

**Indirect Treatment Comparison of the Efficacy of Long-Acting Injectable Cabotegravir
Compared With Lenacapavir for HIV Pre-exposure Prophylaxis**

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SUPPLEMENTARY MATERIAL

Table S1. Systematic Literature Review Eligibility Criteria

PICOS	Inclusion criteria
Population	• Cisgender women, men who have sex with men, and transgender women aged ≥ 18 years who have a greater likelihood of acquiring HIV • Adolescents who have a greater likelihood of acquiring HIV
Interventions/Comparators	• Long-acting injectable PrEP (eg, cabotegravir for PrEP, lenacapavir for PrEP) • Oral PrEP (eg, TDF/FTC, TAF/FTC) • Placebo or no PrEP
Outcomes	• HIV incidence • HIV acquisitions averted • Adherence to PrEP • Adverse events • Incidence of other STIs • Behavioral changes (eg, condom use) • Drug resistance
Study design	Randomized controlled trials
Other	English language only

Cabotegravir, long-acting injectable cabotegravir; FTC, emtricitabine; lenacapavir, long-acting injectable lenacapavir; PICOS, population, intervention, comparison, outcomes, and study criteria; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

Table S2. ITC Sensitivity Analyses Results

Sensitivity analysis (oral lead-in + injection phase)				
Comparisons	Men who have sex with men and transgender women		Cisgender women	
	HR (95% CrI) for risk of HIV acquisition	Reduction in risk of HIV acquisition (95% CrI), %	HR (95% CrI) for risk of HIV acquisition	Reduction in risk of HIV acquisition (95% CrI), %
No PrEP as common comparator				
Cabotegravir vs no PrEP	0.07 (0.03, 0.15)	93 (85, 97)	0.05 (0.02, 0.14)	95 (86, 98)
Lenacapavir vs no PrEP	0.04 (0.01, 0.18)	96 (82, 99)	0.00 (0.00, 0.04)	100 (96, 100)
Lenacapavir vs cabotegravir (no PrEP as a common comparator)	0.62 (0.12, 3.15)	—	0.00 (0.00, 0.95)	—
TDF/FTC as common comparator				
Cabotegravir vs TDF/FTC ^a	0.26 (0.14, 0.49)	74 (51, 86)	0.04 (0.01, 0.12)	96 (88, 99)
Lenacapavir vs TDF/FTC ^a	0.10 (0.02, 0.51)	90 (49, 98)	0.00 (0.00, 0.11)	100 (90, 100)
Lenacapavir vs cabotegravir (TDF/FTC as a common comparator)	0.39 (0.07, 2.21)	—	0.00 (0.00, 3.00)	—

Cabotegravir, long-acting injectable cabotegravir; FTC, emtricitabine; HR, hazard ratio; ITC, indirect treatment comparison; lenacapavir, long-acting injectable lenacapavir; PrEP, pre-exposure prophylaxis; TDF, tenofovir disoproxil fumarate. ^aAdjusted to PURPOSE 1 and 2 levels of adherence to TDF/FTC.

Figure S1. PRISMA diagram. Following identification, screening, and eligibility assessment, 21 records were identified from a recently conducted systematic literature review,¹ with 4 included in the indirect treatment comparison. RCT, randomized controlled trial.

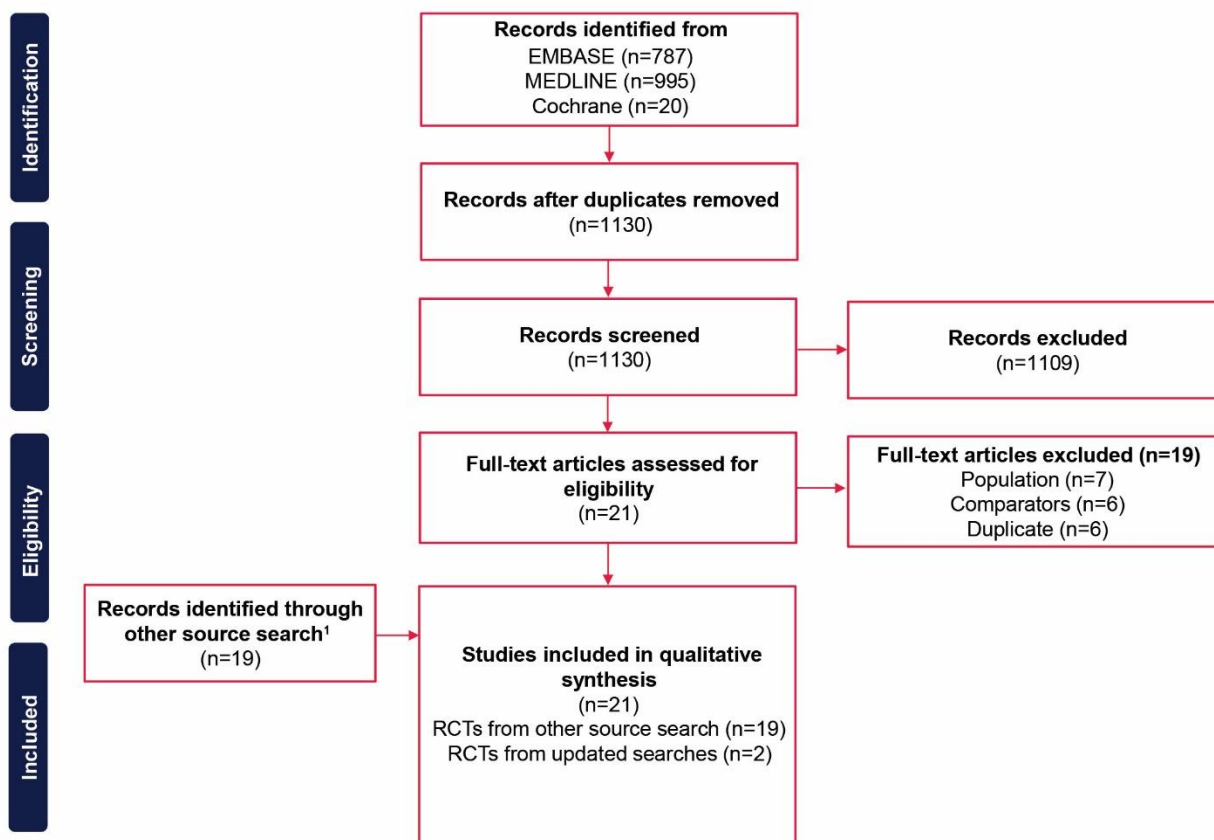


Figure S2. Summary of bias risk among SLR studies (N=21). ITT, intention-to-treat; SLR, systematic literature review.

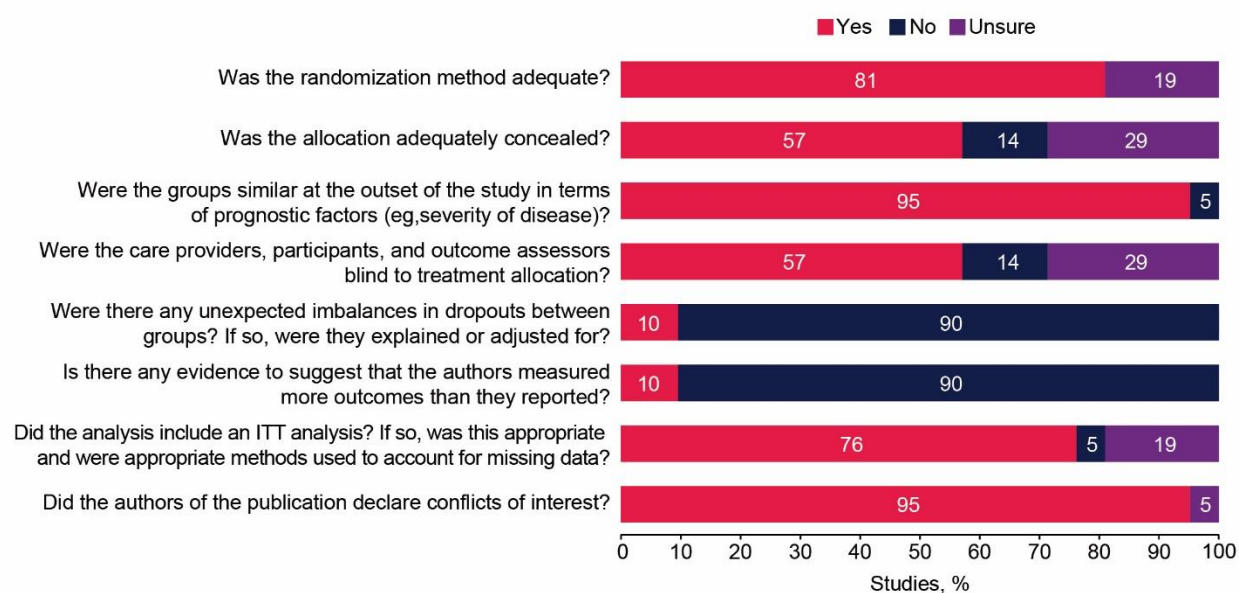


Figure S3. Sensitivity analyses (oral lead-in and injection phases with re-adjudicated efficacy data from HPTN trials). **(A)** Predicted risk of HIV acquisition for lenacapavir versus cabotegravir and **(B)** predicted reduction in the risk of HIV acquisition for cabotegravir or lenacapavir versus no PrEP or oral TDF/FTC. Cabotegravir, long-acting injectable cabotegravir; FTC, emtricitabine; HR, hazard ratio; lenacapavir, long-acting injectable lenacapavir; PrEP, pre-exposure prophylaxis; TDF, tenofovir disoproxil fumarate. ^aHPTN 083 included men who have sex with men and transgender women.² PURPOSE 2 included cisgender gay, bisexual, and other men; transgender women and men; and gender non-binary individuals who have sex with men.³

^bAdjusted to PURPOSE 1 and 2 levels of adherence to TDF/FTC.

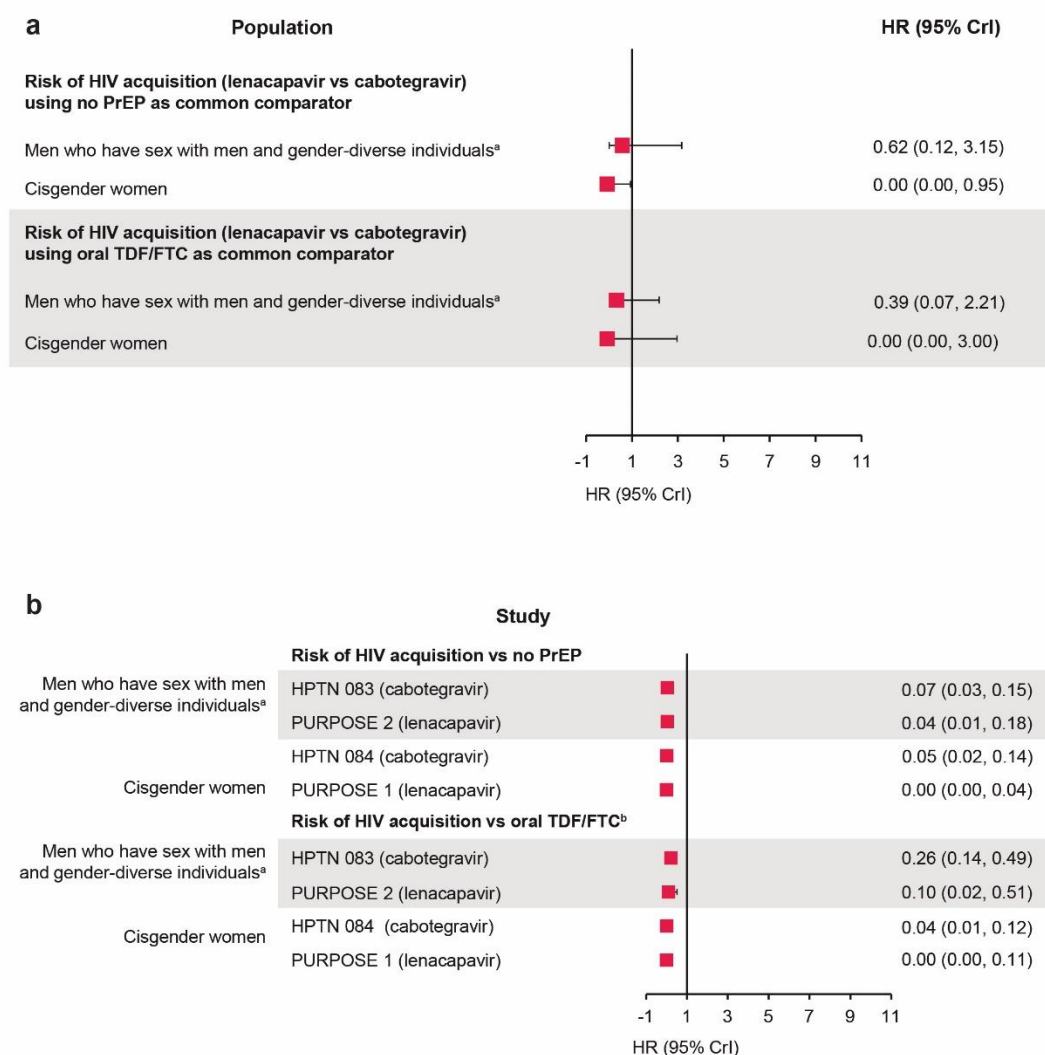
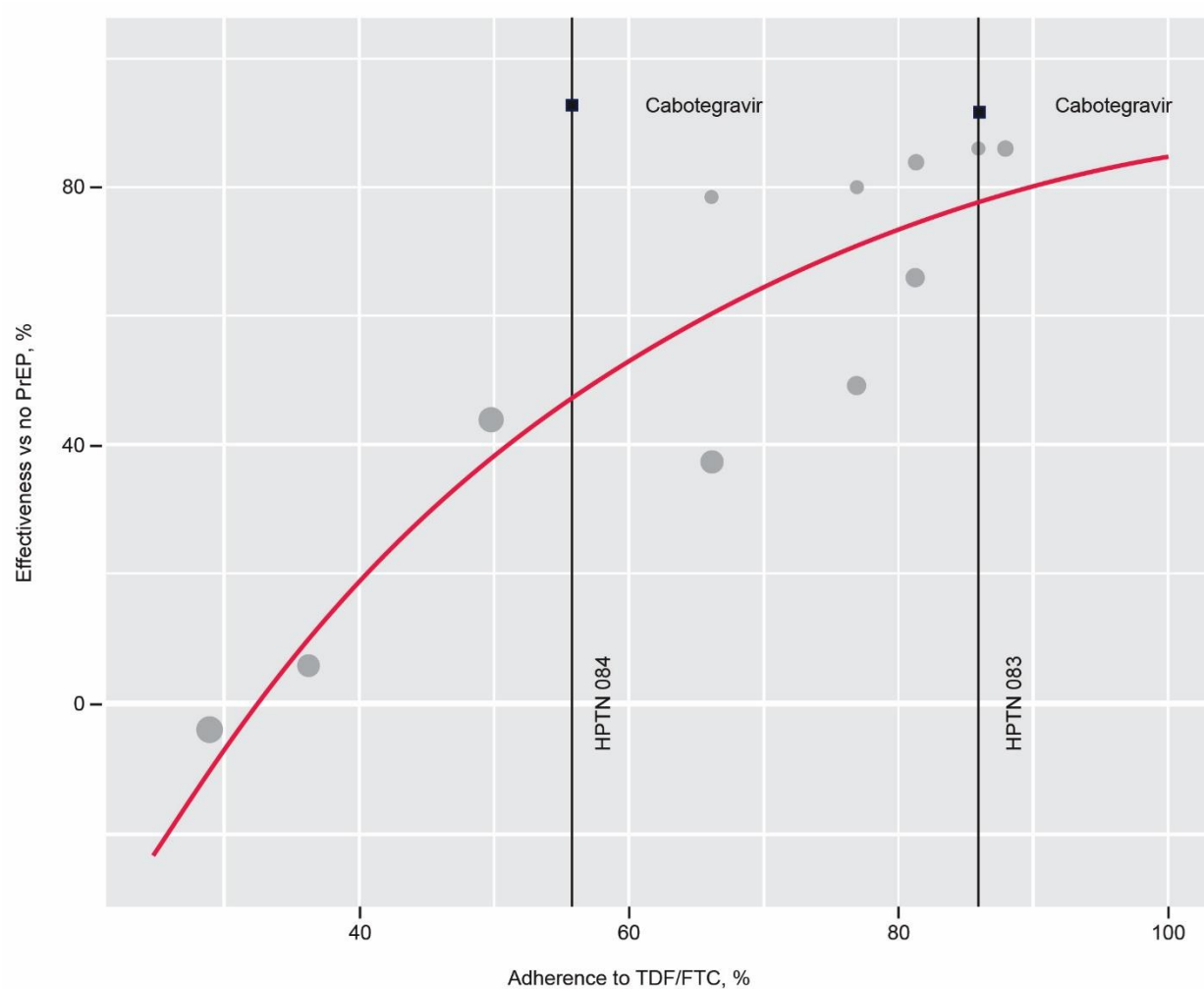


Figure S4. The relationship between effectiveness and adherence in the base case (logarithmic relationship) meta-regression model.⁴ Cabotegravir, long-acting injectable cabotegravir; FTC, emtricitabine; PrEP, pre-exposure prophylaxis; TDF, tenofovir disoproxil fumarate. Image reproduced with no modification from Hawkins et al. Indirect treatment comparison of long-acting injectable cabotegravir as pre-exposure prophylaxis when compared with no pre-exposure prophylaxis for HIV prevention. *Infect Dis Ther.* 2025;14:1739-1753.

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SUPPLEMENTARY REFERENCES

1. Huic M, Reinsperger I. Oral and parenteral preexposure prophylaxis (PrEP) to prevent HIV in people at risk: a systematic review of clinical effectiveness and safety with assessment of organisational, economic, patient/social, ethical and legal elements. AIHTA Project Report No.: 152; 2023. Vienna: HTA Austria – Austrian Institute for Health Technology Assessment GmbH. https://eprints.aihta.at/1436/1/HTA-Projektbericht_Nr.152.pdf. Accessed April 2, 2025.
2. Landovitz RJ, Donnell D, Clement ME, et al. Cabotegravir for HIV prevention in cisgender men and transgender women. *N Engl J Med*. 2021;385(7):595–608.
3. Kelley CF, Acevedo-Quiñones M, Agwu AL, et al. Twice-Yearly lenacapavir for HIV prevention in men and gender-diverse persons. *N Engl J Med*. 2025;392(13):1261–76.
4. Hawkins N, O'Brian P, Thompson J, et al. Indirect treatment comparison of long-acting injectable cabotegravir as pre-exposure prophylaxis when compared with no pre-exposure prophylaxis for HIV prevention. *Infect Dis Ther*. 2025;14:1739–53.