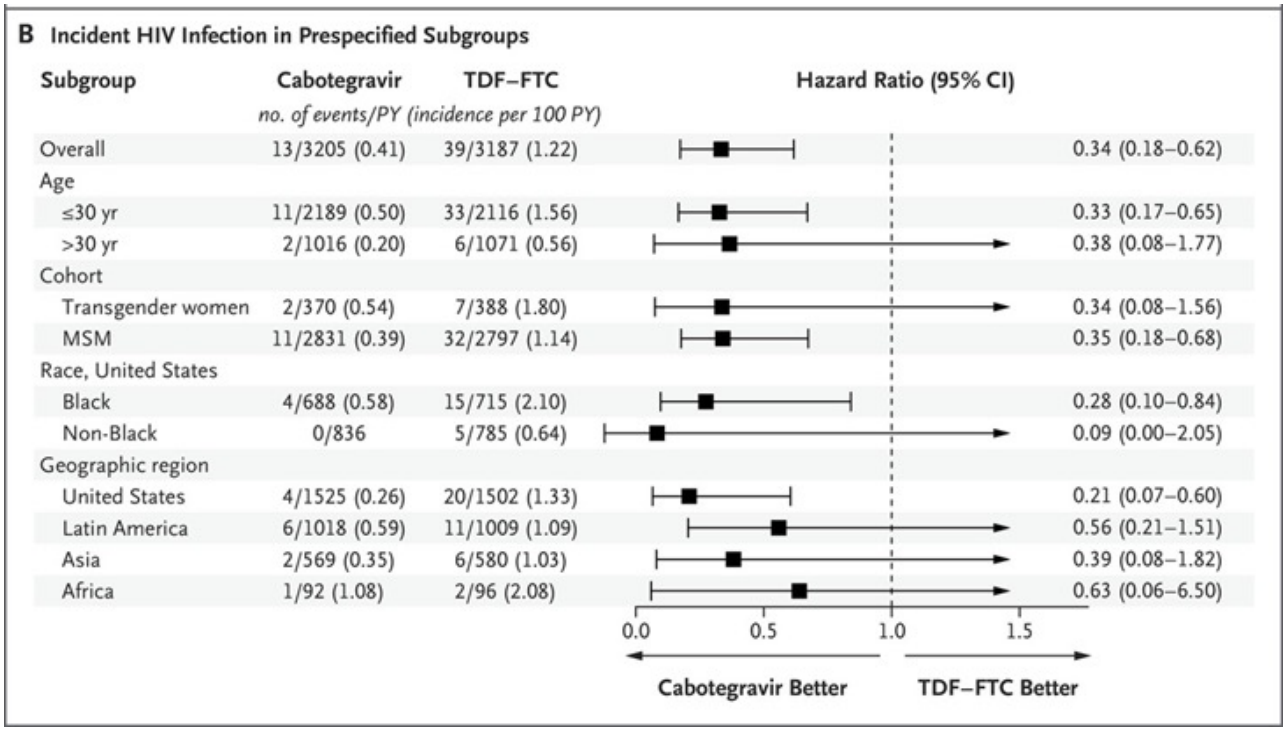
Efficacy: 88%

Delaney-Moretlwe et al Lancet 2022



HPTN 083 Subgroup Analysis

- CAB-LA associated with lower HIV incidence among:
  - Youth <30 yrs
  - MSM
  - US Black participants

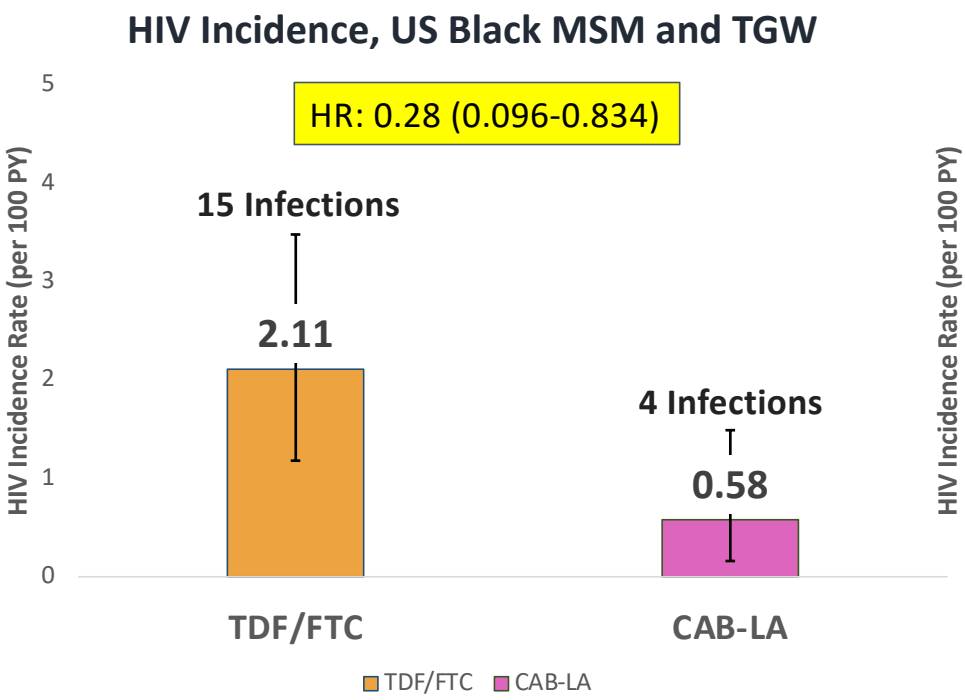


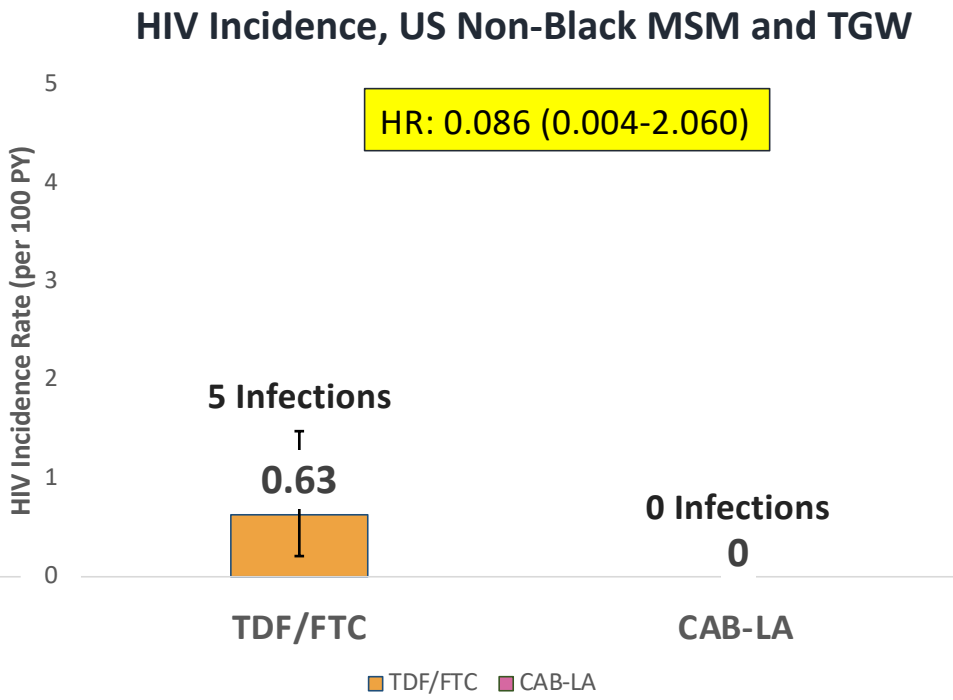
B Incident HIV Infection in Prespecified Subgroups

Subgroup	Cabotegravir	TDF–FTC	Hazard Ratio (95% CI)
	no. of events/PY (incidence per 100 PY)		
Overall	13/3205 (0.41)	39/3187 (1.22)	0.34 (0.18–0.62)
Age			
≤30 yr	11/2189 (0.50)	33/2116 (1.56)	0.33 (0.17–0.65)
>30 yr	2/1016 (0.20)	6/1071 (0.56)	0.38 (0.08–1.77)
Cohort			
Transgender women	2/370 (0.54)	7/388 (1.80)	0.34 (0.08–1.56)
MSM	11/2831 (0.39)	32/2797 (1.14)	0.35 (0.18–0.68)
Race, United States			
Black	4/688 (0.58)	15/715 (2.10)	0.28 (0.10–0.84)
Non-Black	0/836	5/785 (0.64)	0.09 (0.00–2.05)
Geographic region			
United States	4/1525 (0.26)	20/1502 (1.33)	0.21 (0.07–0.60)
Latin America	6/1018 (0.59)	11/1009 (1.09)	0.56 (0.21–1.51)
Asia	2/569 (0.35)	6/580 (1.03)	0.39 (0.08–1.82)
Africa	1/92 (1.08)	2/96 (2.08)	0.63 (0.06–6.50)

Landovitz et al NEJM 2021

HIV Incidence and Efficacy among US Black MSM and TGW





CROI 2023 Abstract #161

High interest in non-Daily PrEP among MSM

- Australian study of PrEP-experienced MSM showed higher interest among those concerned about side effects and daily adherence.
  - **Long acting injectable (LAI) – 59.7%**
  - Daily – 52.0%
  - Implant – 45.3%
  - Event driven – 42.8%

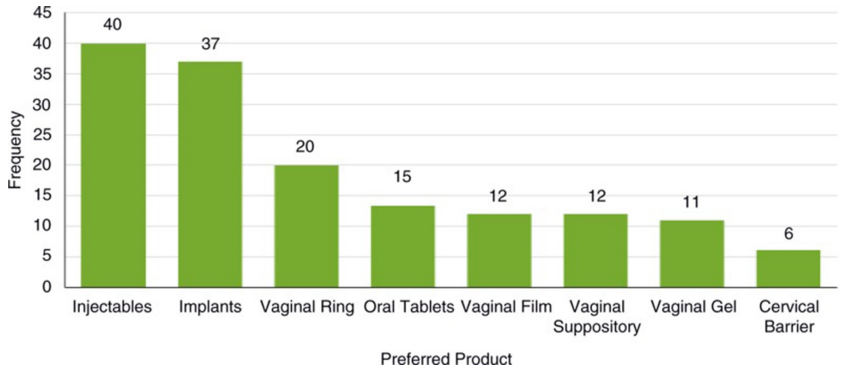
- US study of interest in different PrEP options among MSM recruited online
  - Daily – 35.4%
  - Implant (non-visible) - 34.3%
  - **LAI – 25.2%**
  - Implant (visible) – 4.3%

Chan et al AIDS and Behavior 2022 volume 26, 88–95
Greene et al AIDS and Behavior 2017 volume 21, 1336–1349

High Interest in non-daily PrEP among women

- Survey of 136 women in US and Africa in HPTN 076
  - @Baseline product preferences
    - **LAI – 74%**
    - Daily pill – 15%
    - Vaginal ring – 4%
  - @ Follow-up (week 28)
    - **LAI – 89%**
    - Daily pill – 10%
    - Vaginal ring – 0%

Product preferences from VOICE-D (MTN-003D)



Tolley et al JIAS 2019; Luecke et al JIAS 2016

Higher adherence when given a choice (MTN-034)

Oral PrEP adherence	Chose oral PrEP	Chose ring/neither	p-value
Red/yellow at least once	32 (20%)	129 (80%)	<0.001
Always green	39 (58%)	28 (42%)	

Non-use (red): TFV-DP levels of <16fmol/DBS punch
Some use (yellow): TFV-DP levels of 16-700fmol/DBS punch
High adherence (green): TFV-DP levels of ≥ 700fmol/DBS punch

Ring adherence	Chose ring	Chose oral PrEP/neither	p-value
Red/yellow at least once	134 (67%)	65 (33%)	0.85
Always green	19 (66%)	10 (35%)	

Non-use (red): RD levels showing release of <0.9mg
Some use (yellow): RD levels showing release of 0.9 to <4.0mg
Consistent with 28 days of use (green): RD levels showing release of ≥4.0mg

High adherence to oral PrEP in the crossover period was strongly associated with choice of oral PrEP (p<0.001)

No such association was observed for ring choice (p=0.85)

Ngure et al CROI 2022 Abstract #88 LB

PrEP product level considerations

TDF/FTC or TAF/FTC

Pros

- Daily and on-demand options
- Flexibility in implementation
- Minimal clinical monitoring for most patients
- Available for all populations
- Quarterly HIV testing
- Cost – generic TDF/FTC available

Cons

- Requires daily adherence or complex regimen
- Pills may not be acceptable or preferred for all populations.

Injectable PrEP

Pros

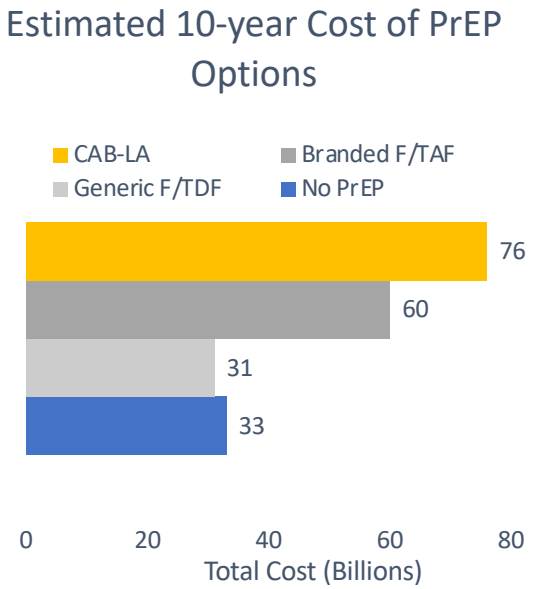
- Superior efficacy
- Daily adherence not required
- Discretion in use

Cons

- Every 2 month visits
- HIV testing requirements
- Cost and access
- Breakthrough HIV infections

Coverage and Cost Considerations

- Cost: Medical vs Pharmacy benefit
  - Generic TDF/FTC has reduced cost substantially
    - CAB-LA ~ $3,700 per dose (~$25,900 per year)
  - Will determine patient and up-front provider costs
  - Covered by national program and PrEP-AP
- Access and Assistance Programs
  - Manufacture programs are often available in US
  - Availability through national programs globally
- CAB-LA Cautionary Tale:
  - Cost/Insurance navigation for CAB-LA is often so complex and time-consuming that access is limited even when it's "covered".



https://www.apretudecopayprogram.com/terms-and-conditions

Neilen et al Ann Intern Med. 2022 Feb 1

Clinical Considerations

- HIV testing
  - Turnaround time for HIV Ab testing
  - POC rapid HIV testing availability at healthcare sites
  - Viral load testing at every visit – availability and cost
- Visit structures
  - Potentially additional visits and staff – provider, lab, and injection visits
  - Same day starts will be more challenging
- Missed or delayed injections
  - Coverage with oral CAB or TDF/FTC or TAF/FTC
  - PEP regimens

HIV Testing for starting CAB-LA

FDA/prescribing information

- Use a test approved or cleared by FDA for diagnoses of acute or primary HIV-1 infection
- If antigen/antibody-specific test is used and provides negative results, should confirm with an RNA-specific assay, even if results are available after CAB administration

CDC Guidelines

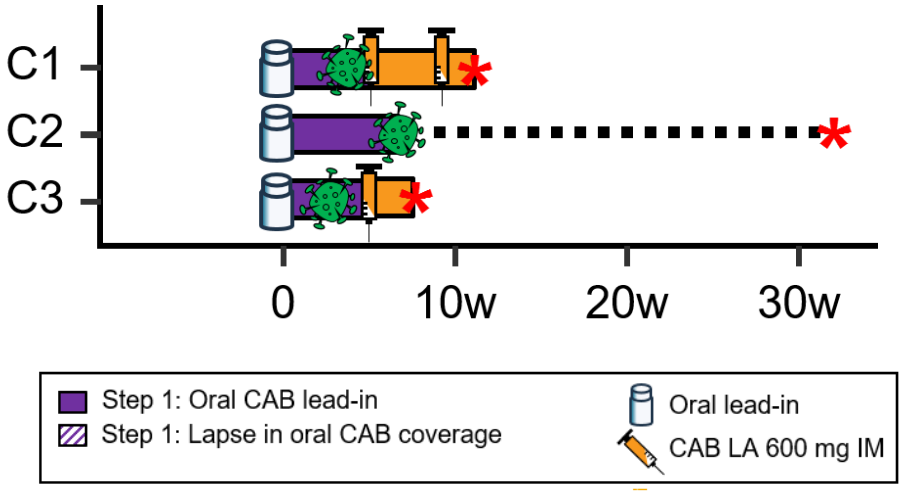
- Use most sensitive test available: HIV-1 RNA assay
- Ideally done within 1 week prior to initiation visit
- If clinician wishes to provide first CAB-LA injection based on result of a rapid Ag/Ab assay, blood should be drawn for HIV RNA assay

Oral CAB lead-in vs. direct-to-inject

Safety

Adverse Events	TDF–FTC (N=2282)	Cabotegravir (N=2280)
	no. (%)	*no. (%)*
Any adverse event of grade 2 or higher	2216 (92.7)	2106 (92.4)
Any adverse event of grade 3 or higher	767 (33.6)	727 (31.9)
Serious adverse event	121 (5.3)	120 (5.3)
Adverse events of special interest		
Seizure	5 (0.2)	2 (0.1)
Liver-related adverse event resulting in discontinuation of oral tablets or both oral tablets and injections	48 (2.1)	47 (2.1)

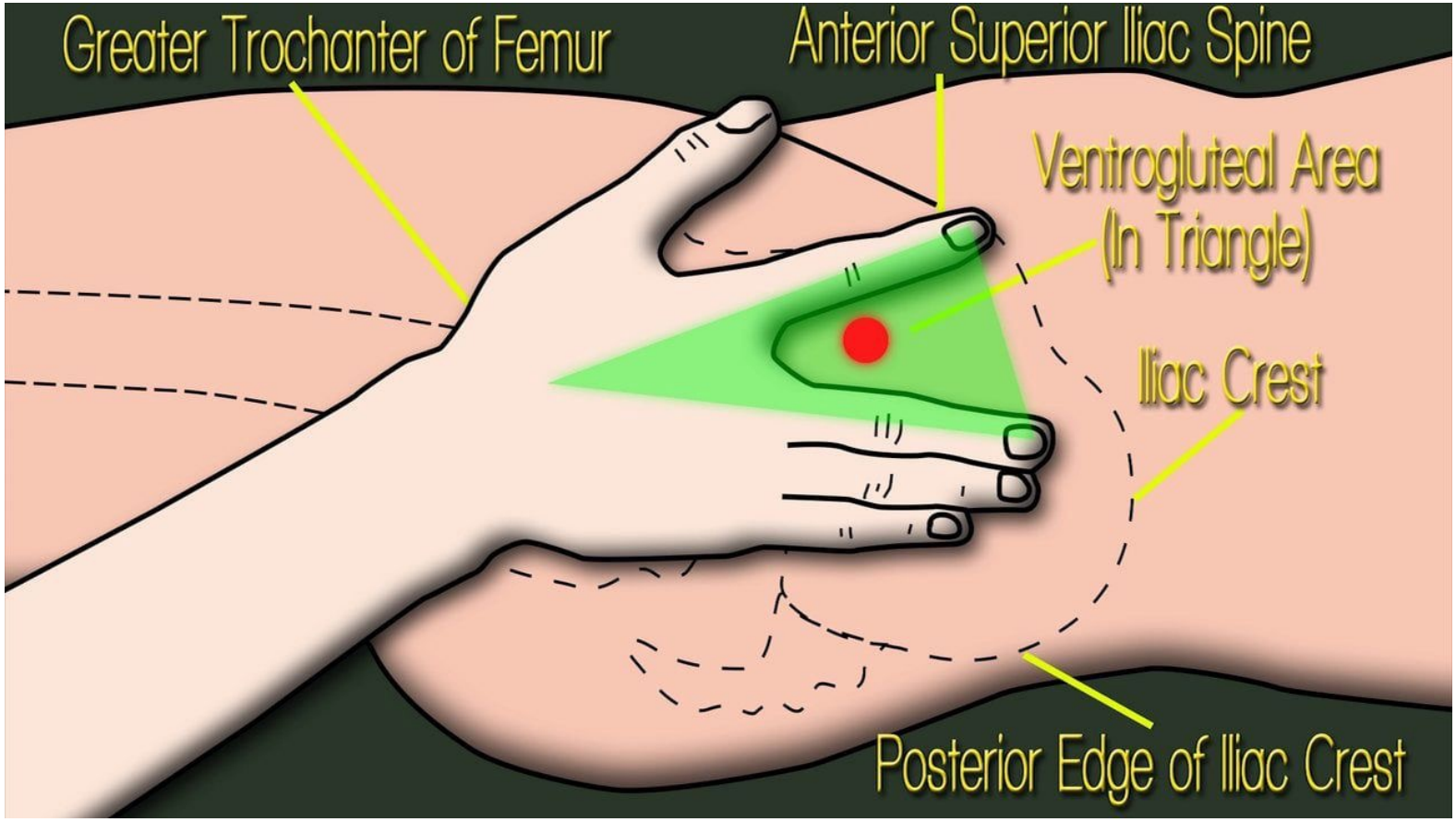
Seroconversions during oral CAB lead-in



In HPTN 083 OLE, 70% pts elected for direct-to-inject CAB-LA

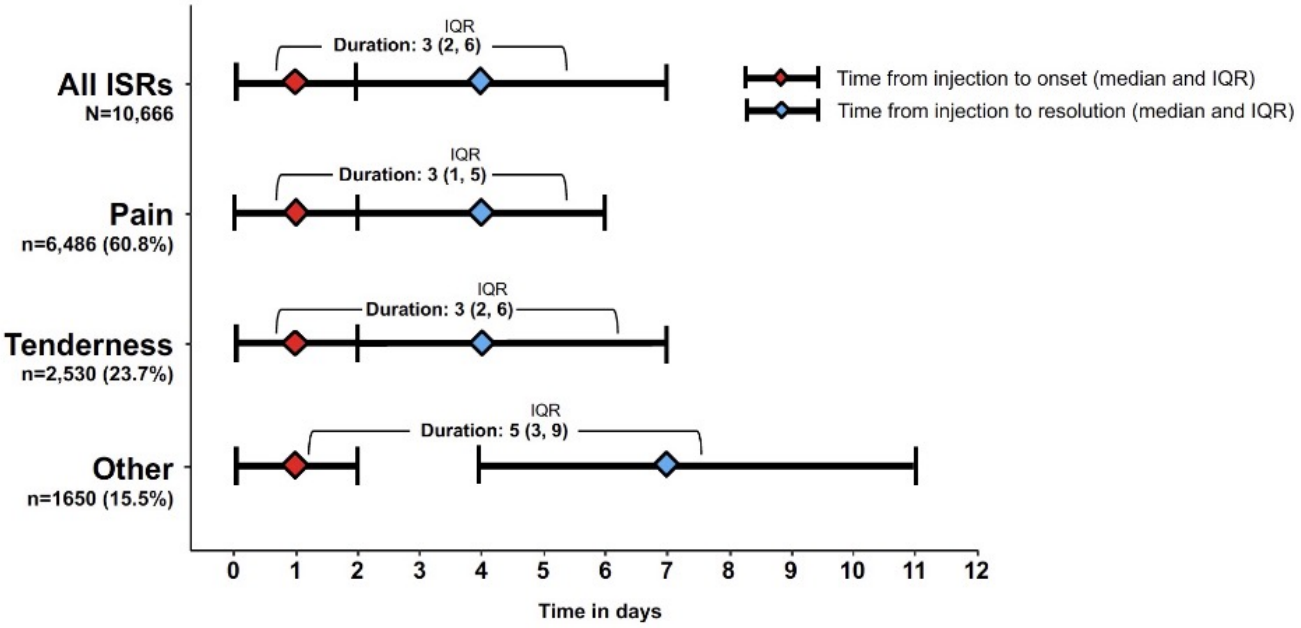
Landovitz et al, NEJM 2021; Marzinke JID 2021

Ventrogluteal injection site preferred



HPTN 083

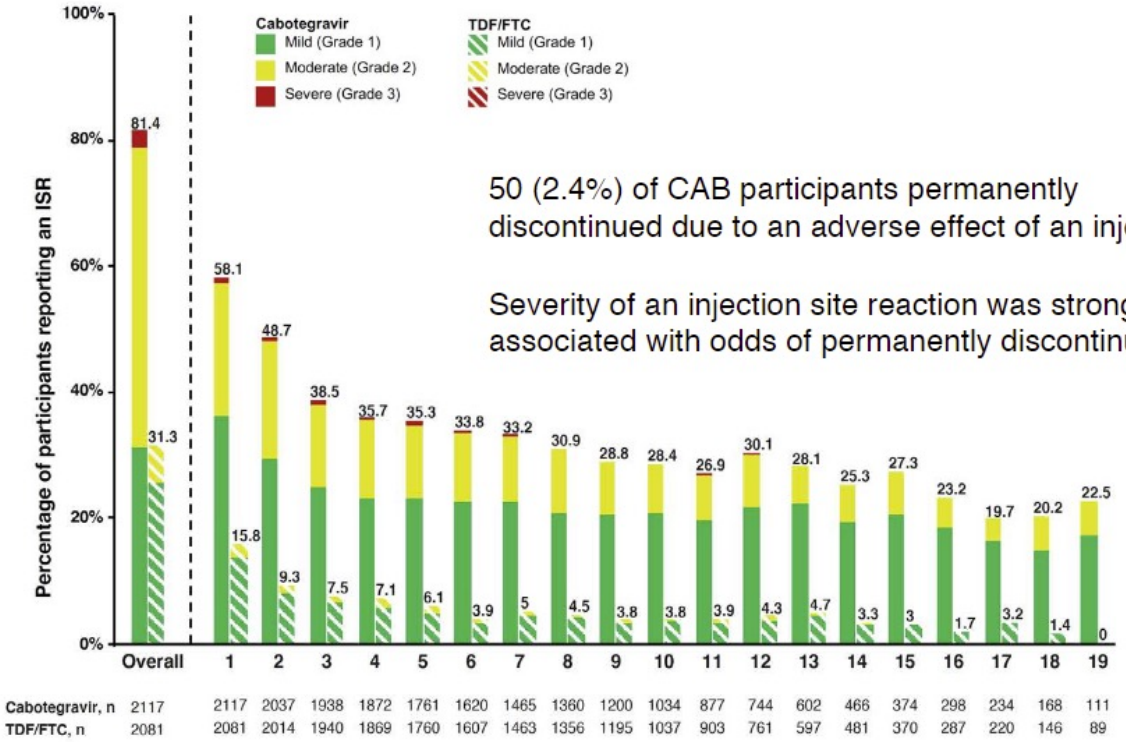
Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW



Supplementary Figure 6 from Landovitz RJ, et al. N Engl J Med. 2021 Aug 12;385(7):595-608

HPTN 083

Oral FTC/TDF vs Injectable CAB-LA for MSM & TGW



50 (2.4%) of CAB participants permanently discontinued due to an adverse effect of an injection

Severity of an injection site reaction was strongly associated with odds of permanently discontinuing

Supplementary Figure 5 from Landovitz RJ, et al. N Engl J Med. 2021 Aug 12;385(7):595-608

Take aways: Injection site reaction management

- ISRs common after 1st and 2nd injections, diminish over time
- OTC pain medication within a couple of hours before or soon after the injection and continue as needed for 1-2 days
- Ensure patient is in a relaxed position for injection, and muscle is relaxed.
- Administer the injection over 1 min
- Consider doing massage at injection site over 1-2 min
- Apply warm compress or heating pad to the injection site for 15-20 minutes after the injection

Covering missed visits - per FDA label

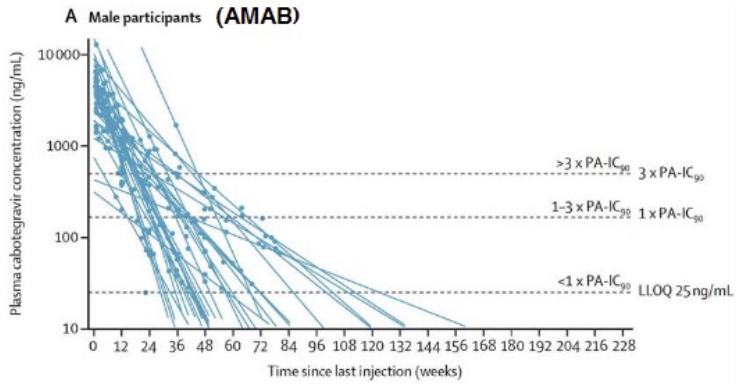
Scenario	Guidance
Injection Schedule	• Injections at 0 and 4 weeks. Subsequent injections every 8 weeks • Goal: +/- 7 days of injection target date
Missed Injections: < 4 weeks late	
Planned	• If >7 days late, can bridge up to 2 months with daily oral CAB (30 mg) • If longer, alternative daily oral PrEP recommended • Start first dose of oral PrEP approximately 2 mo. after last injection
Unplanned	• Reassess if resumption of injection dosing is appropriate • Administer CAB-LA as soon as possible
Missed injection: > 4 weeks late	
Planned & Unplanned	• Reload with initial 4-week interval, then return to 8-week intervals

Covering missed visits – Alternative approach

Scenario	Guidance
Injection Schedule	• Injections at 0 and 4 weeks. Subsequent injections every 8 weeks • Goal: +/- 7 days of injection target date • Provide TDF/FTC to cover gaps
Missed Injections: < 4 weeks late	
Planned or Unplanned	• Counsel patients to start TDF/FTC if they miss their injection visit. • Administer CAB-LA as soon as possible
Missed injection: > 4 weeks late	
Planned or Unplanned	• Reload with initial 4-week interval, then return to 8-week intervals

Cabotegravir takes <u>months</u> to "wash out"

CAB's pharmacokinetic "tail" is a VERY important consideration



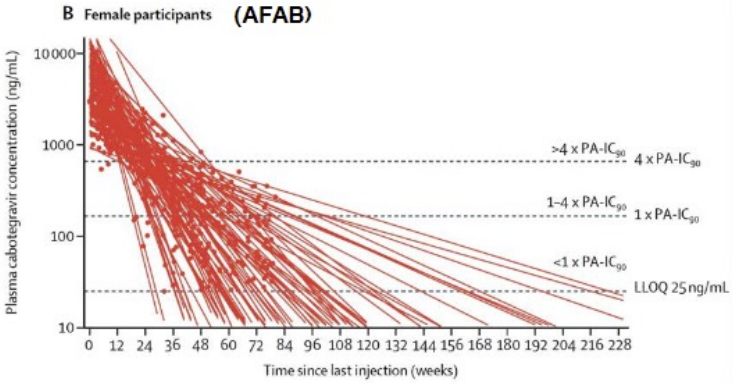
CAB dropped below LLOQ after a median of

10 months

among participants assigned male at birth
(IQR 7-15; range 5-35)

15.5 months

among participants assigned female at birth
(IQR 7-21; range 4-52)



HPTN 077

Landovitz RJ, et al. *Lancet HIV*. 2020;7(7):e472-e481

Take aways: Discontinuing CAB-LA

- Re-educate patients about the “tail” and risks during declining CAB levels
- Assess ongoing risk/indications for PrEP
- Prescribe daily oral F/TDF or F/TAF beginning within 8 weeks after last CAB injection
- Educate about PEP
- CDC guidelines recommend quarterly RNA testing for 1 year after discontinuation!

Clinical Considerations

- Breakthrough HIV infections
  - Management of discordant HIV test results
  - ART choice in the absence of resistance data with low viral load
- Discontinuation
  - Tail coverage for those who cannot tolerate TDF/FTC or TAF/FTC

HPTN 083:
HIV Incidence

- Sensitive RNA screening of 7 persons who received long-acting injectable cabotegravir
  - Detection of baseline infection at study sites using rapid tests and antigen/antibody tests was delayed (median 60 days)
- 5 of 7 cases had major INSTI RAMs detect in samples with low viral loads
  - Use of a RNA assay for screening would have detected infection before a major INSTI RAM was detected (4 cases) or before additional major INSTI RAMs accumulated (2 cases)

Eshleman et al CROI 2022. Abstract # :S8-OA95

Long-acting early viral inhibition (LEVI) Syndrome

	Acute HIV Infection	LEVI
Cause	Phase of natural HIV infection	Long-acting anti-viral PrEP agent (prototype: CAB-LA)
Onset	New infection	Infection during PrEP Initiation of PrEP agent during acute/early infection
Viral replication	Explosive	Smoldering
Symptoms	Fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen glands	Minimal, variable, often no symptoms reported
Detection	Ag/Ab assay, RNA assays (including less sensitive POC and pooled tests), DNA assays, total nucleic acid assays	Ultrasensitive RNA assay (often low or undetectable RNA, low/undetectable DNA, diminished/delayed Ab production)
Assay reversion	Rare	Common for many test types
Duration	1-2 weeks (until Ab detection)	**Months** (until viral breakthrough, drug clearance, or ART start); can persist months after the anti-viral agent is discontinued
Transmission	Very likely	**Unlikely** (except possibly through blood transfusion)
Drug resistance	No (unless transmitted)	Yes (can emerge early when viral load is low)

CROI 2023 Abstract #160

Take aways: Delayed seroconversion on CAB-LA

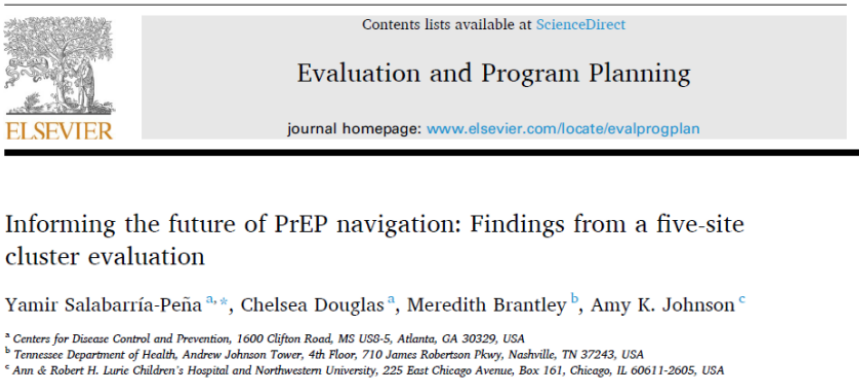
- In HPTN 083, detection of HIV infection was delayed in all 4 baseline cases and 7/12 (58%) incident HIV cases in the CAB arm
- Median delay in CAB arm:
  - **62 days** for baseline cases
  - **98 days** for incident cases
- Use of an **RNA assay for HIV screening** would have:
  - Detected infection at the first HIV-positive visit in all 4 baseline cases and 5/7 incident cases
  - Detected infection before a **major** INSTI RAM was detected (4 cases) or before **additional major** INSTI RAMs accumulated (2 cases)
- **Use most sensitive RNA assay available**

System Considerations

- Supply and storage
  - Space and logistics for onsite storage vs pharmacy delivery
  - Cold-chain for required refrigeration
- Space and staff
  - More frequent visits requiring private rooms
  - Local regulations for who can administer injections
- Patient support
  - Navigation and visit adherence support tools

Patient Navigation

- Varied models including peers, health workers, pharmacists, nurses, or case managers
- Important for insurance/benefit navigation
- Varied results on impact on uptake and persistence
- May be more important for CAB-LA



Contents lists available at ScienceDirect

Evaluation and Program Planning

journal homepage: www.elsevier.com/locate/evalprogplan

Informing the future of PrEP navigation: Findings from a five-site cluster evaluation

Yamir Salabarría-Peña [a,*], Chelsea Douglas [a], Meredith Brantley [b], Amy K. Johnson [c]

[a] Centers for Disease Control and Prevention, 1600 Clifton Road, MS US8-5, Atlanta, GA 30329, USA
[b] Tennessee Department of Health, Andrew Johnson Tower, 4th Floor, 710 James Robertson Pkwy, Nashville, TN 37243, USA
[c] Ann & Robert H. Lurie Children's Hospital and Northwestern University, 225 East Chicago Avenue, Box 161, Chicago, IL 60611-2605, USA

Salabarría-Peña et al Eval Program Plann 2022 Feb;90:101999

Summary

- PrEP uptake has been low and unequitable globally
- Injectable PrEP is highly effective
- Provider, system, and cost barriers are continued threats to Injectable PrEP implementation.
- Addressing these barriers is required to provide an authentic choice for our patients.

Injectable PrEP Users Panel

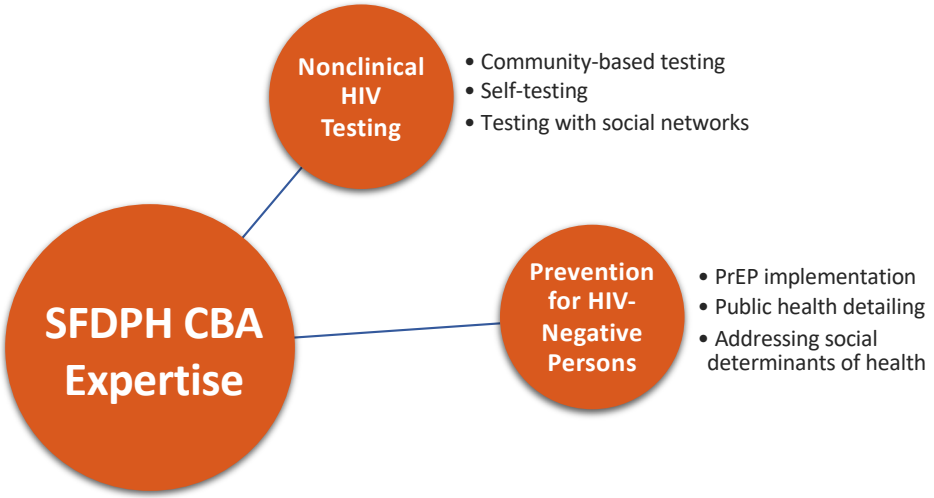
Frank Sidders, MPH (he/him/his)
CBA Manager, getSFcba
San Francisco Department of Public Health

getSFcba

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

Questions?

SFDPH CBA Program



Capacity Building Initiatives
SFDPH, Center for Learning & Innovation

Visit: **www.getSFcba.org**
Email: **get.SFcba@sfdph.org**

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

getSFcba

EVALUATION

Please share with us your feedback!

https://www.surveymonkey.com/r/injPrEPSession1

getSFcba

POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH
CENTER FOR LEARNING & INNOVATION

Join us for the next webinar session, September 19th