



Long-Acting Injectable PrEP: High-volume providers breakout

February 29, 2024

Ending
the
HIV
Epidemic





COMMUNITY HEALTH
CENTER NETWORK



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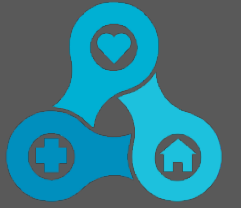
Plan and purpose for this session



Learning objectives:

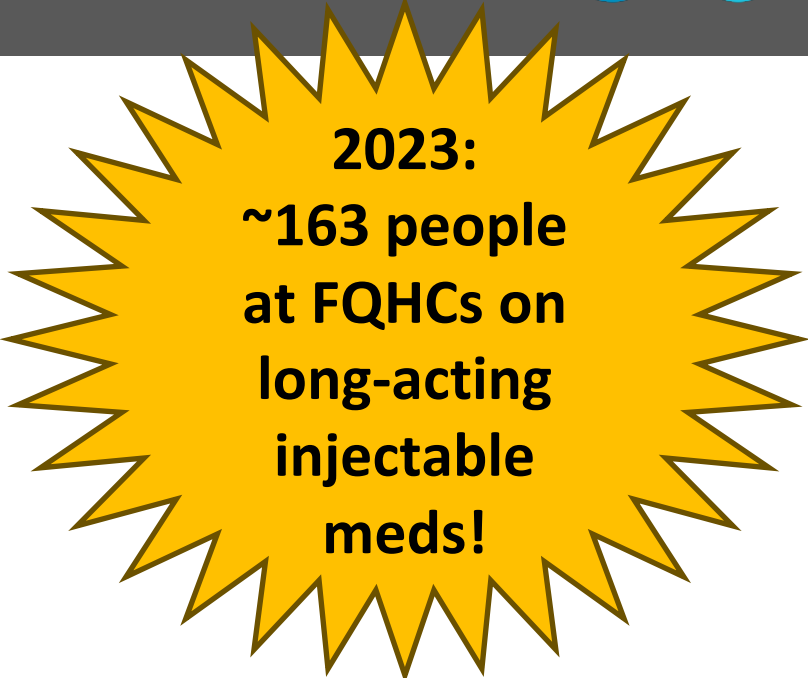
1. Compare clinical workflows from sites with established panels of patients on long-acting injectable (LAI) PrEP.
2. Identify tools to expand LAI services: referrals, recruitment, panel management.
3. Discuss complex cases and management strategies: managing missed visits, labs, LEVI syndrome, CAB tail, integration with behavioral health.

Incredible Injectables!



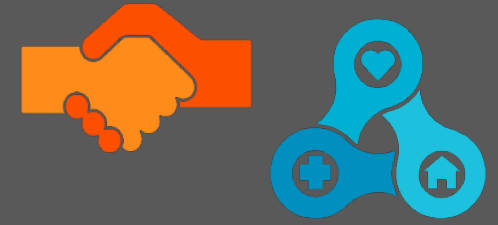
Accomplishments in 2023:

- Quarterly East Bay HIV provider conferences to discuss injectable ART and PrEP.
- [Injectables resource page: ebgtz.org/resource/injectables](https://ebgtz.org/resource/injectables)
- Work flows developed and implemented at many sites.
- Huge scale-up of people on injectables.
- **It takes a massive team effort and collaboration!**



**2023:
~163 people
at FQHCs on
long-acting
injectable
meds!**

Introductions



1. Name, pronouns, role, organization
2. Your injectable program: approximate # of patients on injectable PrEP and # of staff supporting injectables.
3. Do you have clinical workflows you are able/willing to share?
(We have examples from LifeLong, GBWC, AHS.)

EB injectable resources/updates: ebgtz.org/resource/injectables

When poll is active respond at PollEv.com/ebgtz

Send **ebgtz** to **37607**



What topics do you want to prioritize? (Choose 2)

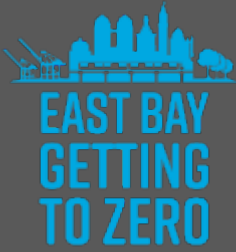


What topics do you want to prioritize? (Choose 2)

Join by Web PollEv.com/ebgtz

Join by Text Send **ebgtz** to **37607**





Injectable PrEP work flows

- **LifeLong Medical Care**
- **Glenn Burke Wellness Clinic at the Oakland LGBTQ Center**
- **Asian Health Services**
- **Others?**

Panel Management

- 1. Patient tracking tools**
- 2. Patient contact/reminders**
- 3. Setting up appointments and following up missed visits**

Recruitment and referrals

- 1. What types of outreach/inreach are you doing?**
- 2. Do you accept outside referrals?**
- 3. How do you prioritize patients for LAI PrEP when you are reaching your clinic's capacity limits?**

Missed visits

1. **Manufacturer missed visit suggested protocol**
2. **GBWC protocol**
3. **Strategies and counseling for oral PrEP backup**
4. Data from HPTN 084 suggests that there may be up to 6 weeks of forgiveness with late injections for people assigned female at birth.

Dose Missed	Time Since Previous Dose	Recommendation
Second Injection	≤ 2 months	Administer dose as soon as possible, then continue every 2-month schedule.
	> 2 months	Restart initiation dosing (2 doses separated by 1 month), followed by every 2-month schedule.
Third injection or after	≤ 3 months	Administer dose as soon as possible, then continue every 2-month schedule.
	> 3 months	Restart initiation dosing (2 doses separated by 1 month), followed by every 2-month schedule.

Lab monitoring

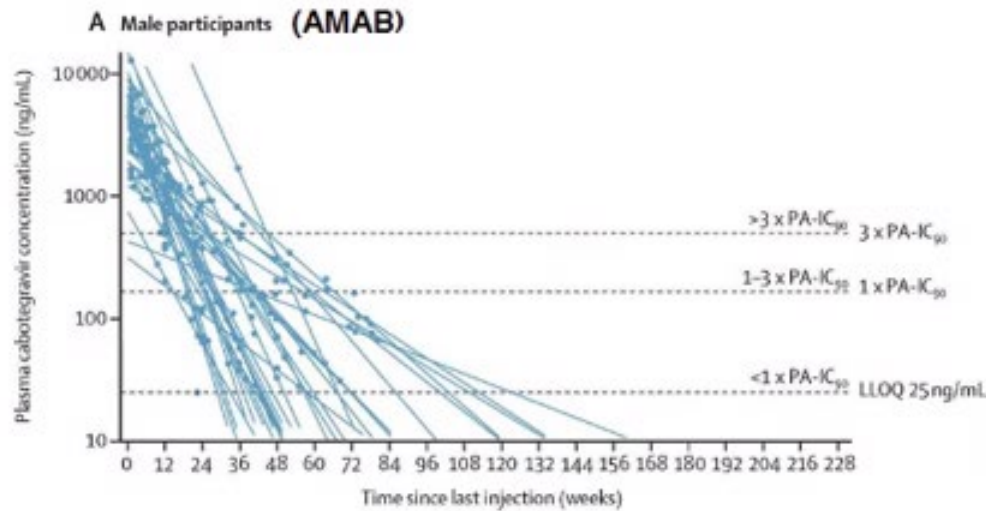
- 1. HIV RNA and Ag/Ab every 2-3 months**
- 2. STI screening every 4 months**
- 3. When applicable: hep C screening each year, pregnancy tests**

Managing the CAB “Tail”

- Cabotegravir has a long half-life and there’s a theoretical risk of resistance if a person seroconverts when the drug levels drop after discontinuation. We have not had documented/known cases of this yet.
- Current guidelines:
- If PrEP is indicated, prescribe daily oral PrEP beginning within 8 weeks after the last injection.
- Obtain HIV RNA viral load and HIV Ag/AB quarterly for 12 months after discontinuing injections.
- Use Symtuza for rapid ART if they have been on injectable PrEP and get an INSTI genotype.
- See [updated rapid ART protocols here](#).

Cabotegravir takes months to “wash out”

CAB’s pharmacokinetic “tail” is a VERY important consideration



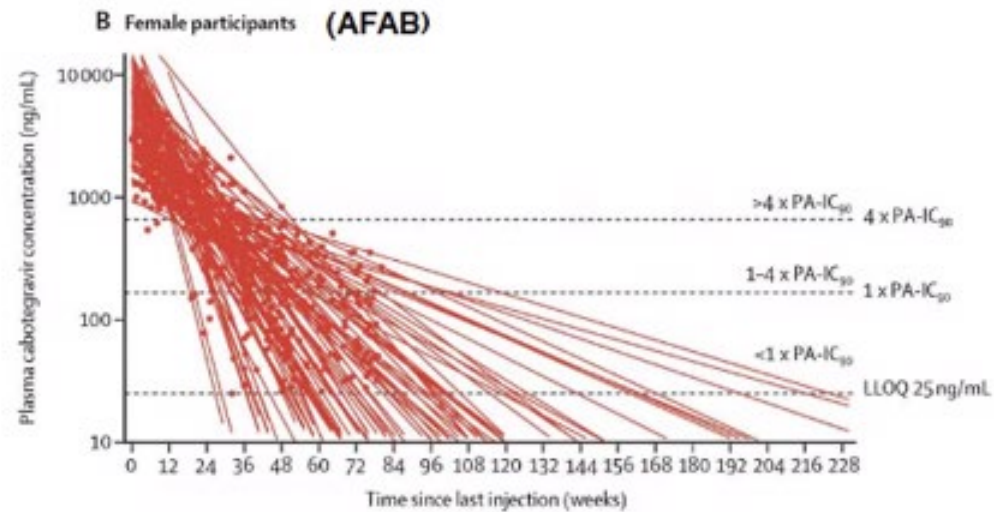
CAB dropped below LLOQ after a median of

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)

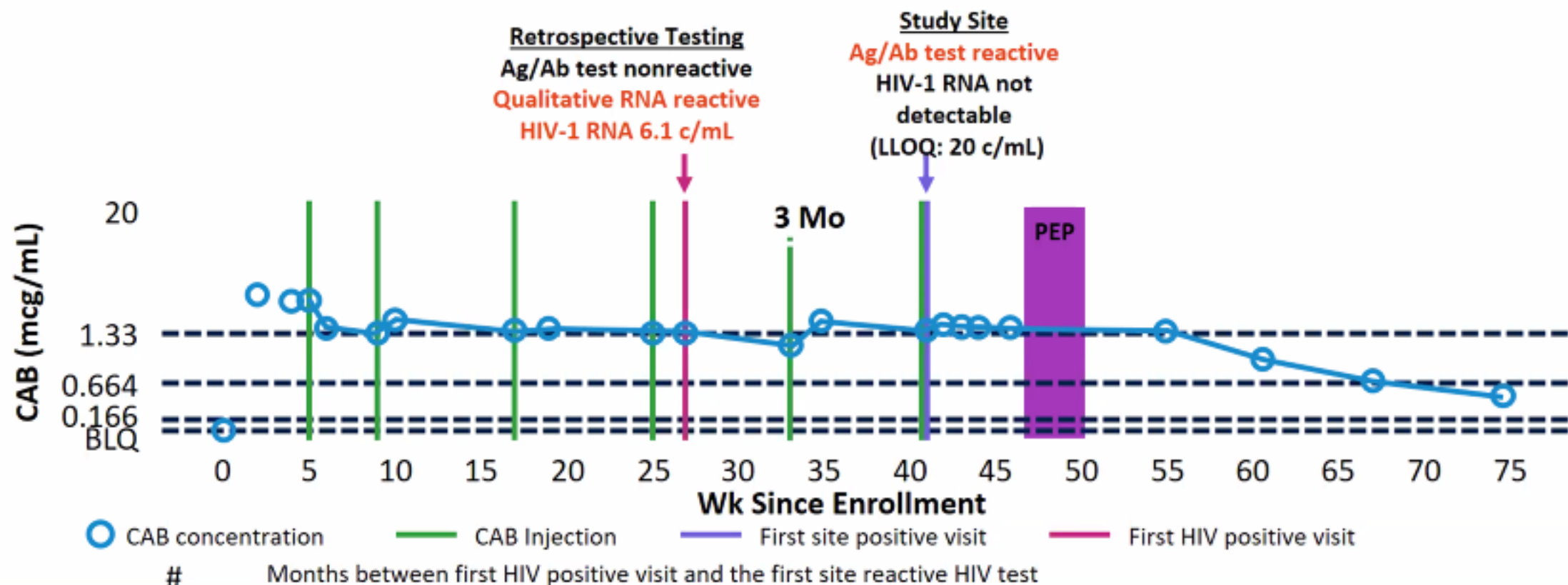


LEVI: Long-acting Early Viral Inhibition Syndrome (Rare and the reason we get RNAs)

- **CAB-LA PrEP is highly effective.**
- **Failures are rare and can be hard to detect.**
- The HPTN 083 study reported 0.3% cases of HIV infection while on CAB-LA PrEP: 18 out of 2,282 cases total, which is a very very low failure rate.
- Half had delayed diagnoses due to minimal or no symptoms and labs that were difficult to interpret: very low RNA/DNA levels and delayed Ab production.
- This is dubbed LEVI syndrome (Long-acting Early Viral Inhibition syndrome).
- 10 developed integrase resistance mutations, which limits treatment options.
- RNA testing would've picked up some seroconversions before resistance emerged.
- **To catch acute infections and seroconversions earlier and reduce integrase resistance, we recommend getting both RNAs and HIV Ag/Ab tests at initiation and every 2-3 months while on CAB-LA PrEP.**

LEVI Syndrome Patient Case: Detection of Infection

- Retrospective sensitive HIV-1 RNA testing detected HIV infection 3 mo earlier than study site



Limited Updated Data from CROI 2023

6 infections occurred despite on-time injections among 2,282 participants randomized to CAB-LA

Type of case	# Cases
Infected despite on-time injections	6
28 other infections	
No recent CAB exposure (within 6 months)	16
HIV+ at enrollment	4
Infected while receiving oral CAB	3
Infected after ≥ 1 delayed injection	3
Infected near the time of CAB re-initiation	2

Summary of INSTI Resistance	Cab Exposure	>6 Months since Cab Exposure
# Cases	18	16
INSTI Resistance	10	0

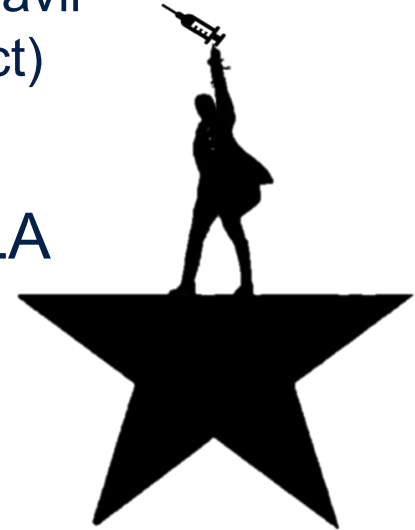
Slide credit:
Dr. Matthew Spinelli

Long-Acting Early Viral Inhibition (LEVI) Syndrome

	AHI	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)

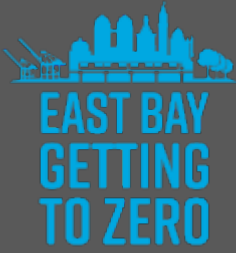
Summary: LEVI Syndrome

- Long-Acting PrEP has superior efficacy, but in rare cases of breakthrough, clinical management is complicated
- Long-acting Early Viral Inhibition (LEVI) Syndrome can occur due to:
 - Initiating Cab-LA during acute infection; prevent this by checking a viral load
 - Rare Cabotegravir breakthrough with adequate drug levels; delayed cabotegravir injections; potential for poor adherence to the oral lead -in (offer direct to inject)
- HIV tests should be interpreted with caution in the context of Cab -LA
 - Antigen/Antibody tests may remain negative or turn positive and revert
 - Viral Loads can be extremely low and will often revert over time
 - Qualitative HIV RNA is preferred, but use most sensitive assay available

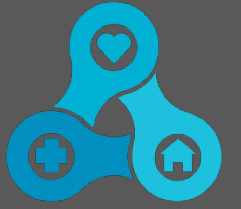


LEVI Syndrome outbreaks: What to do about it

- 1. Get *both* HIV RNA and HIV Ag/Ab tests at initiation and every 2-3 months while on CAB-LA PrEP to catch acute infections and seroconversions earlier.**
- 1. If someone seroconverts (positive HIV RNA, DNA *or* Ag/Ab) while on CAB-LA PrEP, get a genotype including integrase resistance and prescribe a PI-based regimen such as Symtuza as rapid ART. If the genotype doesn't show integrase resistance, you can consider switching to INSTI regimen if desired.**
- 1. If someone stops CAB-LA for PrEP, prescribe daily oral F/TDF or F/TAF within 8 weeks after the last CAB injection (2-1-1 could be a reasonable alternative in some situations) and get quarterly HIV RNA and Ag/Ab testing for a year after stopping CAB-LA.**

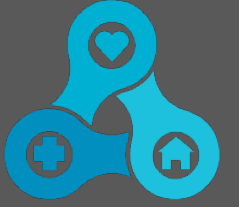


Innovative models: BH integration



- **Combining LAI PrEP with other LAI treatment (psych/SUD)**
- **Bridge**
- **TRUST**
- **ACBH primary care**

Innovative models: LAI PrEP in EDs?



- **What if Emergency Departments (EDs) provided LAI PrEP injections?**
- **... for people already on LAI PrEP?**
- **... for people initiating LAI PrEP, with follow-up coordination?**

Injectables resources

Check out the [EBGTZ Injectables webpage](https://ebgtz.org/resource/injectables) for the latest local resources:
ebgtz.org/resource/injectables

- **Clinical guides, protocols and EHR tools**
- [EBGTZ Injectable PrEP Quick Guide](#)
- [Pacific AETC Injectables Toolkit](#), including clinical protocols, checklists and patient education
- [SFDPH Injectable PrEP Pocket Card PDF](#); also [on this webpage](#)
- [Ward 86 Long-acting Injectable Antiretroviral Protocol](#)
- [LifeLong Long-acting Injectable ARV Protocol](#)
- [Epic SmartPhrases for Cabenuva and Apretude from LifeLong](#)

- **Training videos**
- [Apretude clinical training video from Viiv](#): [click to watch here](#) or [watch on the Viiv website](#)
- [Ventrogluteal injection site training video](#)
- [Thigh injection \(vastus lateralis\) site training video](#)



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Next steps and upcoming meetings

Upcoming events and working group meetings:

- Next clinical conference discussing injectables: May 14, 2024, 12-1 pm on Zoom.
- More East Bay HIV meetings here: www.EBGTZ.org/events
- Join our East Bay HIV network lists/groups: email ZJ Eskman: zj@ebgtz.org

Thank you & Evaluation!

