CROI 2025: Updates in HIV Prevention & STIs

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Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

MPOX

ACTG A5418

STOMP
Study of Tecovirimat for Mpox

Design and Sample Size	2:1 Randomized, Blinded, Placebo-controlled (n=530) Open label for children, persons with pregnancy or severe disease, severe immune suppression or severe skin disease (n≅250)
Study Population	Symptomatic mpox
Design	Superiority; randomized participants allowed open label tecovirimat for disease progression or severe pain at day 5
1^0 Outcome	Time to clinical resolution (all skins lesions scabbed or epithelialized; all visible mucosal lesions healed)
2^0 Outcomes	Daily pain score, HMPXV detection in various compartments, Pt reported outcomes
Duration	57 days (in person or fully remote enrollment)
Agent	Weight based oral Tecovirimat

Wilkin T, et al. CROI 2025 – OA 201

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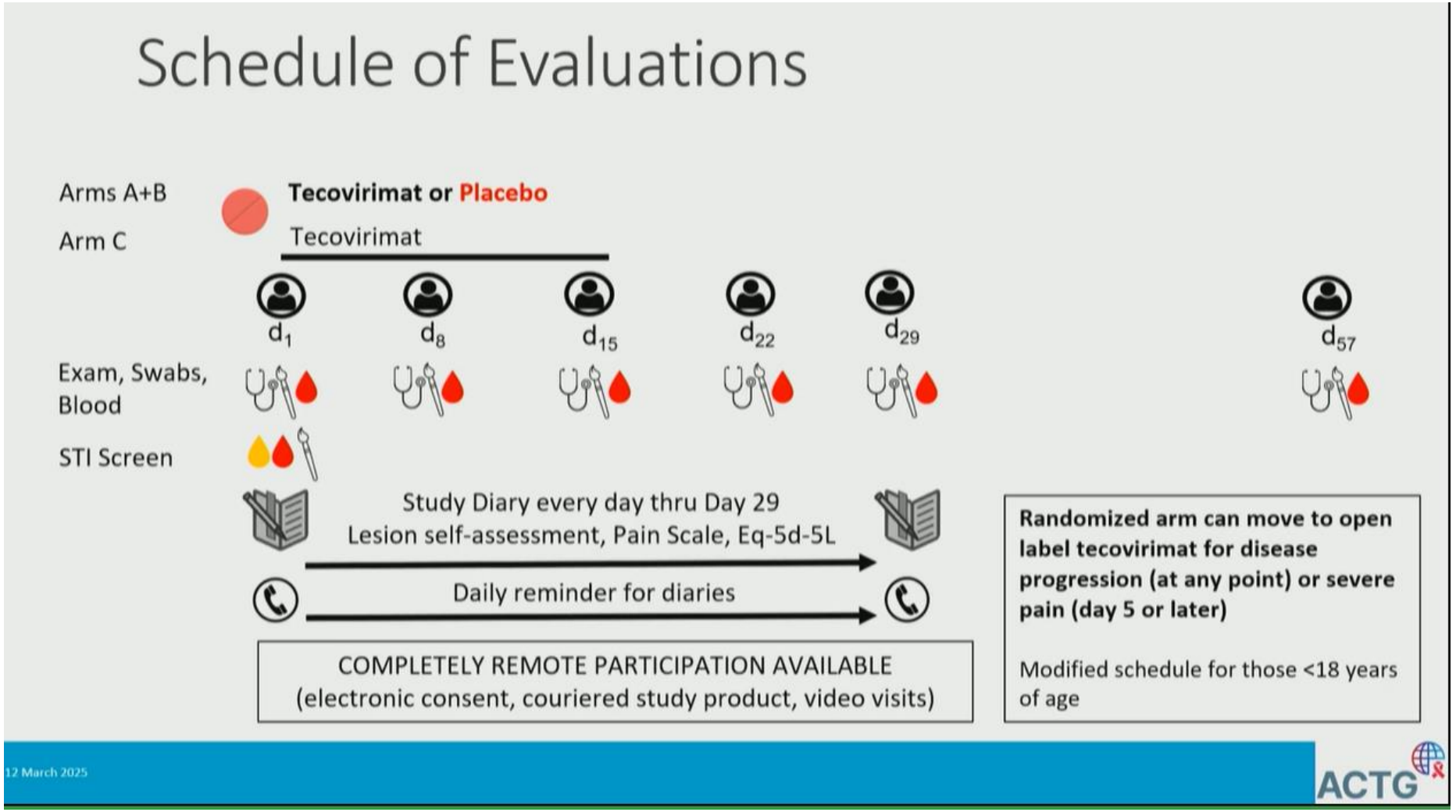
STOMP: Study procedures



Wilkin T, et al. CROI 2025 – OA 201
Fischer II WA, et al. CROI 2025 – OA 159

STOMP: Participant characteristics

Baseline characteristics for randomized population with lab-confirmed mpox (n=344)

	Tecovirimat (n=232)	Placebo (n=112)	Total (n=344)
Age	34 [27, 40]	34 [28, 41]	34 [28,40]
Male sex	228 (98%)	111 (99%)	339 (99%)
Remote enrollment	53 (23%)	28 (25%)	81 (24%)
White race	121 (52%)	61 (54%)	182 (53%)
Hispanic	107 (46%)	44 (39%)	151 (44%)

713 enrolled; 413 randomized; 68 excluded for lack of mpox diagnosis; 1 excluded enrollment violation; 344 analysis set

ACTG

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STOMP: Participant characteristics

Baseline characteristics for randomized population with lab-confirmed mpox (n=344)

	Tecovirimat (n=232)	Placebo (n=112)	Total (n=344)
Days from symptom onset	8 [6, 10]	8 [6, 10]	8 [6, 10]
Severe pain (7-10 NRS)	81 (35%)	35 (32%)	116 (34%)
Lesion number	9 [5, 18]	8 [3, 17]	9 [4, 18]
Proctitis	85 (37%)	37 (33%)	122 (35%)
Living with HIV	86 (38%)	31 (28%)	117 (35%)
Prior smallpox vaccine	54 (23%)	24 (21%)	78 (23%)

713 enrolled; 413 randomized; 68 excluded for lack of mpox diagnosis; 1 excluded enrollment violation; 344 analysis set

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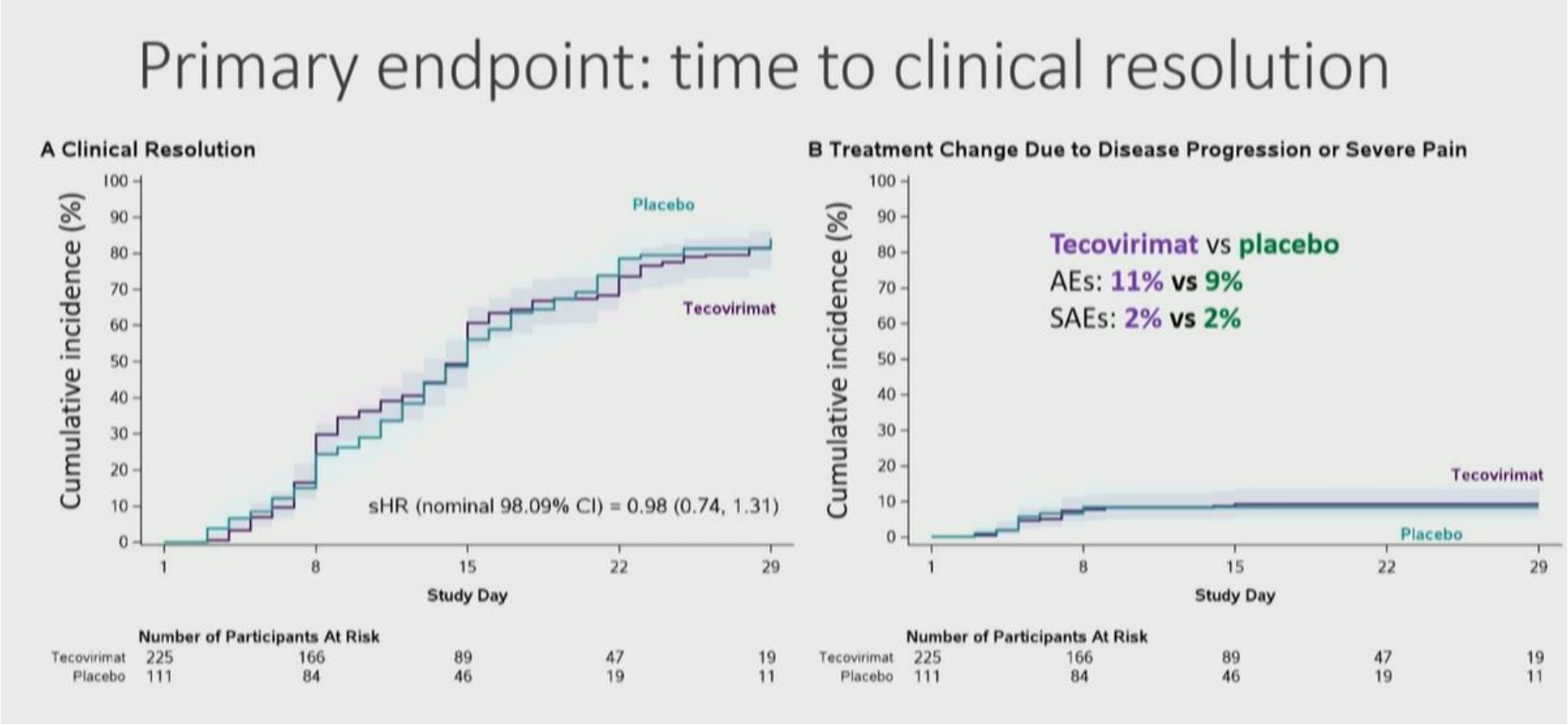
STOMP: Tecovirimat did not improve clinical outcomes

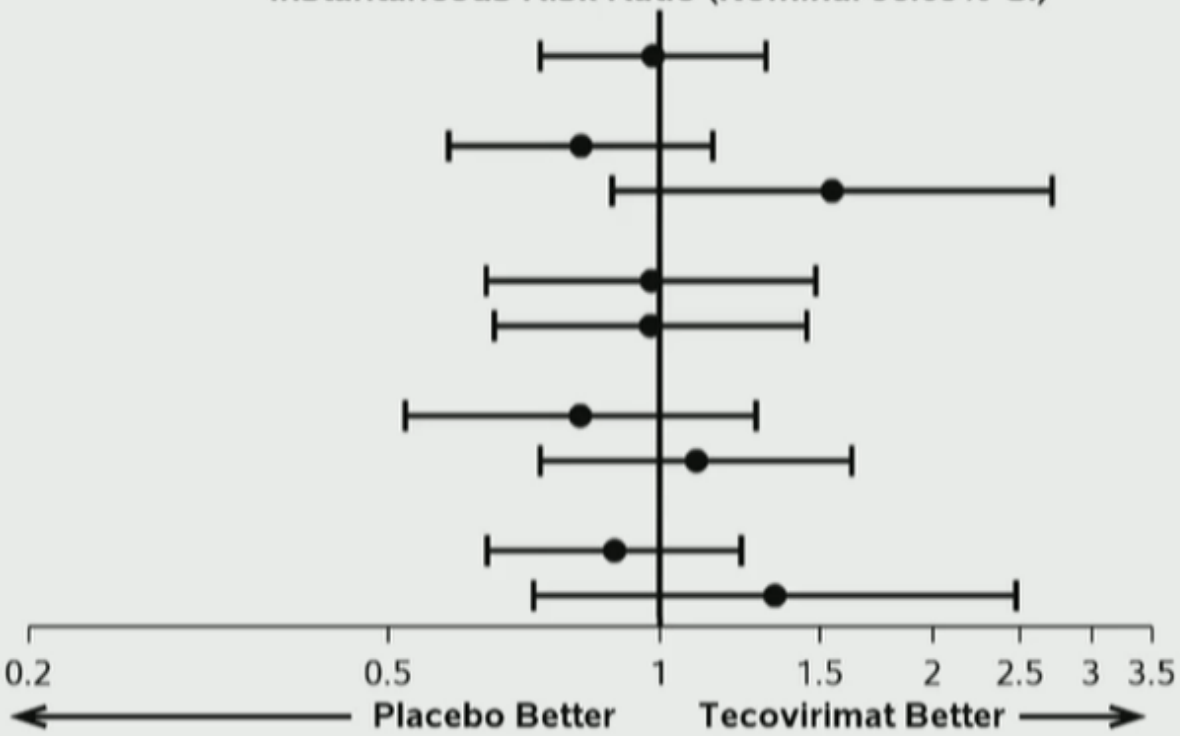


- Cumulative probability of clinical resolution by 28 days: 87% (95% CI: 80-92)
- Arm C: median time to clinical resolution from treatment initiation: 14 days (95% CI: 13-16)

Wilkin T, et al. CROI 2025 – OA 201
Fischer II WA, et al. CROI 2025 – OA 159

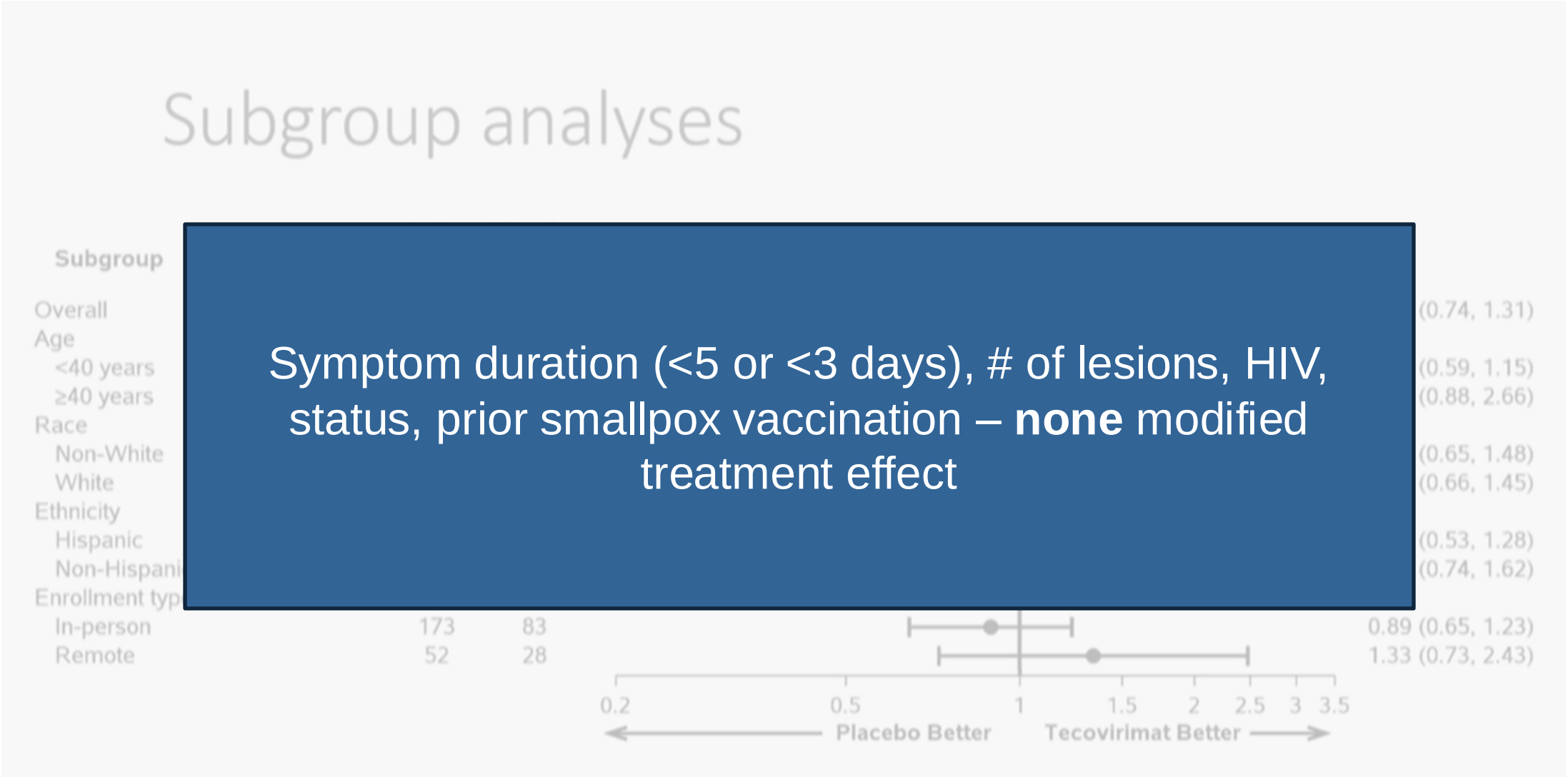
STOMP: No treatment effect modification in subgroup analysis

Subgroup	Active N	Placebo N	Instantaneous Risk Ratio (Nominal 98.09% CI)
Overall	225	111	0.98 (0.74, 1.31)
Age			
<40 years	165	79	0.82 (0.59, 1.15)
≥40 years	60	32	1.53 (0.88, 2.66)
Race			
Non-White	107	50	0.98 (0.65, 1.48)
White	118	61	0.98 (0.66, 1.45)
Ethnicity			
Hispanic	105	44	0.82 (0.53, 1.28)
Non-Hispanic	117	63	1.09 (0.74, 1.62)
Enrollment type			
In-person	173	83	0.89 (0.65, 1.23)
Remote	52	28	1.33 (0.73, 2.43)



Wilkin T, et al. CROI 2025 – OA 201

STOMP: No treatment effect modification in subgroup analysis



Symptom duration (<5 or <3 days), # of lesions, HIV, status, prior smallpox vaccination – **none** modified treatment effect

Mpox and STOMP trial: Summary and conclusions

- Tecovirimat was safe but did not improve clinical outcomes in US population with clade II mpox
  - No faster resolution of mpox skin lesions or improved pain control (median 14d)
  - No significant reduction in hMPXV detection (trend toward ↓ at day 8)

- Now 2 negative clinical trials (PALM-007, clade I mpox); pending UNITY trial results soon

- Alternative agents and likely combination therapy should be used for mpox (e.g., brincidofovir + tecovirimat) – priority for immunocompromised populations

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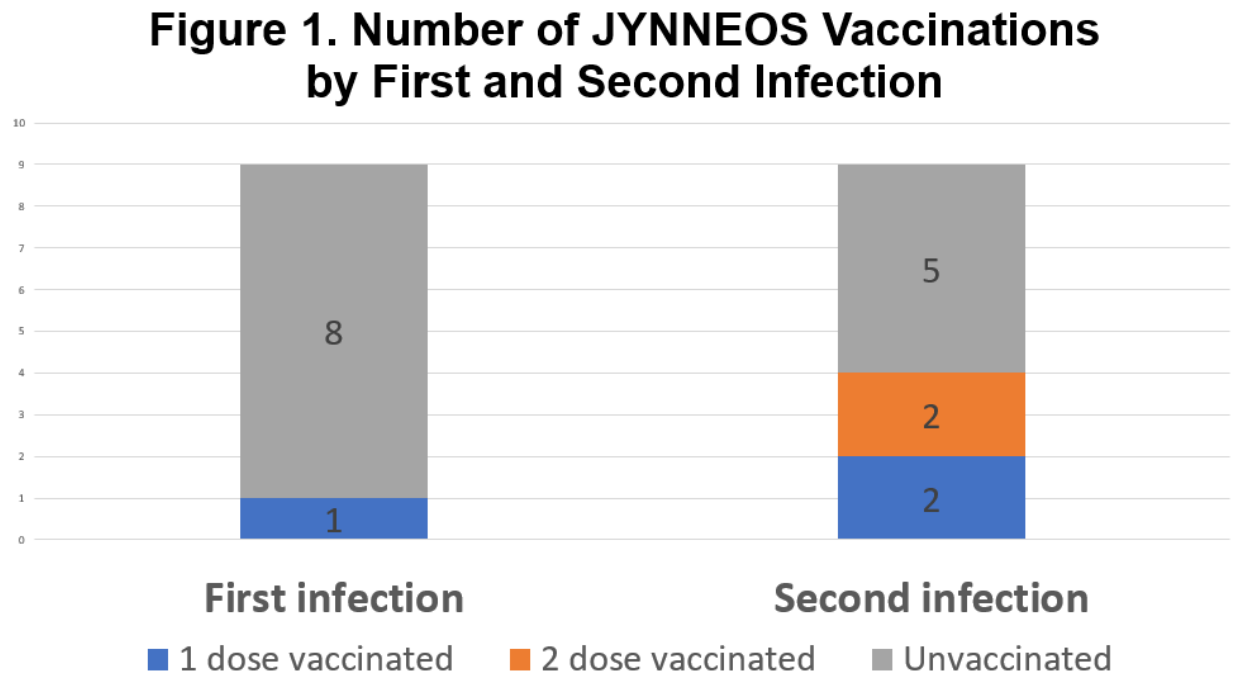
Mpox reinfection is rare but still possible

- Lab-confirmed mpox cases in California from 5/2022 – 8/2024
  - Reinfection = 2 PCR+ results >60d apart
  - Medically reviewed; phylogenetics if possible
- Of 6,476 cases, 9 **(0.14%)** confirmed/probably mpox reinfections
  - All GBMSM
  - Time interval = 266-778d (median 64 wks)
- 3 confirmed phylogenetically distinct
- Consider mpox if compatible sx even if prior infection



Watson JW, et al. CROI 2025 – Poster 1092

DOXY FOR STI PREVENTION

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Doxy-PEP: the Milan experience

- Doxy-PEP effective for CT and syphilis prevention in hospital-based clinic
  - Indications per clinic policy: ≥1 STI or condomless sex with ≥1 casual partner
  - Suggested use: “intensive” sexual activity (>5 partners)

- **Study aim:** Retrospective evaluation of benzylpenicillin, ceftriaxone, doxycycline use for bacterial STI treatment
  - Population: MSM with HIV or on PrEP receiving doxy-PEP in a real-world setting
  - Period: Aug 2022 – July 2024
  - Quantified as days of therapy (DOT) per 1000 person-days for users vs non-users
  - Analysis
    - Observed DOT after doxy-PEP Rx + DOT for incident STI treatment
    - Expected DOT for STI treatment in the absence of doxy PEP

Raccagni AR, et al. CROI 2025 – OA 1284
Raccagni AR, et al. *Lancet Infect Dis* 2025

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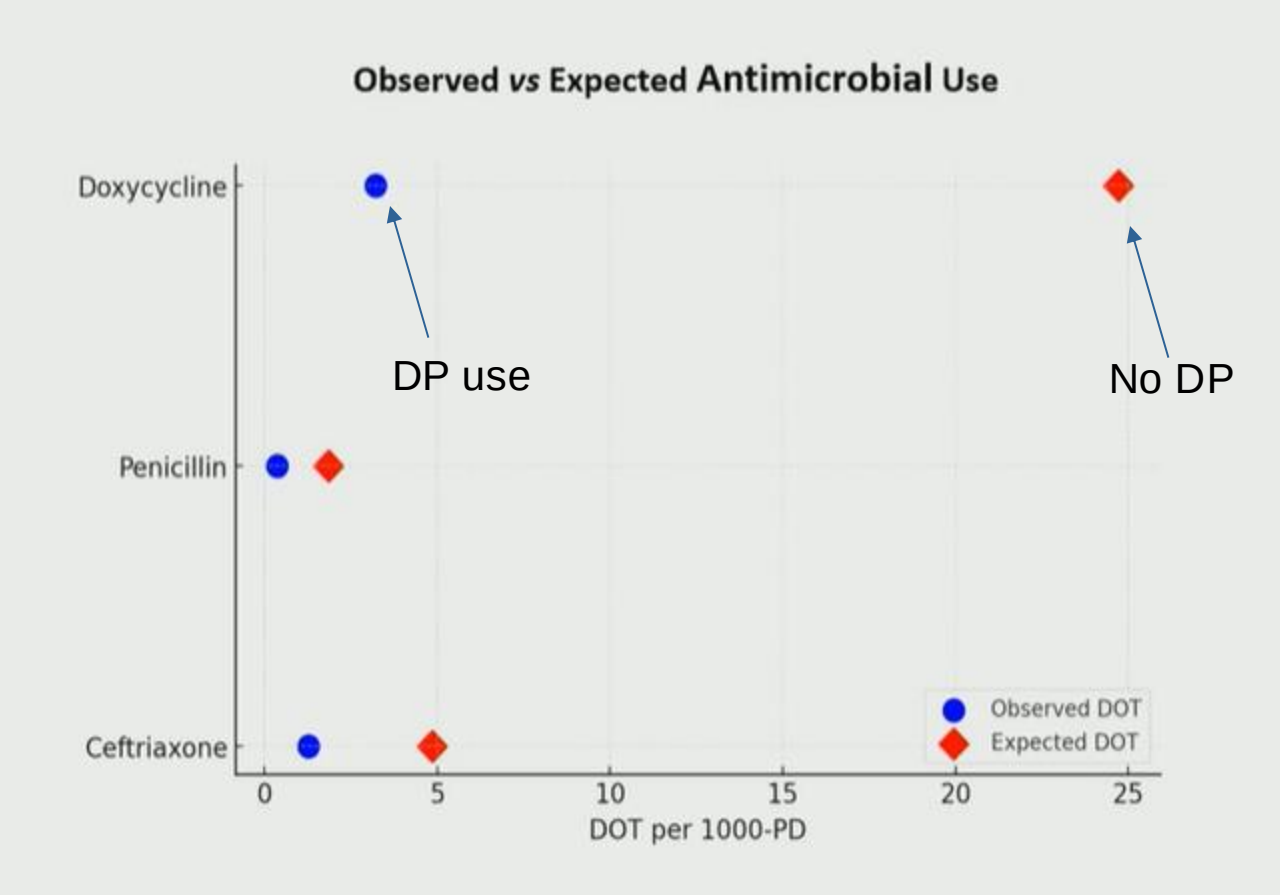
Doxy-PEP dramatically reduces antibiotic use for STI treatment

- Rx for 754 MSM, 222 (29.4%) of whom took ≥1 dose
- PWH 24% vs on PrEP 71%

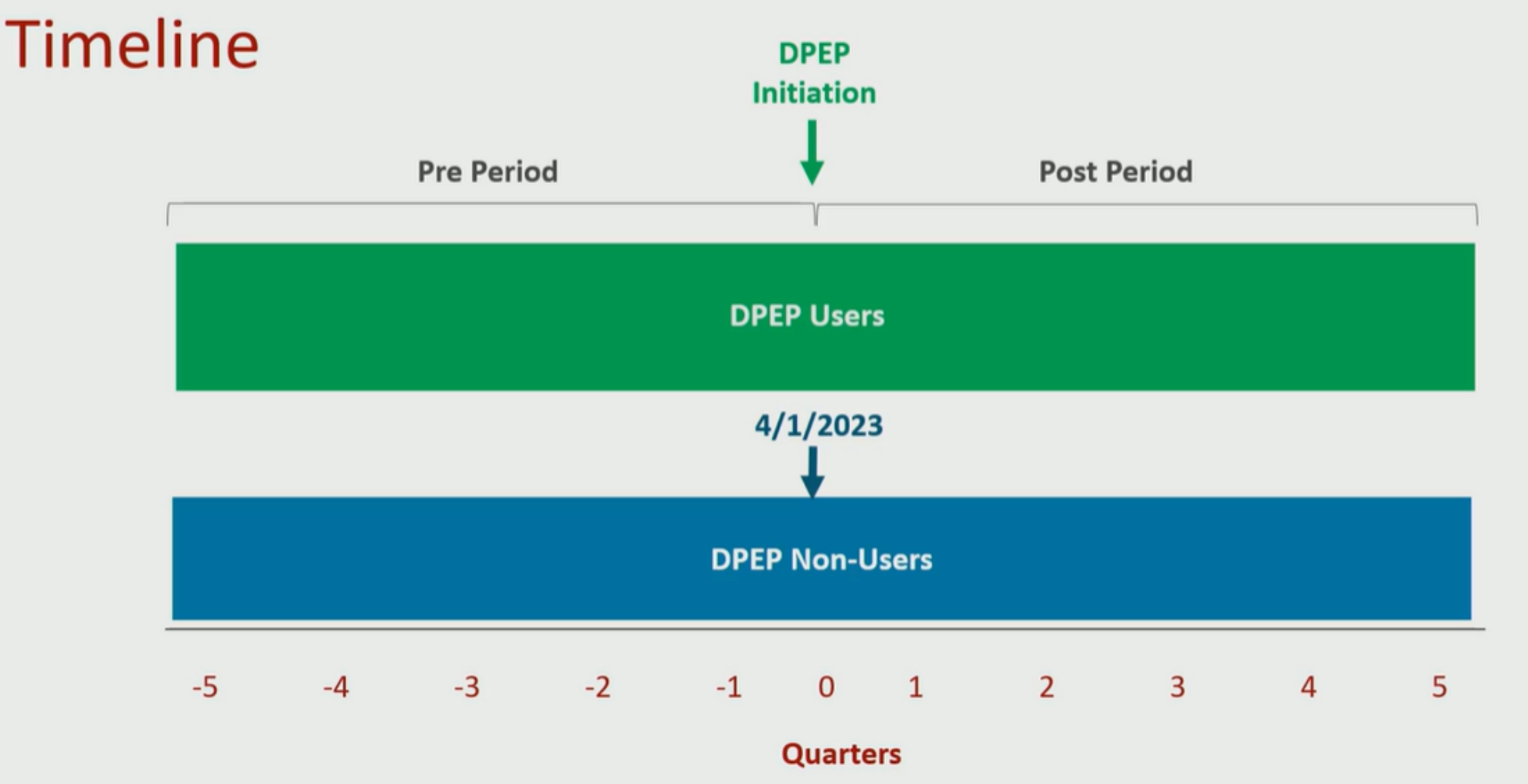
Doxy PEP timing	Median (IQR) f/u in users, mo	N, bSTI	N, by STI
Pre	16 (12-19)	401	Tp 70, CT 139, NG 192
Post	11 (7-13)	146	Tp 26, CT 32, NG 88
64% reduction in bacterial STI			

- Doxy-PEP group had lower DOT rate even when accounting for both therapeutic and prophylactic use



Raccagni AR, et al. CROI 2025 – OA 1284

Doxy-PEP effectiveness analysis update from San Francisco



Scott H, et al. CROI 2025 – OA 163

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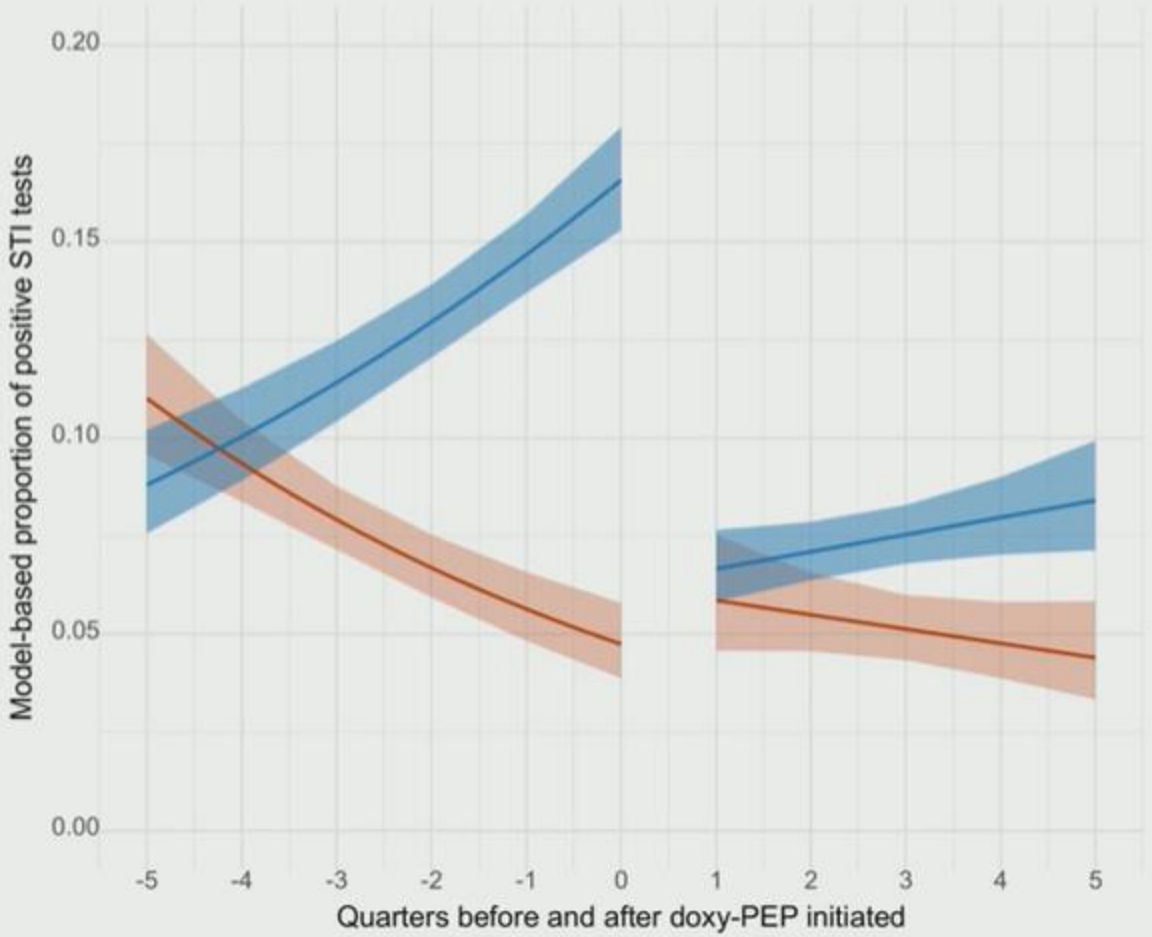
Sustained doxy-PEP effectiveness at Magnet SHC in SF



DPEP Users vs Non-Users	Odds Ratio	95% CI	p-value
Pre-Period	3.78	3.04 – 4.68	<0.001
Post-Period	1.01	0.67 – 1.55	0.917

	Odds Ratio	95% CI	p-value
Any STI	0.34	0.28 - 0.42	<0.001
Chlamydia	0.19	0.13 – 0.29	<0.001
Syphilis	0.11	0.02 – 0.54	0.006
Gonorrhea	0.56	0.44 – 0.71	<0.001

Scott H, et al. CROI 2025 – OA 163

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Global implementation updates for doxy as STI prevention

- Philadelphia NHBS: 37% heard of doxy-PEP but only 5.5% used in last 12 mo (Nassau, Poster 1276)
- PRIDOX, Spain: 197 (22.4%) PrEP users started doxy-PEP (Gómez-Ayerbe, Poster 1275)
  - CT incidence ↓ 75%, syphilis ↓ 85%, gonorrhea ↓ 30% (*NS**) over 48 wks follow-up
  - No difference from 0 to 48 wks in MDR *E. coli*, MRSA or NG

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  - No difference from 0 to 48 wks in MDR *E. coli*, MRSA or NG
- Young Black MSM with HIV and/or syphilis, especially with meth use, want doxy-PEP in Chicago (Pagkas-Bather, Poster 1280)
- Applying CDC criteria to community Milanese SHC population, 55% of pts provided doxy-PEP would not have new STI in next 12 mo – unnecessary Rx? (Rossotti, Poster 1282)
- DuDHS in Vancouver: No significant change in rectal microbiome α or β diversity through 48 wks in immediate doxy-PrEP vs deferred 24 wks (Burgener, Poster 1276)

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Doxy for STI prevention: Summary and conclusions

- Doxy-PEP use is rolling out across US and in some countries globally
- More work to reach those who are interested and could benefit
- Doxy-PEP reduced use of antibiotics needed for STI treatment in a real-world clinical setting
- Criteria for most appropriate use may require refinement for individual clinic or geographic populations
- Effectiveness for STI prevention is sustained in one of SF's largest SHCs
- Two studies of doxy-P(r)EP found little to no impact on microbiome or emergent AMR in potential pathogens of interest using

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HIV PREVENTION: LENACAPAVIR

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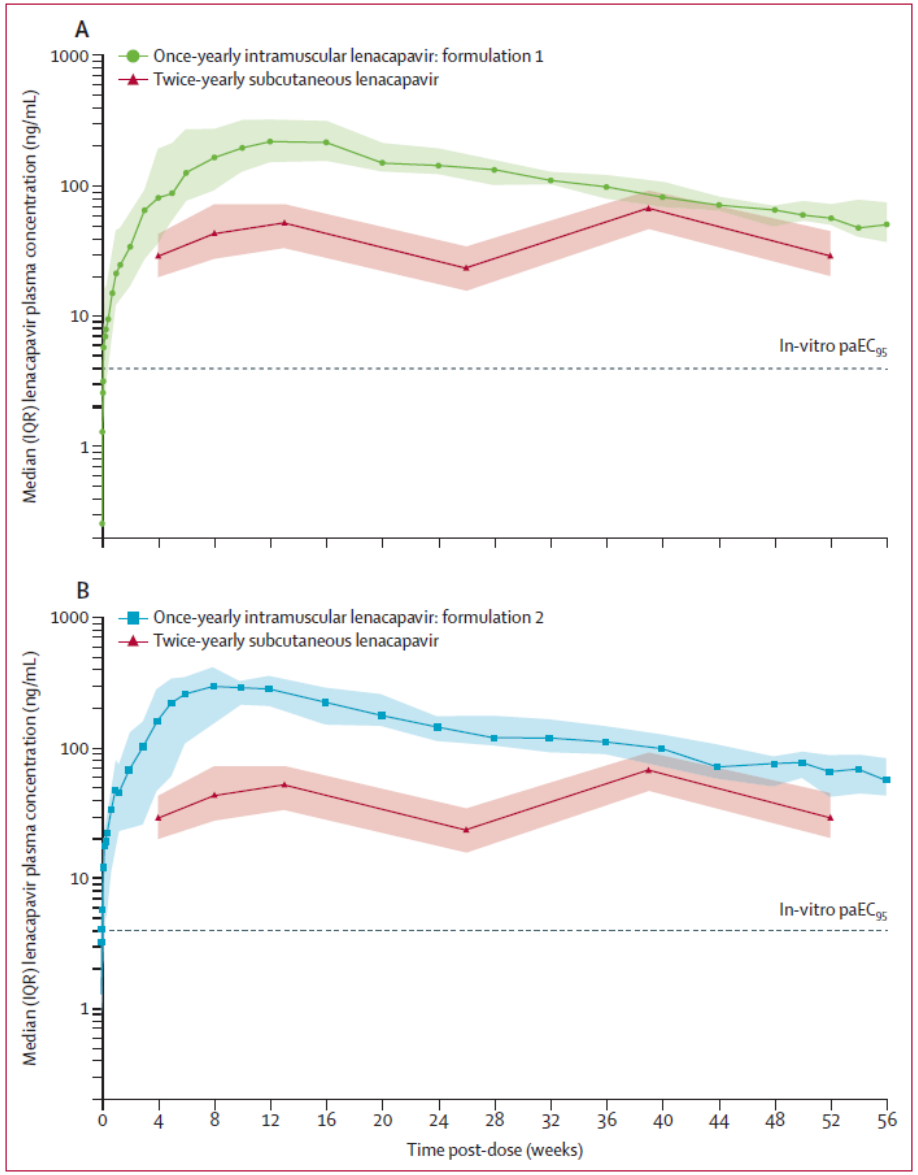
Phase 1 study of once-yearly LEN for PrEP

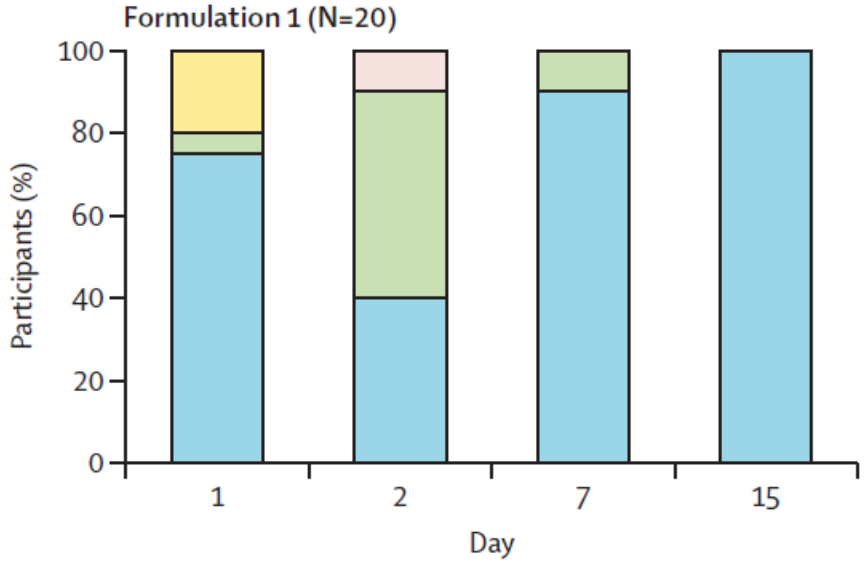
- Evaluated PK, safety, tolerability of LEN IM as 5000mg dose (two 5mL ventrogluteal injections)
  - Formulation 1: 5% w/w ethanol (n=20)
  - Formulation 2: 10% w/w ethanol (n=20)
- Ppts were representative of population; ages 33-37, BMI 26-28

	Lenacapavir formulation 1 (N=20)	Lenacapavir formulation 2 (N=20)
C_{max}, ng/mL	247·0 (184·0–346·0)	336·0 (233·5–474·3)
T_{max}, days	84·1 (56·1–112·0)	69·9 (55·3–105·5)
$AUC_{days\ 1–365}$, h*µg/mL	1011·1 (881·0–1490·2)	1274·0 (1177·3–1704·8)
$C_{trough\ (day\ 365)}$, ng/mL	57·0 (49·9–72·4)	65·6 (41·8–87·1)

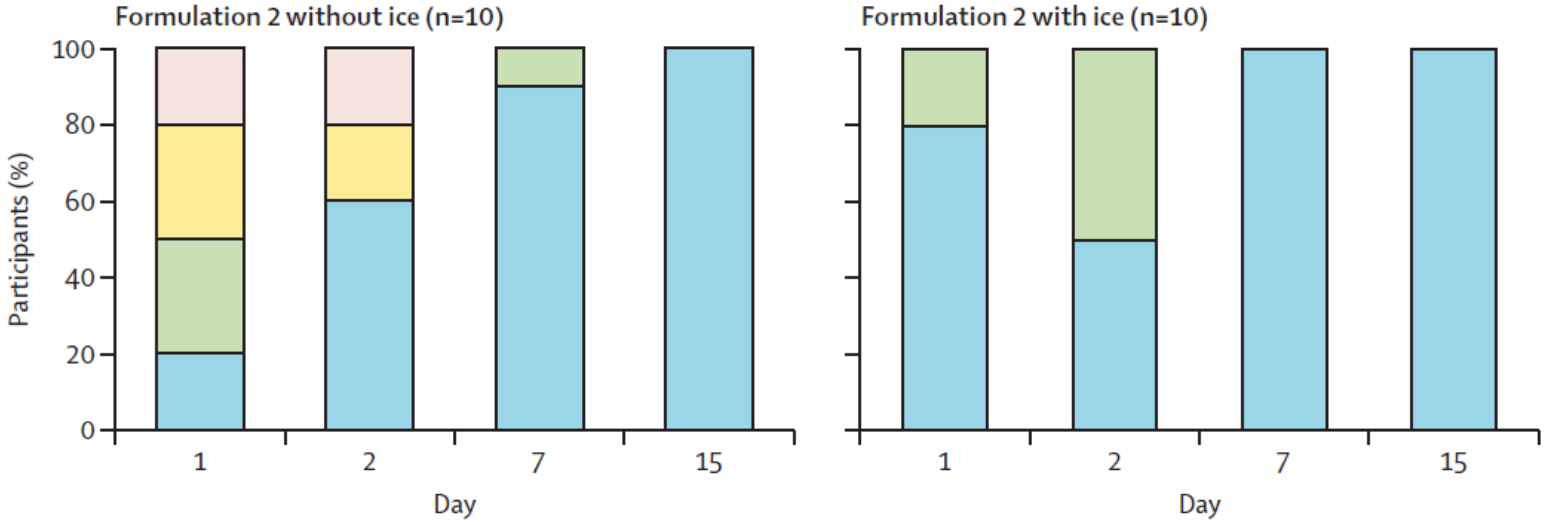


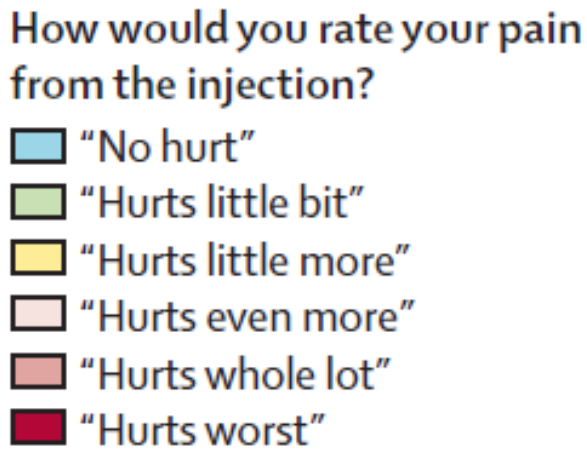
Singh R, et al. CROI 2024 – OA 154; Jogiraju V, et al. *Lancet* 2025

Injections site reactions common; better with ice before injection



- Study drug-related TEAEs common
  - 85% in formulation 1: injection site pain, bruising, swelling
  - 80% in formulation 2: injection site pain, gait disturbance, headache, “feeling hot,” dizziness





Singh R, et al. CROI 2024 – OA 154
Jogiraju V, et al. *Lancet* 2025

Lenacapavir: Summary and conclusions

- Once-yearly IM LEN maintained plasma concentrations beyond 12 months at levels above that known to be efficacious for twice-yearly SC LEN for PrEP
- Intramuscular LEN was safe, but injection site pain was common, resolved after a few days and was improved with pretreatment using ice
- Planned phase 3 study for once-yearly IM LEN for PrEP is already planned and may be able to use an even lower dose
- LEN could have significant public health impact for ending HIV epidemic if it is available, scalable and acceptably priced

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HIV PREVENTION: CABOTEGRAVIR

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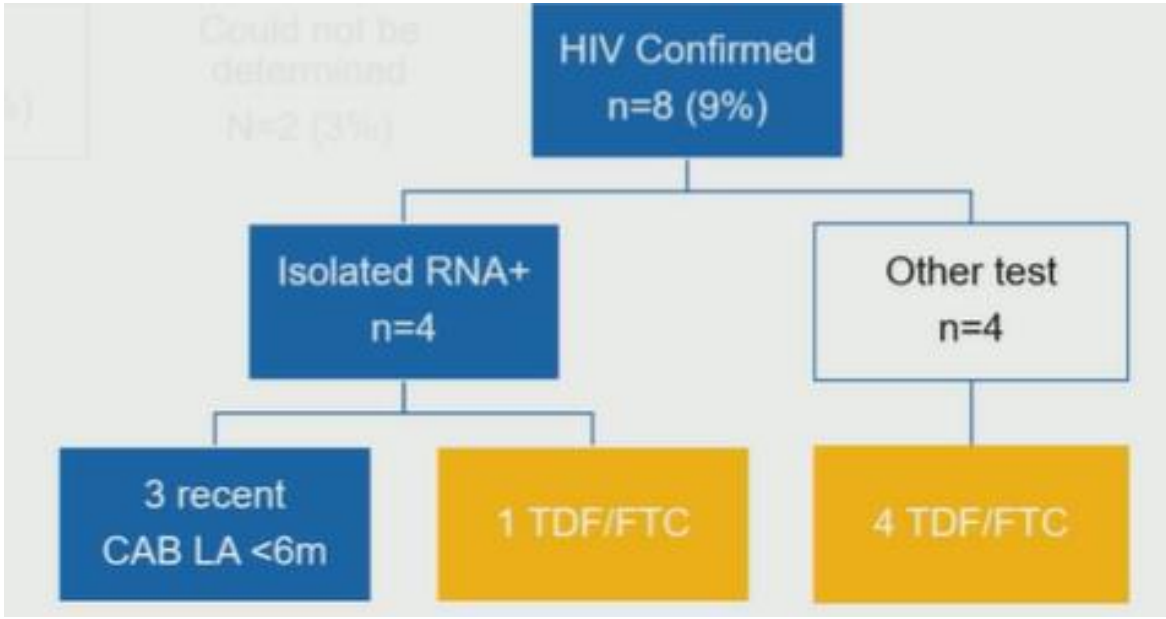
Challenges with diagnosing HIV in setting of CAB-LA

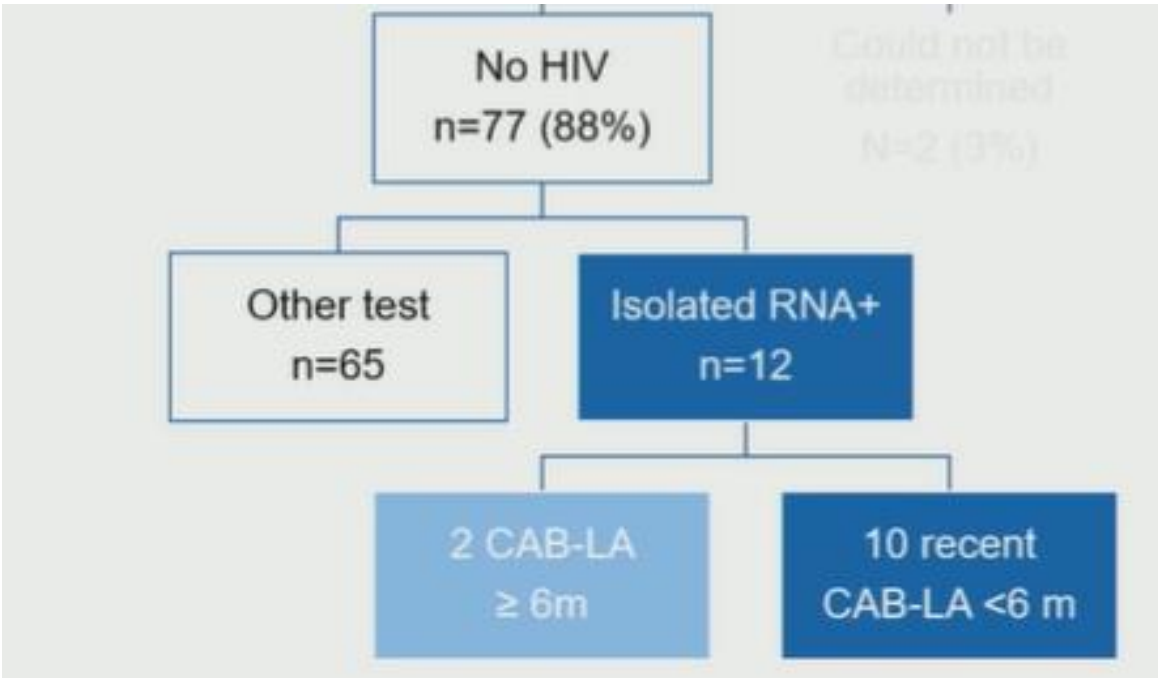
- Analysis of HPTN 084 OLE data evaluating HIV RNA performance for screening
  - Included 2,462 ppts in 24,244 visits with RNA screening = 3,229 person-years
  - 87 (4%) ppts had ≥1 reactive HIV test requiring adjudication
    - No HIV (n=77, 88%)
    - Unable to determine (n=2, 3%)
    - **HIV confirmed (n=8, 9%) as true cases**
  - For isolated HIV RNA cases:
    - RNA <LOQ with recent CAB use (quant unhelpful re: FP vs TP)
    - Oral F/TDF: RNA = 1000 c/mL



Delaney-Moretlwe S, et al. CROI 2025 – OA 195
Delaney-Moretlwe S, et al. *Lancet* 2022

Challenges with diagnosing HIV in setting of CAB-LA

- **HIV excluded (n=77, 88%) as false cases**
  - **12 (15%) had false positive RNA**
  - 5/12 (42%) had >10wk injection delays
  - Most had recent CAB use in past 6 mo
  - All had CAB paused at some point



HPTN 084: Frequent HIV RNA false positives with CAB use

	FPR (95% CI)	PPV (95%)	Sensitivity* (95% CI)
Overall	75% (47.6%, 92.7%)	25% (7.3%, 52.4%)	62.5% (24.5%, 91,5%)
CAB-LA use < 6 m	76.9% (46.2%, 95.0%)	23.1% (5.0%, 53.8%)	100.0% (29.2%, 100.0%)
CAB-LA use ≥ 6m	100% (15.8%, 100.0%)	0% (0%, 84.2%)	0%

*Sensitivity based on HIV RNA with other screening tests

Delaney-Moretlwe S, et al. CROI 2025 – OA 195

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HPTN 083: ART outcomes after HIV acquisition on CAB

47 new HIV diagnoses in initial blinded, 1st year post-unblinding + OLE periods

ART regimen	Time from CAB-LA	Number	% VS	Median f/u duration, days
INSTI-based (DTG or BIC anchor)		18 of 21	**85.7%**	236
	<6 mo	6 of 6	100%	342
	>6 mo	12 of 15	80%	316
Other anchors (b/PI + 2NRTIs)		22 of 26	**84.6%**	316
	<6 mo	16 of 16	100%	334
	>6 mo	6 of 10	80%	162

Landovitz RJ, et al. CROI 2025 – OA 197

*Virologic suppression (VS) in studies = <50 c/mL
Unsuppressed VL range for non-INSTI group: 2,330 to 664,821

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HPTN 083: ART choice and outcomes after HIV acquisition

47 new HIV diagnoses in initial blinded, 1st year post-unblinding + OLE periods

9 of 44 cases (20.5%) had INSTI RAMs before initiating ART

All eventually suppressed on first regimen chosen regardless of last CAB dose

*Virologic suppression (VS) in studies = <50 c/mL

Profile and management of CAB-LA PrEP failures

- SeroPrEP: observational study enrolling newly diagnosed PWH despite PrEP use

- 7 participants with prior CAB-LA PrEP use in routine clinical care
  - 4/7 had nonreactive HIV ag/ab at first detectable HIV RNA

- Resistance: 5 of 7 with emergent RAMs
  - High-frequency (1 of 5) : E138K, Q148QK, N155NH
  - Low-frequency (4 of 5): G118R, E138K, G140R, S147G, Q148R, N155NK, R263K

- ART outcomes: all started DRV-based ART and reached VL <200 c/mL
  - 3 with low-freq. major INSTI RAMs switched to INSTI regimen with VS at 13-31 wks

Koss CA, et al. CROI 2025 – Poster 1228

CAB-LA: Summary and conclusions

- Single isolated HIV RNA test performs poorly for diagnosing HIV infection in context of CAB-LA use
- Most isolated positive HIV RNA tests are expected to be false positives given low HIV incidence in setting of highly effective CAB-LA
- HIV RNA may not be cost effective as screening test and has potential for negative clinical consequences including prolonged PrEP interruptions
- HIV VS rates were 77% (HPTN 083) and 100% (SeroPrEP) for people newly diagnosed with CAB-LA experience; similar short-term outcomes btwn INSTI or other (PI-based) regimens
- Need to understand clinical significance of low-freq. RAMs and how durable VS is on INSTI-based ART after CAB-LA failure

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HIV PREVENTION: PrEP FOR WOMEN

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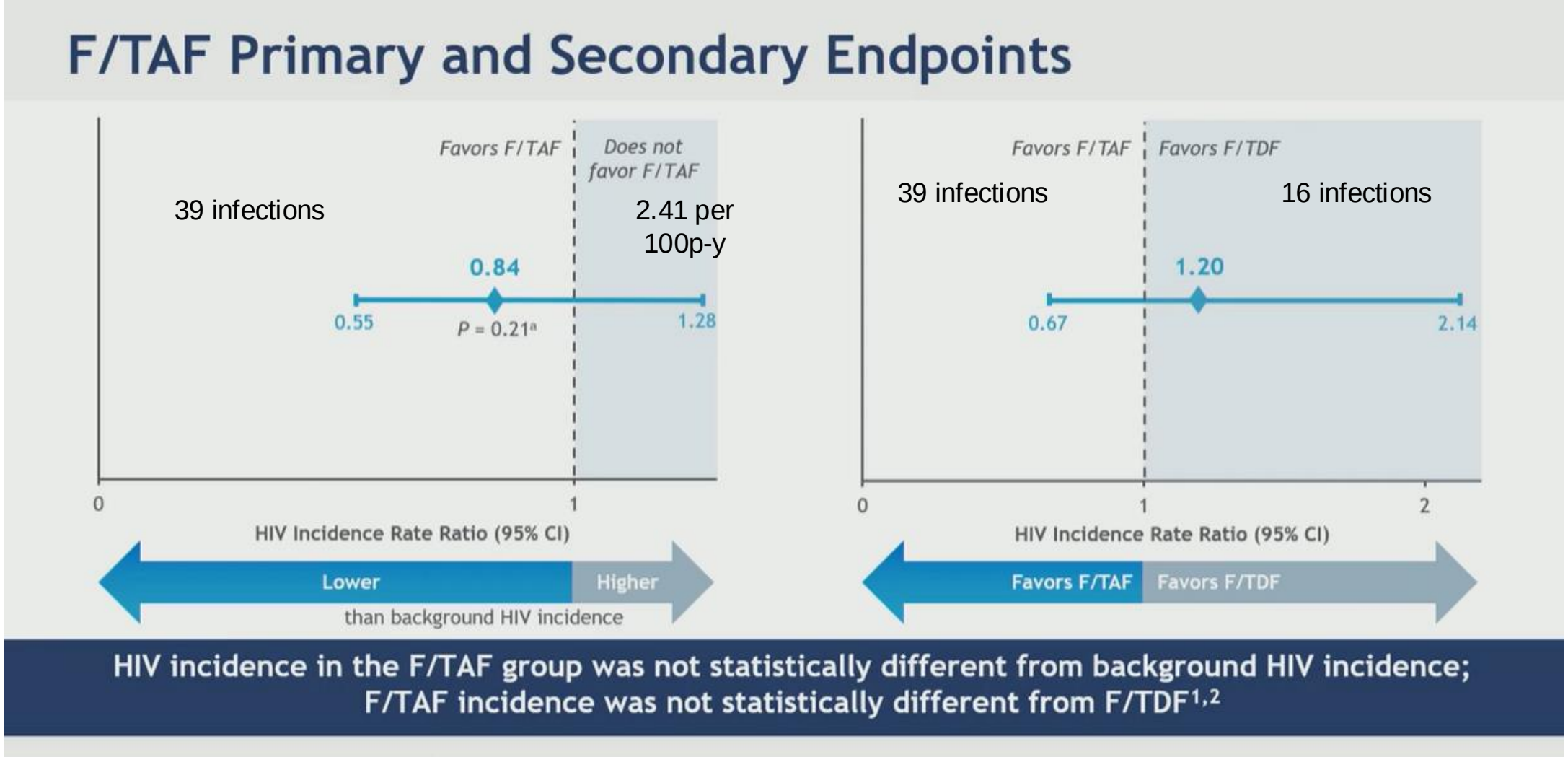
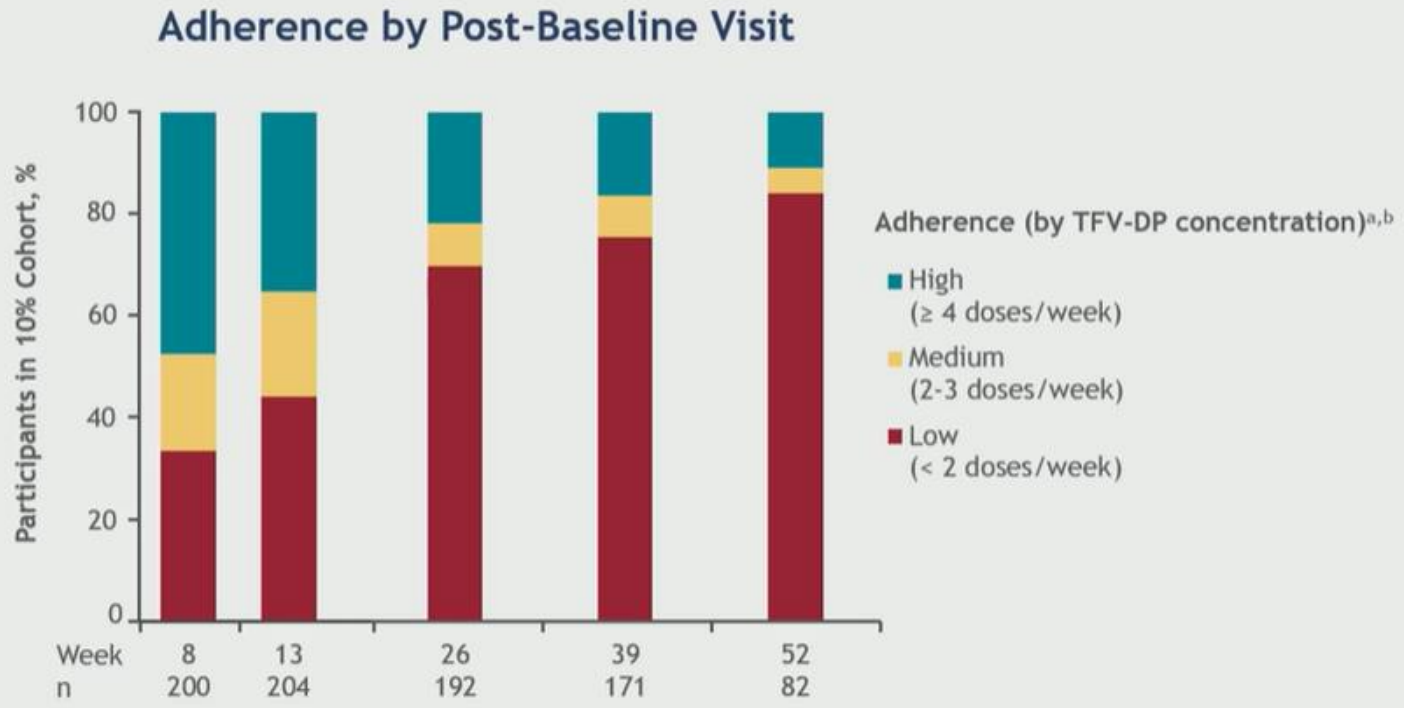
Lack of efficacy for F/TAF in women in the PURPOSE 1 trial



Kiweewa FM, et al. CROI 2025 – OA 194; Bekker LG, et al. *NEJM* 2024

Low adherence to F/TAF in women in the PURPOSE 1 trial

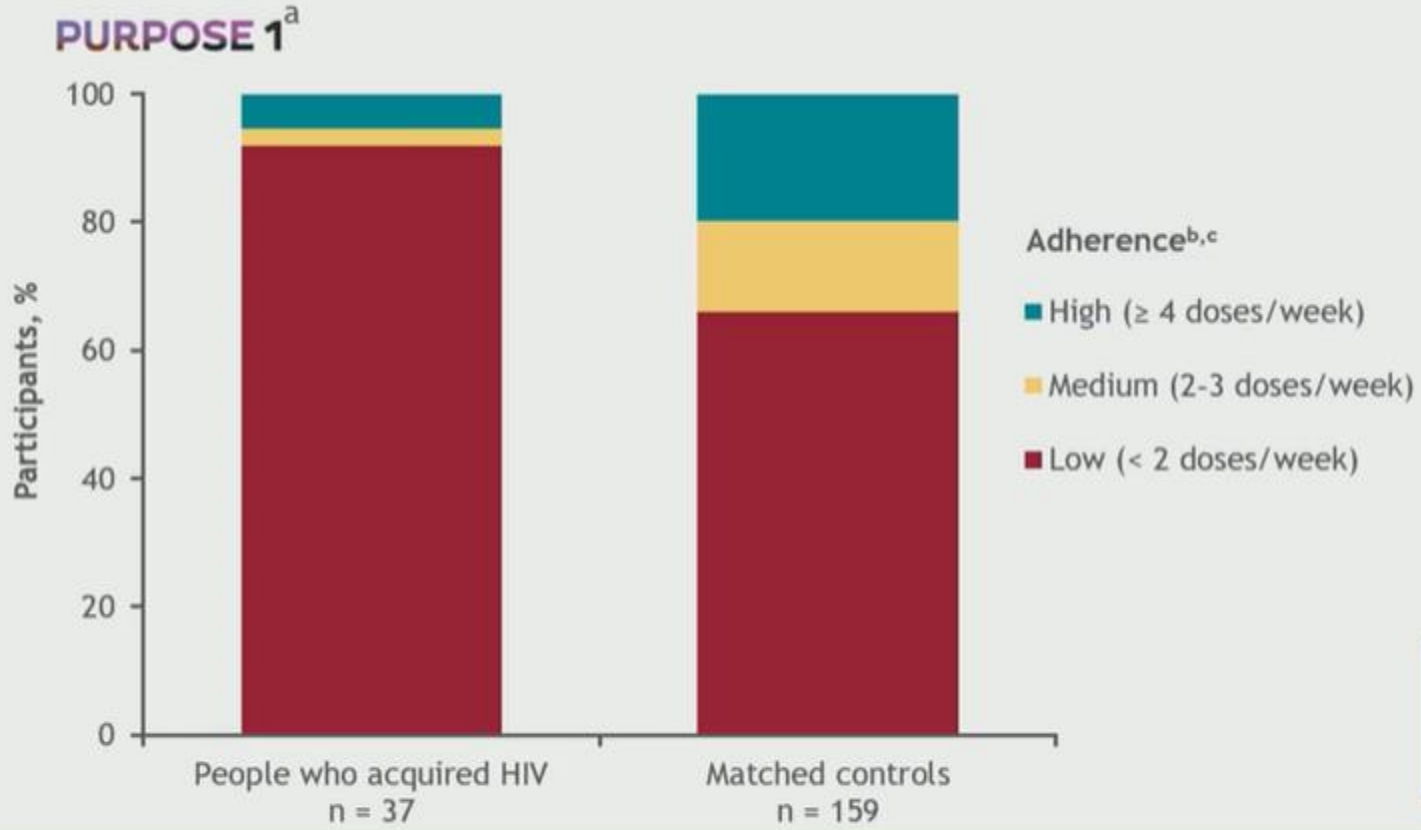
Adherence to Oral F/TAF Was Low

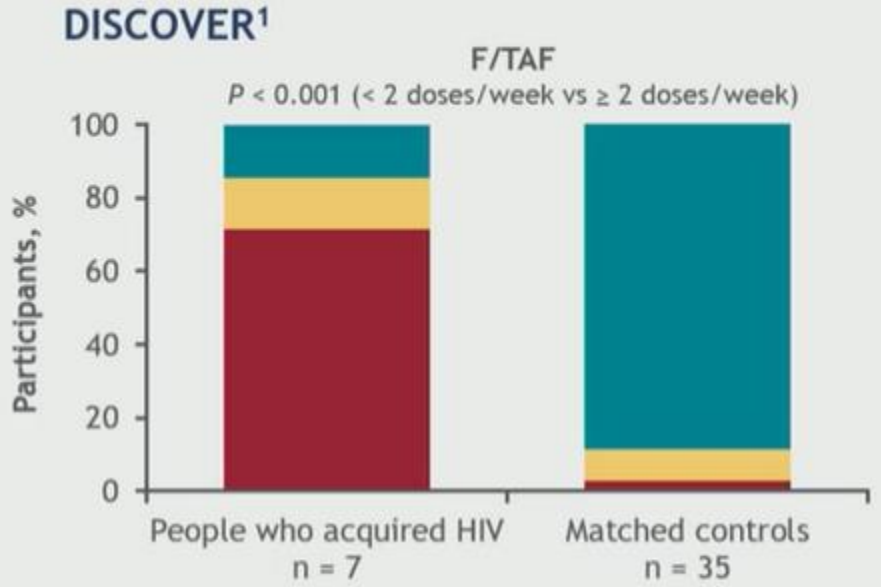


Most participants in the F/TAF group had low adherence to oral tablets, and adherence declined over time[1,2]

Kiweewa FM, et al. CROI 2025 – OA 194; Bekker LG, et al. *NEJM* 2024

Lower odds of HIV a/w medium or high F/TAF adherence





F/TDF adherence-efficacy analyses from post-approval studies in women also show increased efficacy with increased doses/week[2]

Odds of HIV acquisition were 89% lower among women in PURPOSE 1 who took ≥ 2 pills per week (odds ratio: 0.11; 95% CI: 0.012-0.49; *P* = 0.0006)[3,4]

Kiweewa FM, et al. CROI 2025 – OA 194; Bekker LG, et al. *NEJM* 2024

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New PURPOSE 1 takeaways

- All but 1 case of incident HIV in PURPOSE 1 was due to low F/TAF adherence
  - Emergent ARV resistance was rare (1 case of TFV + FTC transmitted RAM)
  - F/TAF did not cause a delay in HIV diagnosis as few had detectable HIV VL
- Medium or high adherence to F/TAF is efficacious for HIV prevention in women

Kiweewa FM, et al. CROI 2025 – OA 194; Bekker LG, et al. *NEJM* 2024

Evaluating on-demand PrEP in South African women

Stansfield SE, et al. CROI 2024 – Poster 1290

- Synthetic cohort of women in HPTN 067
- Simulated hypothetical use of 3 PrEP regimens using data from previously published adherence-efficacy curves
  - Women with adherence <2.8 pills/week assigned to 2-1-1 PrEP
- Median effectiveness
  - 86% for daily PrEP
  - 57% for 2-1-1 2 pills before sex + 1 pill daily x2d after sex
  - 47% for time-driven 2 pills/wk + 1 pill after sex
  - 1.4 pills/wk for event-driven 1 pill before sex + 1 pill after sex
- On-demand PrEP may yield better protection with fewer pills for women with low daily adherence

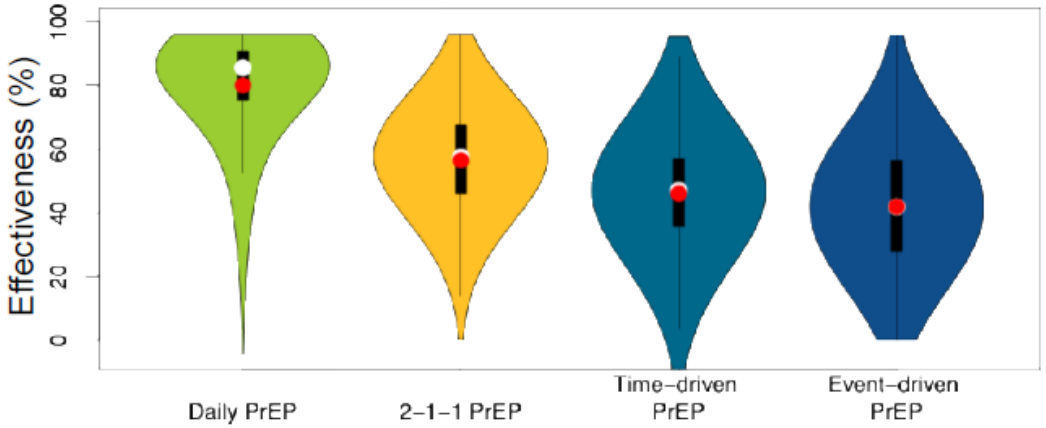


Figure 1: Estimated effectiveness of simulated HPTN 067 PrEP regimens & 2-1-1 PrEP when all women received the same regimen. *Red points show mean percent effectiveness and white points (may overlap) show median percent effectiveness.*

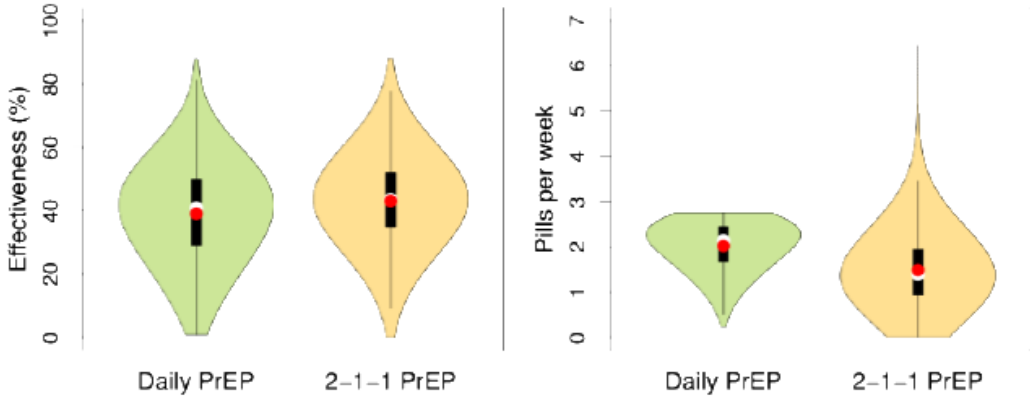


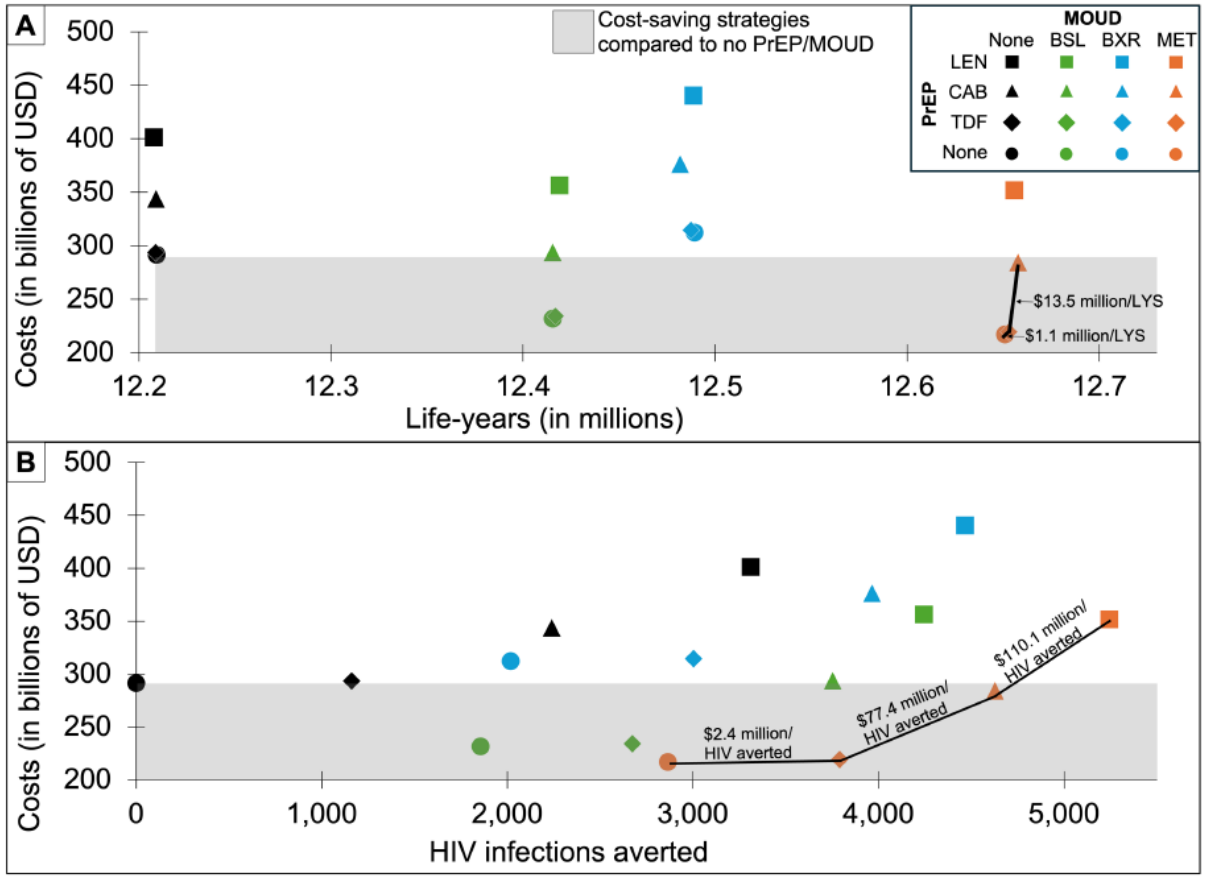
Figure 2: Estimated effectiveness (%) & pills taken per week on daily PrEP or 2-1-1 PrEP for the 8% of women with low daily PrEP adherence (<2.8 pills/week). *Red points show mean percent effectiveness and white points (may overlap) show median percent effectiveness.*

HONORABLE MENTIONS

POTPOURRI

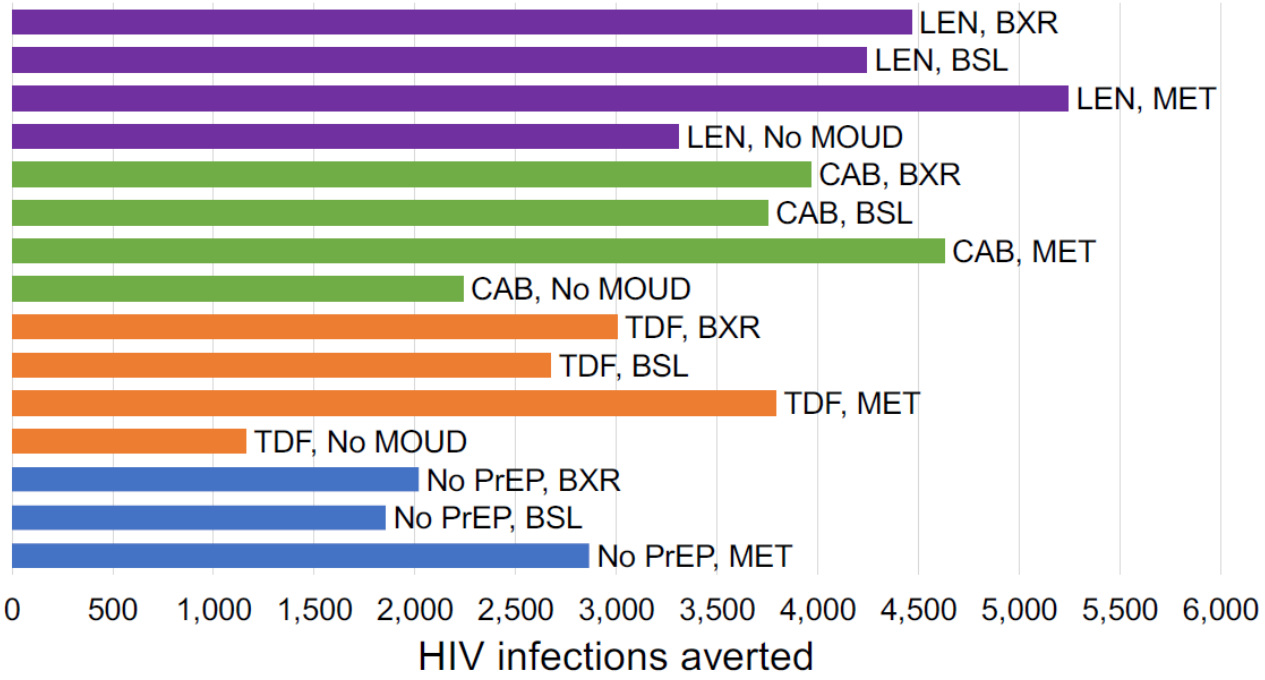
PrEP +/- MOUD reduces morbidity and mortality for PWID with OUD but is not cost effective at current PrEP prices

Figure 3. Cost-effectiveness (efficiency frontiers)



PrEP strategies: TDF = daily oral TDF/FTC; CAB = bimonthly IM cabotegravir; LEN = biannual SQ lenacapavir
MOUD strategies: MET = daily oral methadone; BSL = daily SL buprenorphine; BXR = monthly SQ buprenorphine

Figure 2. HIV infections averted (vs. No PrEP or MOUD)



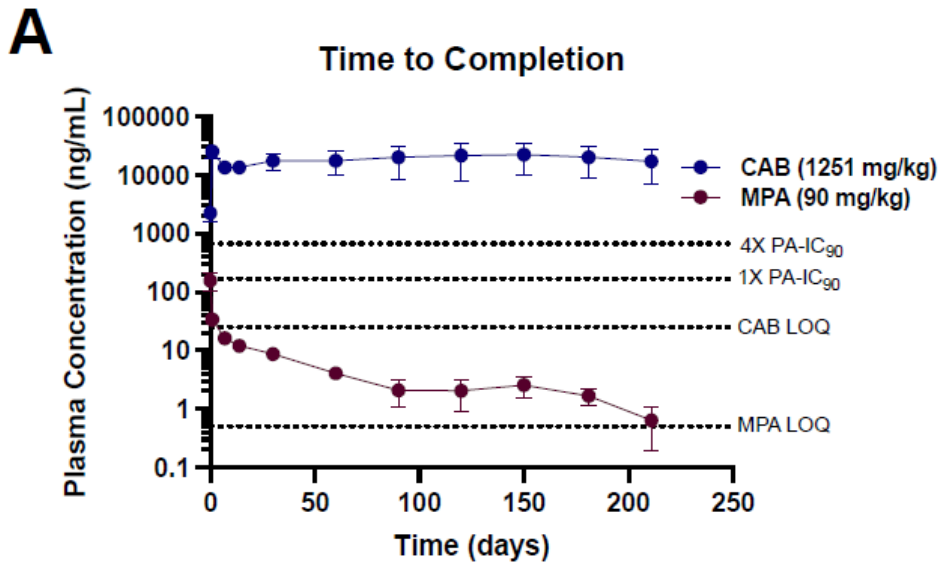
PrEP	US$ cost/interval
Oral F/TDF	$300/yr
IM CAB	$23,214 bimonthly
SQ LEN	$39,000 biannually

Chiosi J, et al. CROI 2025 - Poster 1294

Future of HIV, STI, and pregnancy prevention

- Grindr survey of 827 MSM with HIV in 46 US states/territories *(Martinson, Poster 1358)*
  - 59% aware of doxy-PEP, 13% prescribed
  - Of 306 meeting CDC criteria
    - 20% prescribed and taking
    - 90+% not on doxy-PEP were interested and would start if offered by provider

- Multipurpose interventions for women and girls
  - Biodegradable, removable in-situ forming implants with CAB + MPA maintained therapeutic levels for 210 and 180d, respectively, in mice *(King, Poster 1236)*
  - Islatravir intravaginal ring was 100% efficacious in pigtail macaques SHIV challenged x12 wks *(Srinivasan, Poster 1238)*



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