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PLAIN LANGUAGE SUMMARY

Using a microsimulation model, we found that using Ag/Ab testing alone to monitor for HIV infection among people using injectable, bi-monthly cabotegravir-based HIV PrEP would save costs with similar clinical outcomes compared to CDC-recommended combined Ag/Ab+RNA testing.

BACKGROUND

- HIV detection is challenging among people acquiring HIV while on long-acting, injectable cabotegravir (CAB-LA) pre-exposure prophylaxis (PrEP) due to low/undetectable viral loads, delayed antibody production, and the absence of acute retroviral syndrome.
- US CDC recommends simultaneous antigen/antibody (Ag/Ab) and RNA testing at each CAB-LA injection visit.
- Objective:** To determine the optimal HIV monitoring strategy among US men (MSM) and transgender women (TGW) who have sex with men receiving CAB-LA HIV PrEP.

METHODS

- Design: CEPAC microsimulation model
- Population: US men and transgender women who have sex with men, representing HPTN 083 OLE participants.
- Outcomes: misdiagnoses, quality-adjusted life-years (QALYs), HIV-related costs, and incremental cost-effectiveness ratios (ICERs).
- Strategies: simultaneous Ag/Ab and RNA testing (current CDC guideline, *Ag/Ab+RNA*), Ag/Ab alone (*Ag/Ab-only*), and RNA alone (*RNA-only*) at each CAB-LA injection visit.
- Time horizon: 10 years

Table 1. Select model input parameters

Parameter	Value	Source
HIV incidence, per 100 person-years		
Off-PrEP (interruptions) / On CAB-LA	5.32 / 0.26	1,2
Test costs		
RNA / AgAb	34.5 / 92.6	3
Without ARV exposure		
Ag/Ab sensitivity (acute/chronic), %	81.88 / 99.94	4,5,6
RNA sensitivity (acute/chronic), %	99.03 / 100	7,8
Ag/Ab specificity, %	99.77	9,10
RNA specificity, %	99.95	11,12
With ARV exposure		
Ag/Ab sensitivity, %	50.00	13, 14
RNA sensitivity, %	75.00	9,10
Ag/Ab specificity, %	99.77	14
RNA specificity, %	99.91	14
CAB-LA administration frequency, months	2	15
Delay to restart PrEP after interruption, mean (SD), months	2.1 (0.7)	13,14

¹ Landovitz, *NEJM* 2021; ² Neilan, *Ann Intern Med* 2022; ³ Medicare-aid CLFS 2024; ⁴ Peters, *JAMA* 2016; ⁵ Pilcher, *PLoS One* 2013; ⁶ Chavez, *J Clin Virol* 2011; ⁷ Manak, *J Clin Microbiol* 2017; ⁸ Pierce, *J Clin Microbiol* 2011; ⁹ Bentsen, *J Clin Virol* 2011; ¹⁰ Nasrullah, *AIDS* 2013; ¹¹ Aptima HIV-1 Quantitative Package Insert; ¹² Alinity HIV-1 AMP Package Insert; ¹³ Landovitz, *IAS* 2024; ¹⁴ Landovitz, *CROI* 2024; ¹⁵ CDC 2021 PrEP guidelines

At current test costs, Ag/Ab-only for HIV monitoring during CAB-LA PrEP use would achieve similar clinical outcomes at lower cost compared with current CDC-recommended Ag/Ab+RNA testing

RESULTS: BASE CASE

Table 2. Model-projected outcomes of on-PrEP monitoring strategies over 10 years

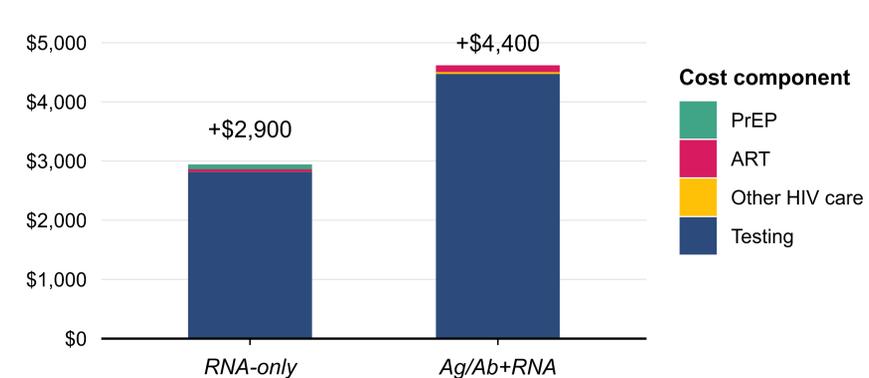
Strategies	Misdiagnosis		Discordant results	PrEP interruption frequency	HIV cases	Time from HIV acquisition to diagnosis, months, per person	QALYs, undisc	Total cost, million USD per 10,000
	FP	FN						
<i>Ag/Ab-only</i>	15.70	3.50	-	1,075	220	6.0	9.80	2,143.6
<i>RNA-only</i>	8.84	1.20	-	697	219	4.9	9.80	2,173.2
<i>Ag/Ab+RNA</i>	0.01	0.52	26.62	1,488	221	3.7	9.80	2,187.8

FP, false positive; FN, false negative. Costs reported in 2024 USD, rounded to the nearest 100, discounted 3%/year. Results calculated from unrounded numbers. QALYs rounded to 2 decimal places.

Base case

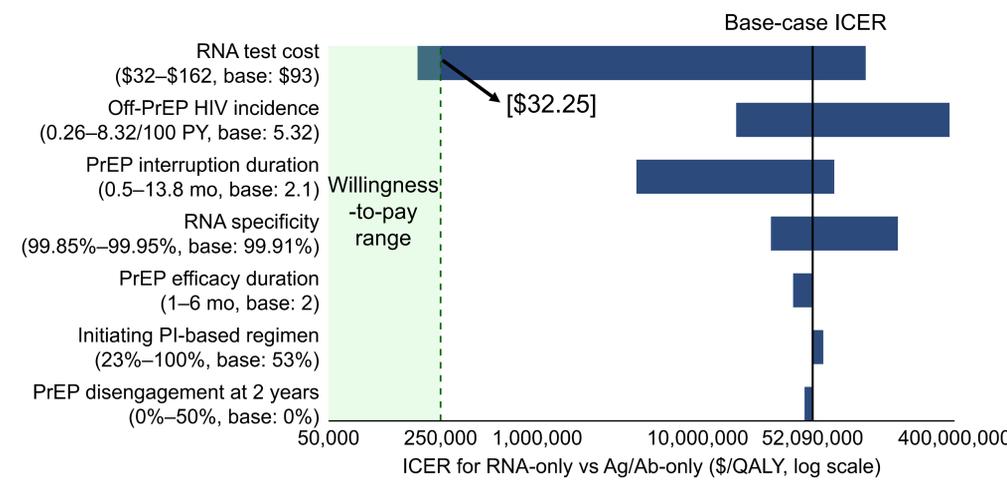
- Ag/Ab-only* would be preferred: lower per-person cost (\$214,400) than *Ag/Ab+RNA* (\$218,800) or *RNA-only* (\$217,300; ICER=\$52.1M/QALY vs. *Ag/Ab-only*).
- Ag/Ab+RNA* would lead to fewest misdiagnosis and earlier HIV diagnoses but more PrEP interruptions due to discordant results, potentially increasing HIV infections.
- QALYs would be equivalent across all strategies (9.80).

Figure 1. Additional cost per person vs. Ag/Ab-only (2024 USD, discounted)



RESULTS: SENSITIVITY ANALYSES

Figure 2. One-way sensitivity analysis: ICER for RNA-only vs. Ag/Ab-only (\$/QALY, log scale)



Sensitivity analyses

- Ag/Ab-only* would be preferred when assessing uncertainty in model input parameters, including in both deterministic and probabilistic sensitivity analyses.
- RNA-only* would be preferred only if RNA test cost decreased below \$32.25 (66% reduction).
- Results would be robust to extended dosing intervals and PrEP disengagement rates.

LIMITATIONS

- Assumed constant HIV risk behavior during PrEP interruptions.
- Longitudinal psychological/behavioral consequences of false-positive diagnoses may not have been fully captured.
- HIV transmission (sexual/parenteral) not explicitly modeled; low viral loads among those on CAB-LA suggest low sexual transmission risk.

CONCLUSIONS & ONGOING WORK

- At current HIV RNA test costs, *Ag/Ab-only* monitoring at CAB-LA injection visits would reduce costs with similar clinical outcomes compared to CDC-recommended simultaneous *Ag/Ab+RNA* testing.
- Ongoing analyses include evaluating pre-PrEP initiation screening strategies and alternative testing approaches.

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