



NATIONAL LGBTQIA+ HEALTH
EDUCATION CENTER

A PROGRAM OF THE FENWAY INSTITUTE

Long-acting Injectable PrEP

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May 19, 2022

Our Roots

Fenway Health

- Independent 501(c)(3) FQHC
- Founded 1971
- Mission: To enhance the wellbeing of the LGBTQIA+ community as well as people in our neighborhoods and beyond through access to the highest quality health care, education, research, and advocacy
- Integrated primary care model, including HIV and transgender health services

The Fenway Institute

- Research, Education, Policy



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The National LGBTQIA+ Health Education Center offers educational programs, resources, and consultation to health care organizations with the goal of providing affirmative, high quality, cost-effective health care for lesbian, gay, bisexual, transgender, queer, intersex, asexual, and all sexual and gender minority (LGBTQIA+) people.

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- ECHO Programs
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www.lgbtqiahealtheducation.org

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I have no relevant financial disclosures.

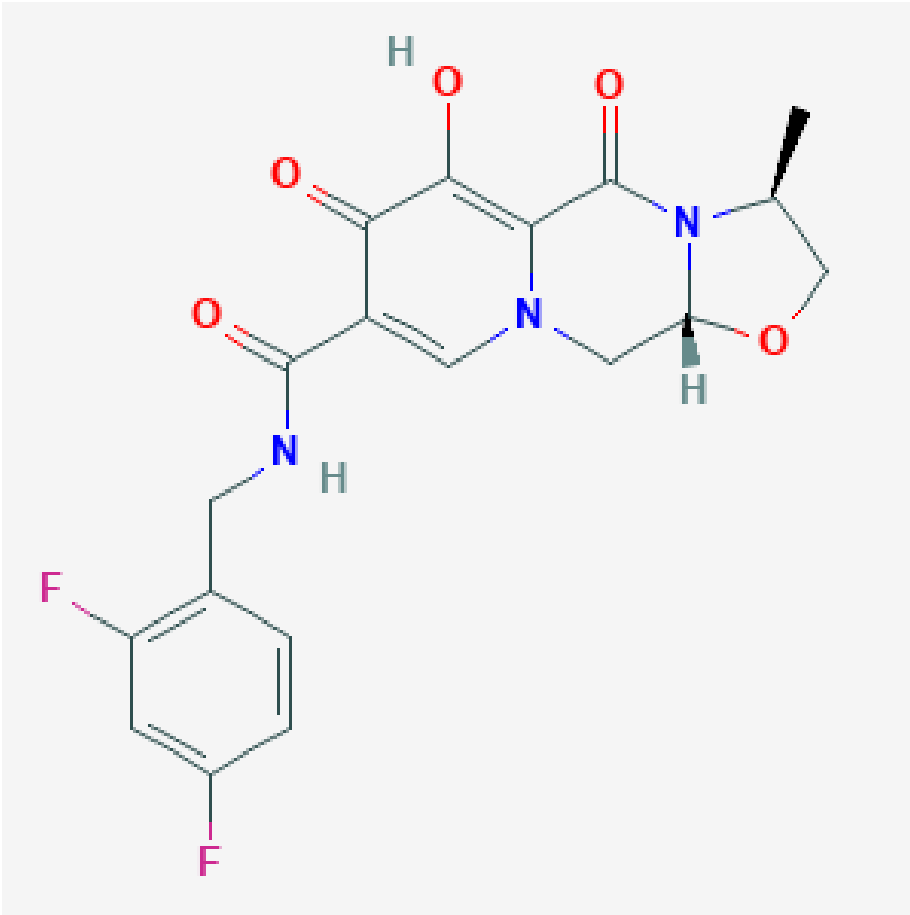
Learning Objectives



Image from oceanographicmagazine.com

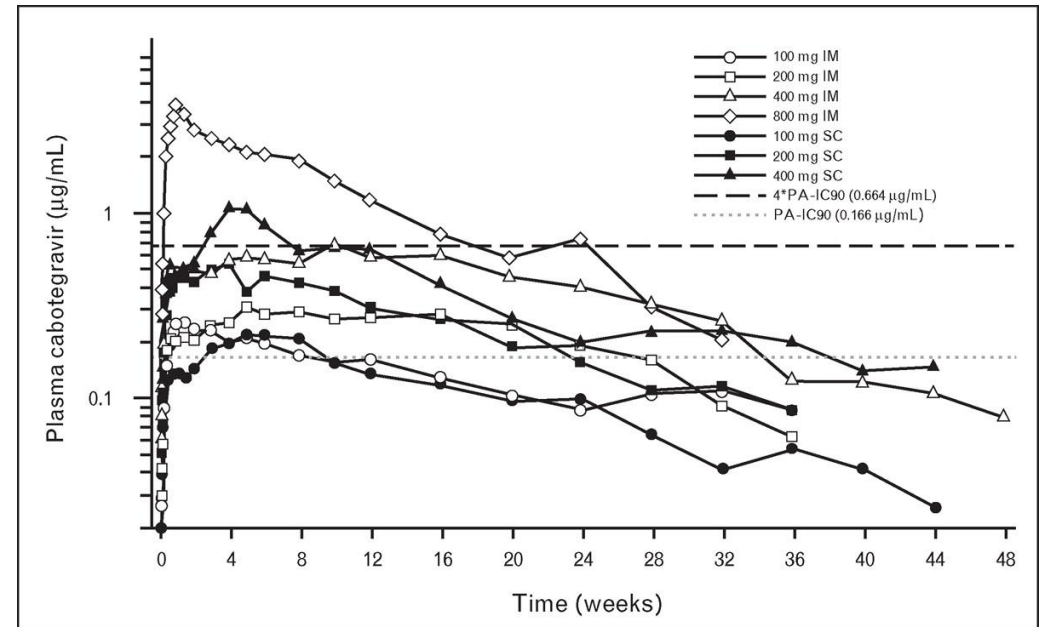
1. Summarize the evidence for long-acting injectable HIV prevention
2. Analyze the advantages and disadvantages of long-acting injectable antiretrovirals
3. Discuss the implementation of long-acting injectable HIV prevention

Long-acting Cabotegravir (CAB-LA)



pubchem.ncbi.nlm.nih.gov/compound/Cabotegravir#section=2D-Structure, Trezza C 2015

- Integrase inhibitor (structurally similar to dolutegravir)
- Elimination half-life = 40 days
- Prolonged subtherapeutic tail



Long-acting Cabotegravir/Rilpivirine for HIV treatment (CAB/RPV)

- Indicated for people with HIV-1 who “are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure or known or suspected resistance to either cabotegravir or rilpivirine”
- Monthly or bi-monthly intramuscular injections



Cabenuva prescribing information,

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf

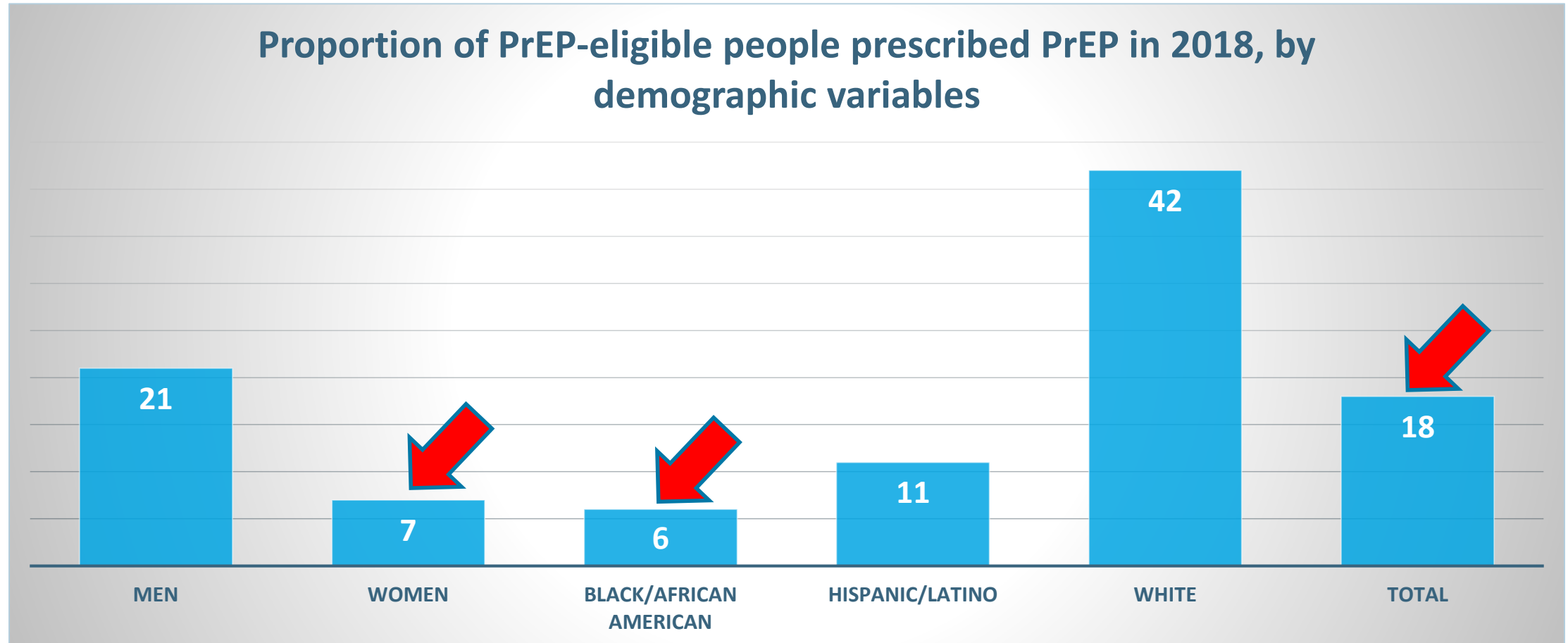
Image from <https://www.poz.com/article/cabenuva-every-month-maintains-viral-suppression-two-years>

Poll

What proportion of Americans with indications for PrEP have been prescribed it?

- A. 1%
- B. 10%
- C. 20%
- D. 30%

Most people who could benefit from PrEP are not taking it.



Case

- A 27-year-old cisgender gay man presents in follow-up.
- He injects methamphetamine daily, often sharing injection equipment with others.
- He has insertive/receptive sex with cisgender men and does not use condoms.
- 2 months ago, he was diagnosed with early latent syphilis and was treated with long-acting benzathine penicillin.
- He is prescribed oral TDF/FTC for PrEP but struggles to take it, often missing weeks of pills at a time.
- Today, he is asymptomatic, and a routine HIV antibody/antigen test is negative.

Poll

Would you recommend CAB-LA for PrEP for him?

- A. Yes
- B. No
- C. I'm not sure

Which barriers will long-acting injectable PrEP overcome?

Patient	Provider	Structural/environmental
Limited knowledge of PrEP	Knowledge of PrEP	Homophobia
Low HIV risk perception	Willingness to prescribe PrEP	Transphobia
Limited knowledge of partners' risks	"Purview paradox"	Sexism
Medical mistrust	Competing priorities	Racism
Financial concerns	Failure to elicit HIV risk information	Lack of health care access
Competing priorities	Billing/reimbursement concerns	Insurance climate
Confidentiality concerns		HIV-related stigma
Adherence		

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Potential Advantages and Disadvantages of Long-acting Injectable HIV Prevention

Advantages

- Choice
- Adherence
- Confidentiality
- Reduced stigma
- Does not require GI absorption

Disadvantages

- Cost?
- Schedule of care?
- Injection site reactions
- Long subtherapeutic tails

Kerrigan D, et al. PLoS One. 2018

Choice may lead to uptake.

CROI 2022

APPLYING LESSONS ON EFFICACY AND AUTONOMY FROM CONTRACEPTION TO PrEP

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Disclosure: None



Bixby Center for Global Reproductive Health | **UCSF** University of California San Francisco

Contraception: more choices → greater use



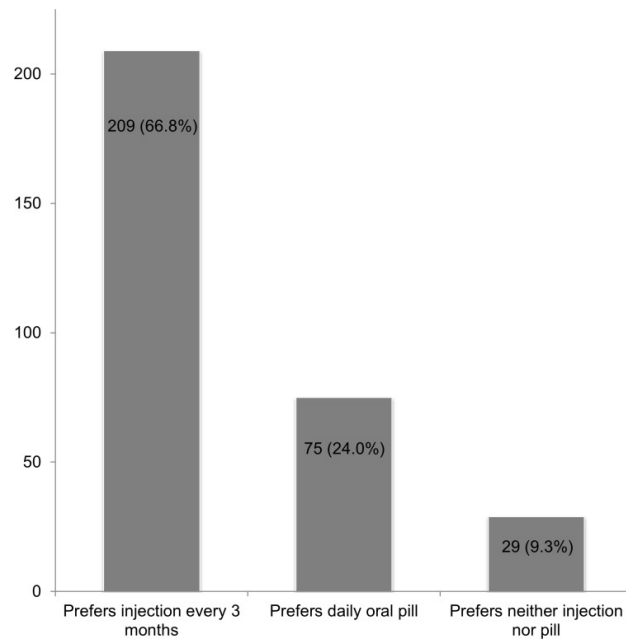
Mean No. of Available Methods	Modern Contraceptive Prevalence Rate (%)
1	10, 12, 14, 15, 16
2	5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28
3	5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80
4	8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80
5	30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90
6	32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80

Ross & Stover, *Global Health Sci Pract* 2013

Perceptions of Long-acting Injectable PrEP among MSM

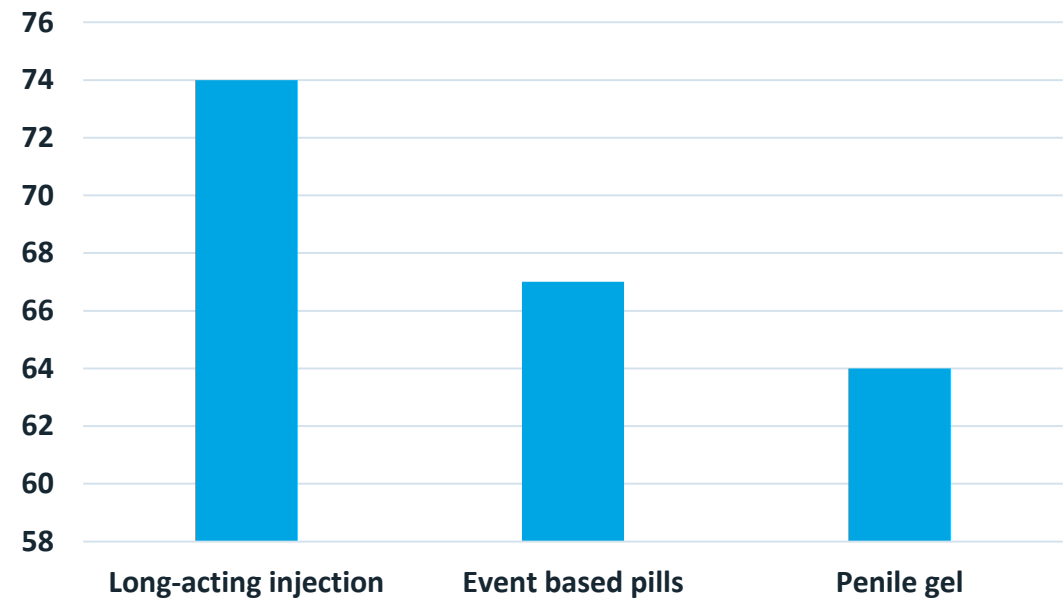
314 MSM in Washington, DC

- Median age 30, 41% non-Hispanic Black



M-cubed study

Proportion of MSM reporting likelihood of using PrEP formulations



Levy ME 2017

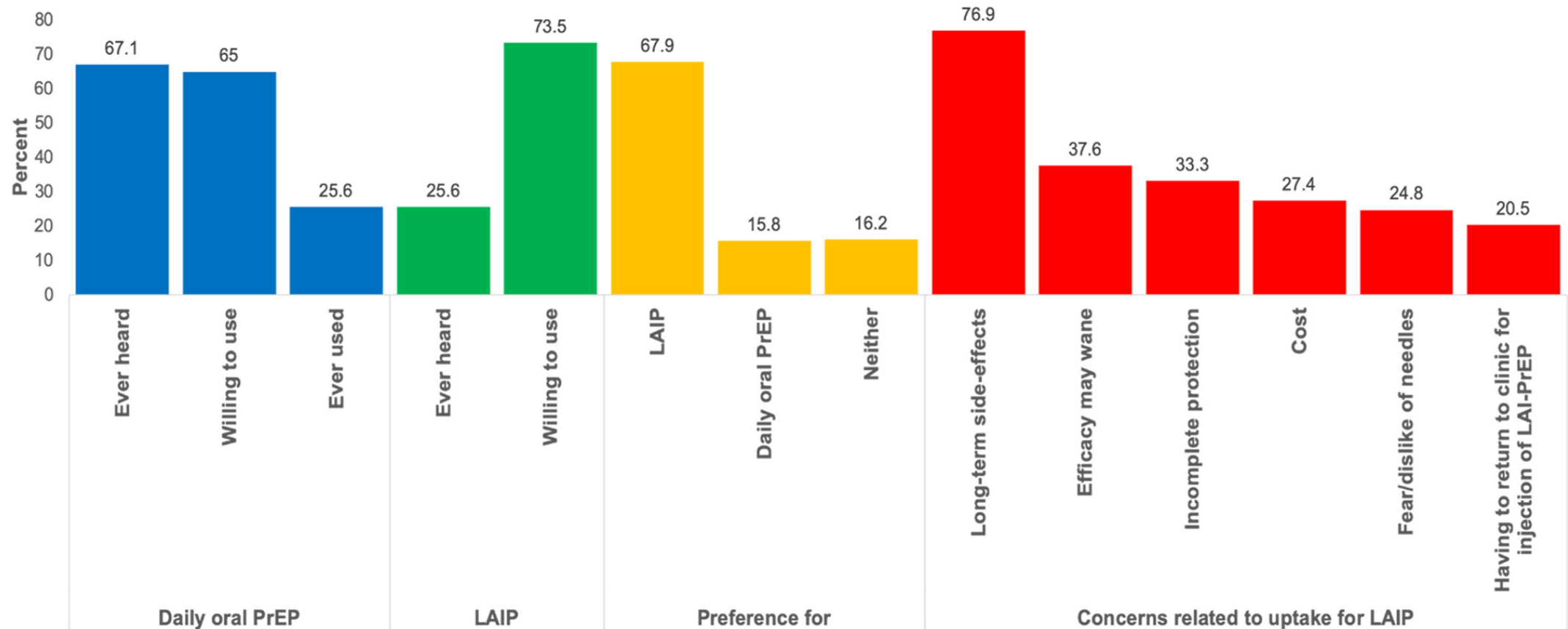
Perceptions of Long-acting Injectable PrEP among Women

- 30 subjects in the Women's Interagency HIV Study
- Median age = 51 years
- 77% Black/African-American
- 60% no education beyond high school
- 57% knew of PrEP
- When asked to choose a formulation:
 - 55% preferred long-acting injectable PrEP
 - 10% preferred oral PrEP
 - 33% no PrEP

Philbin MM 2020

Perceptions of Long-acting Injectable PrEP among People Who Inject Drugs

Perceptions among 234 people with opioid use disorder in CT

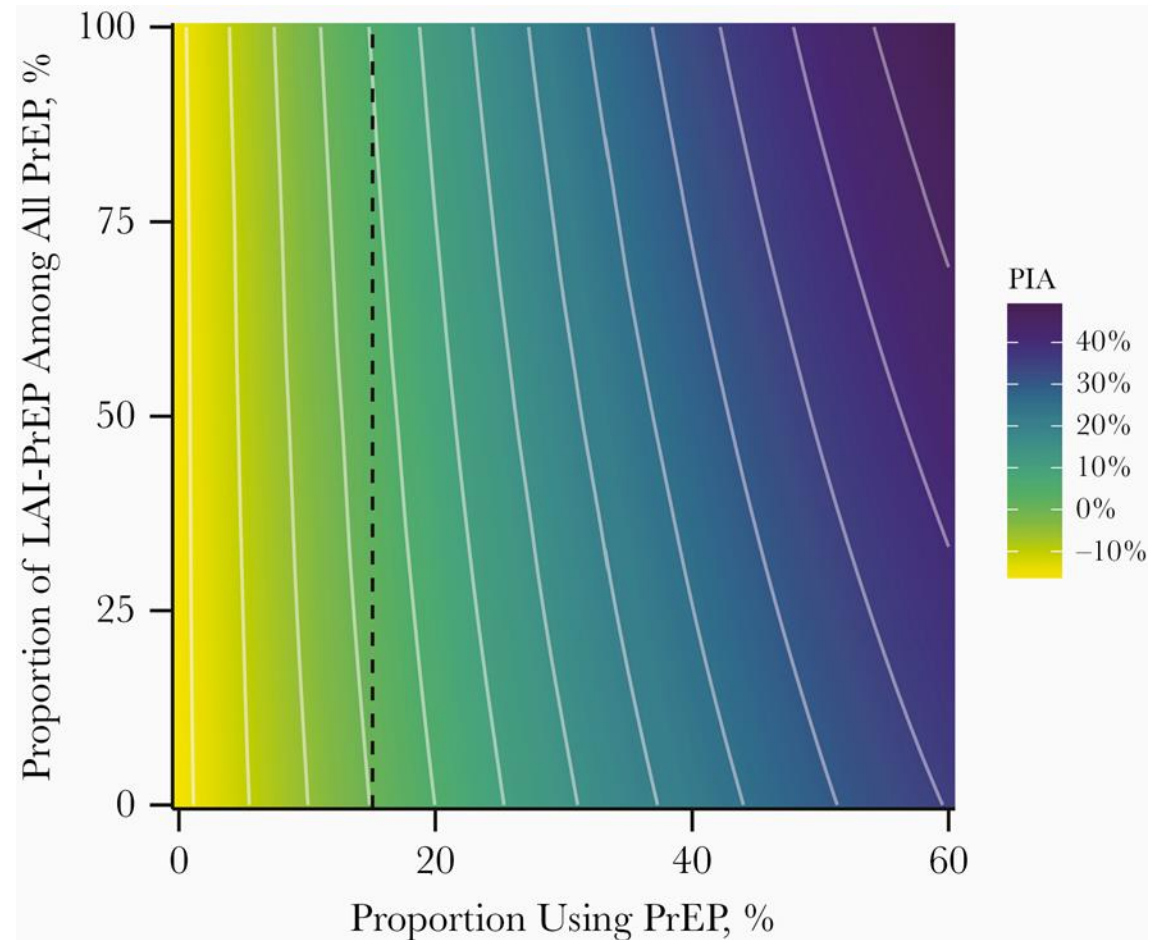


Conclusion from Perception Studies

- Many people report being more likely to use long-acting injectable PrEP than other forms of PrEP.
- Enthusiasm is limited in some populations with low oral PrEP use.
- Prior use of oral PrEP predicts willingness to use long-acting injectable PrEP.
- Perceptions may be different once there are available therapies.

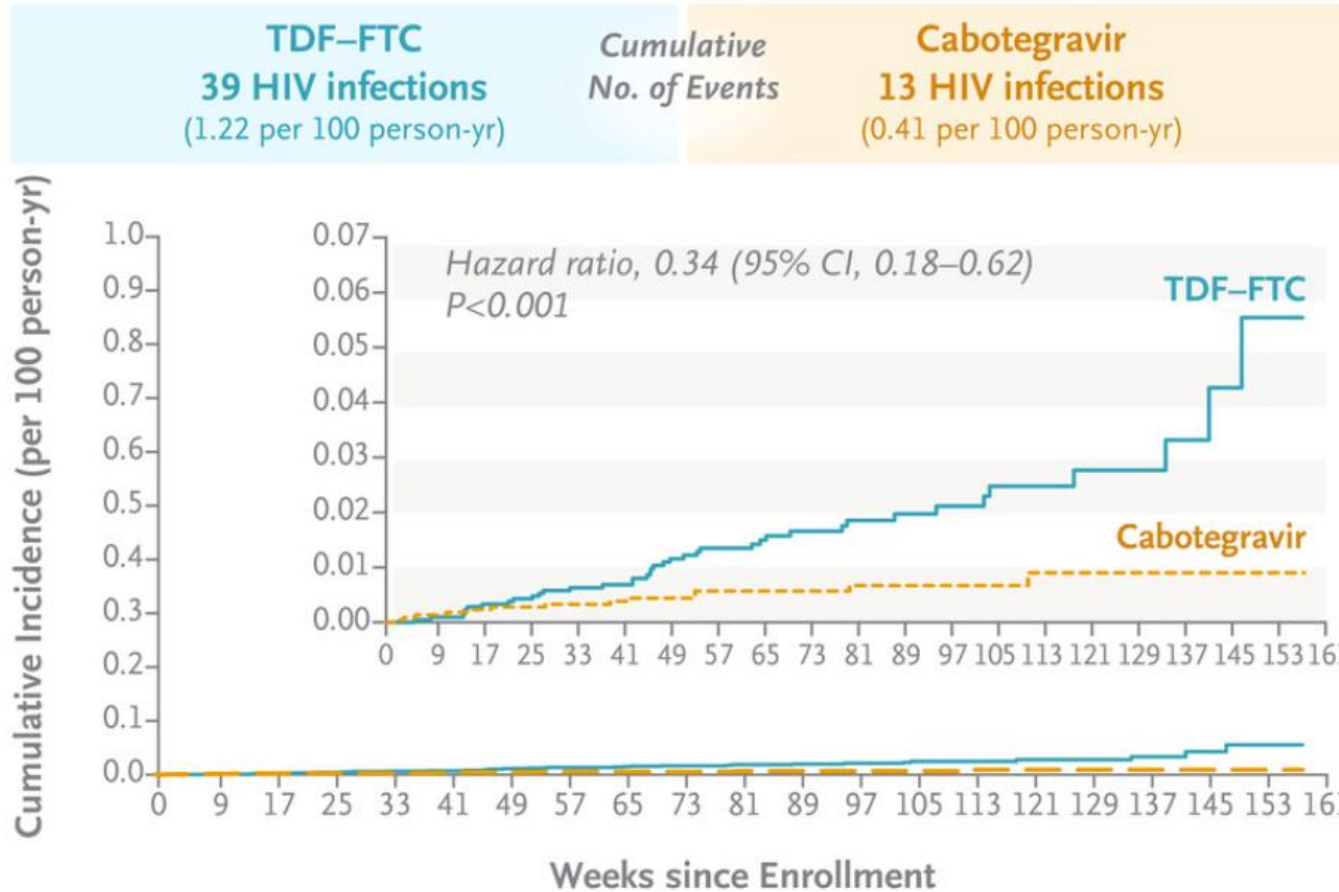
Modelled Impact of Long-acting PrEP among MSM in the Southeastern U.S.

- **Comparison:** 15% of eligible MSM using daily oral PrEP
- If 50% of PrEP users opt for long-acting injectable PrEP, 4% of infections averted over 10 years

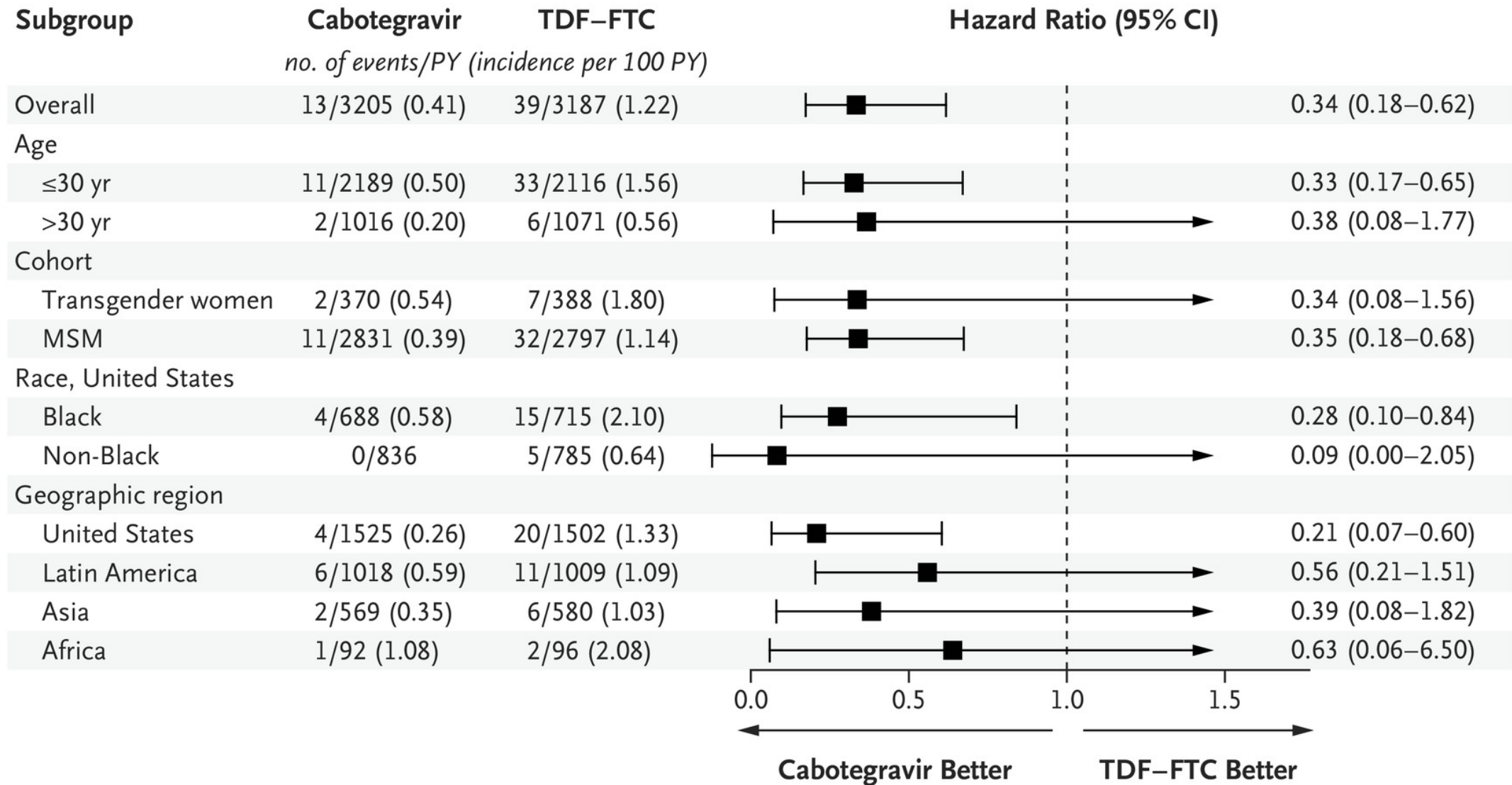


CAB-LA is Superior to TDF/FTC for PrEP.

Incident HIV Infection



B Incident HIV Infection in Prespecified Subgroups



CAB-LA is Superior to TDF/FTC for PrEP among Cisgender Women.

- **HPTN 084:** Randomized clinical trial of CAB-LA versus TDF/FTC for PrEP among 3,224 women in Africa
- CAB-LA reduced the risk of HIV by **88%** in comparison to TDF/FTC.
- Adherence to TDF/FTC was moderate; **42%** took it daily based on drug levels.

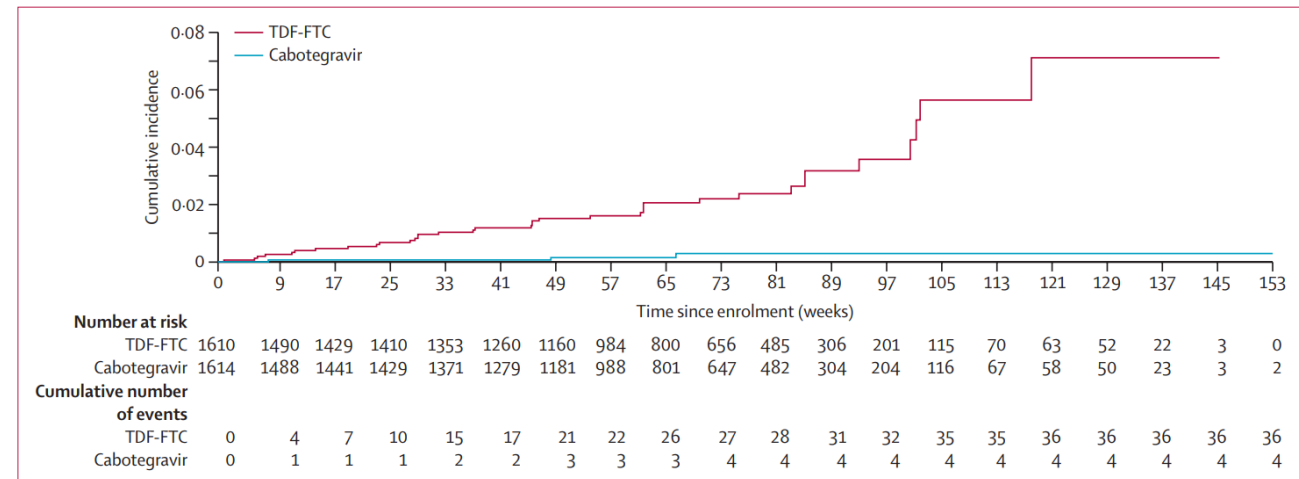


Figure 3: Cumulative HIV incidence by study group

Delany-Moretlwe S, Lancet, 2022

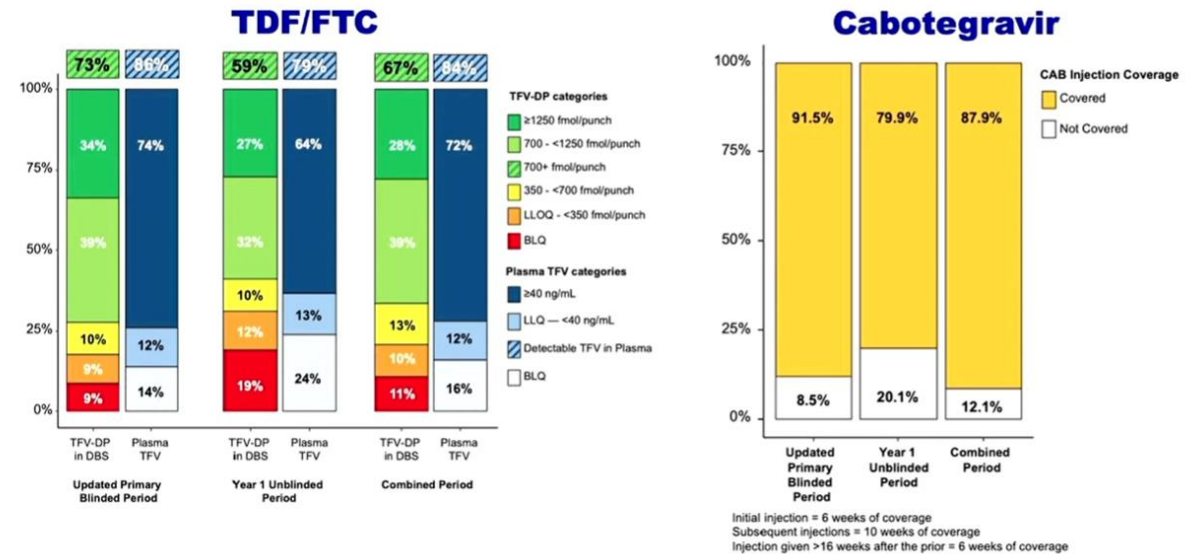
Antiretroviral Resistance in HPTN 083

Context of infection	Integrase inhibitor mutations
Prior to CAB injection	Q148R in 2 of 3 subjects
Infection despite on-time CAB	R263K in 1 of 4 subjects Q148R in 1 of 4 subjects
Tail phase	None in 5 subjects

Updates from HPTN 083 (CAB-LA vs. TDF/FTC for PrEP)

- Updated efficacy analysis from the first unblinded year
- HR 0.33 for HIV in CAB-LA versus TDF/FTC, consistent with the primary blinded results
- However, HIV incidence rose in both CAB-LA and TDF/FTC arms with declines in adherence in both arms

Study Product Adherence



Landovitz R, Abstract 96

Table 7 Timing of CAB PrEP-associated Laboratory Tests

Test	Initiation Visit	1 month visit	Q2 months	Q4 months	Q6 months	Q12 months	When Stopping CAB
HIV*	X	X	X	X	X	X	X
Syphilis	X			MSM^/TGW~ only	Heterosexually active women and men only	X	MSM/TGW only
Gonorrhea	X			MSM/TGW only	Heterosexually active women and men only	X	MSM/TGW only
Chlamydia	X			MSM/TGW only	MSM/TGW only	Heterosexually active women and men only	MSM/TGW only

* HIV-1 RNA assay

X all PrEP patients

^ men who have sex with men

~ persons assigned male sex at birth whose gender identification is female

Why no assessment for viral hepatitis in those at risk?

HIV RNA Assays for Monitoring Those with Antiretroviral Exposure

Rationale:

- Antiretrovirals impact HIV test performance
- Antigen/antibody positivity may be delayed beyond that of an HIV RNA assay for incident infections by a mean of
 - 98 days in those receiving CAB-LA
 - 31 days in those receiving TDF/FTC

Questions and challenges:

- Obtaining HIV RNA assays for people who are un- or underinsured
- Limitations of the USPSTF/ACA provision

HIV RNA Assays for Those Receiving CAB-LA for PrEP

- Low viral load INSTI genotypes for people who acquired HIV despite CAB-LA
- Among 7 cases, RNA assays would have detected HIV before a major INSTI mutation was detected in 4 cases and before additional major INSTI mutations in 2 cases
- **Is CAB-LA a good option for PrEP even when resources do not permit RNA assays?**

Eshleman S, Abstract 95

Questions about CAB-LA

Will it prevent HIV transmission from injection drug use?

- **CDC:** “PWID are likely to benefit from PrEP with any FDA-approved medication with or without an identified sexual behavior risk of HIV acquisition.”

Can CAB-LA be used in adolescents?

- The FDA approved the drug for adults *and* adolescents.
- **CDC:** “CAB is not recommended for adolescents < 18 years old.”
- The HPTN 083-01 study is assessing CAB-LA among people < 18 years.

1. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 update: a clinical practice guideline. 2021. Available at: <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>.

2. FDA news release. 2021 Dec 20. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention>.

Questions about CAB-LA, continued

Will CAB-LA be compatible with pregnancy/breastfeeding?

- **HPTN 084:** 29 pregnancies in the CAB-LA group; no congenital anomalies observed
- **Package insert:**
 - Use during pregnancy “only if the expected benefit justifies the potential risk to the fetus.”
 - Implications of tail phase
 - Antiretroviral Pregnancy Registry (www.apregistry.com)

Delany-Moretlwe S, Lancet, 2022; accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf

Poll

What are your biggest concerns about LA-CAB for PrEP?

- A. Ensuring patients return for injections
- B. Cost/access
- C. Logistics prescribing/administering
- D. Breakthrough HIV infections
- E. Side effects
- F. Something else

Implementing CAB-LA: Many Questions

Two approaches:

- Buy and bill
- Specialty pharmacy

Questions

- Optimal workflows?
- Local PrEP drug-assistance programs?
- Ensuring patients return for their first injection?

Will same-day PrEP be possible for CAB-LA?

Panel: Considerations for same-day PrEP

Reasons to consider same-day PrEP

- Minimise drop-off between PrEP evaluation and initial prescription
- Reduce barriers to PrEP access and delivery (eg, time)
- Standard of care for other medical conditions (eg, oral contraceptives)

Reasons not to consider same-day PrEP

- System barriers (absence of insurance or payment assistance, absence of referral network for PrEP continuity care, absence of laboratory services)
- Patient considerations (history of renal disease, inability to contact for follow-up if abnormal laboratory test results)
- Unknown effect on PrEP persistence and adherence

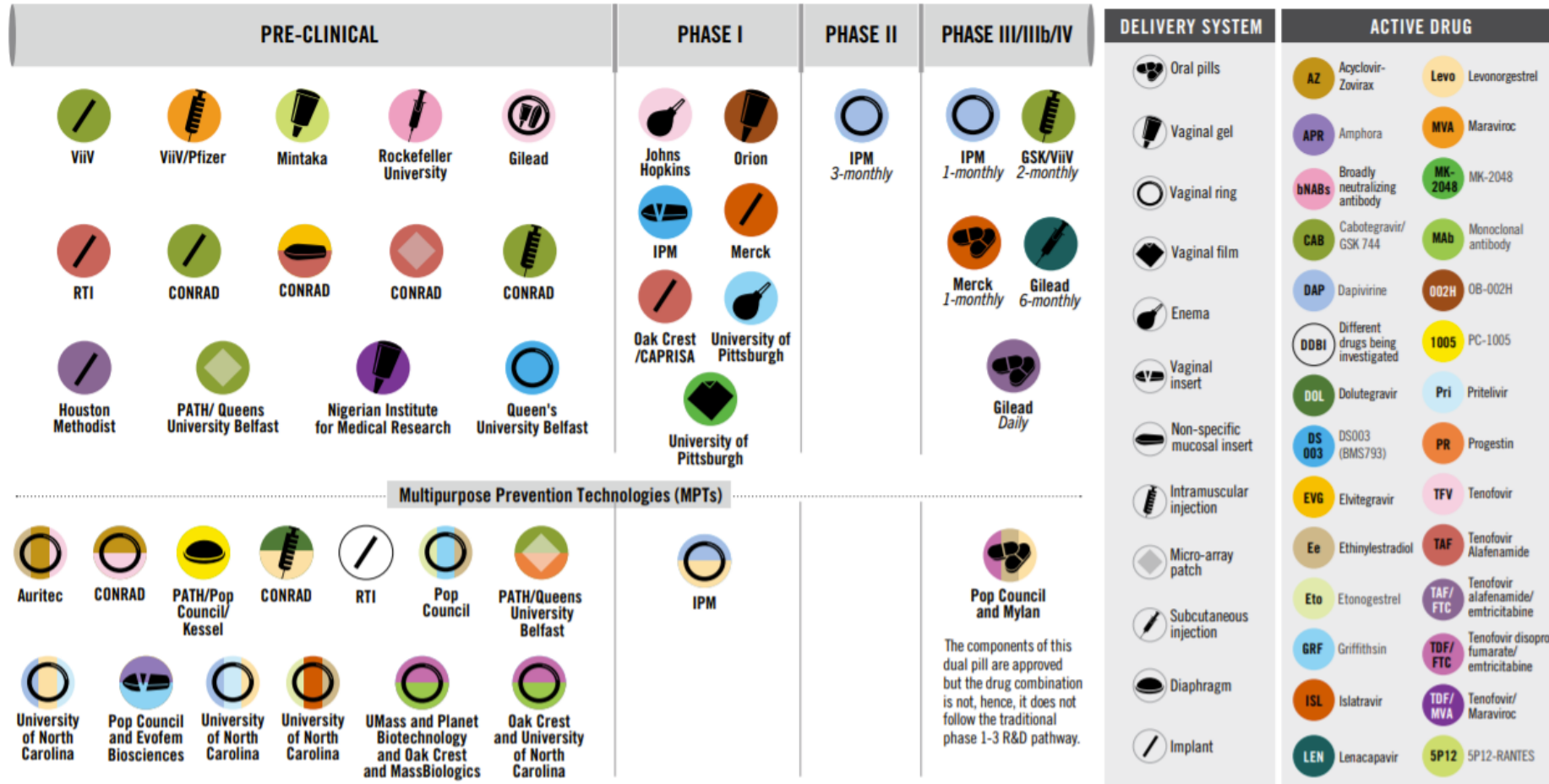
Facility considerations for providing same-day PrEP

- Ability to do point-of-care HIV testing
- Ability to test for creatinine and pregnancy
- Ability to draw blood for laboratory testing
- Ability to contact patients to discontinue PrEP if needed
- Access to insurance navigation and medication assistance programmes for uninsured and underinsured individuals
- Capacity to attend the 1 month or 3 month (or both) follow-up appointments for ongoing PrEP care (onsite or through referral network)

PrEP options in 2021

Medication	Advantages	Disadvantages
Oral TDF/FTC	<ul style="list-style-type: none"> →Prevents HIV acquisition through sex and injection drug use →Effective when used in an on-demand fashion among MSM →Available as a generic 	<ul style="list-style-type: none"> →Should not be used when estimated creatinine clearance is < 60 mL/min →Risks of renal adverse events and decreased bone mineral density
Oral TAF/FTC	<ul style="list-style-type: none"> →Prevents HIV acquisition through sex →Less likely than TDF/FTC to adversely affect kidneys or bone →Can be used if the estimated creatinine clearance is ≥ 30 mL/min 	<ul style="list-style-type: none"> →Use in an on-demand fashion or among cisgender women has not been studied →Risk of weight gain and dyslipidemia
Intramuscular CAB (CAB-LA)	<ul style="list-style-type: none"> →Superior to TDF/FTC for PrEP among MSM, transgender women, and cisgender women →Every-two-month injections obviate the need for taking a pill daily 	<ul style="list-style-type: none"> →Requires more frequent clinic visits than oral PrEP →Injection site reactions are common but tend to be mild →Limited data about safety in pregnancy

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals and more. Also pictured are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and STIs and/or provide effective contraception for women. (Visit www.avac.org/hvad for vaccine and broadly neutralizing antibody pipelines.)



Summary

- CAB-LA is highly effective for PrEP
- CAB-LA's monitoring and administration will affect PrEP program structure and workflow
- The addition of CAB-LA to the PrEP toolkit may increase PrEP uptake overall