

PrEP for HIV Prevention

NAT in PrEP

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Disclosures

This talk may include discussion of non-FDA approved strategies for HIV prevention.

I attended an advisory meeting for ViiV Healthcare in 2025. I have no other conflicts of interest or relationships to disclose.

Disclaimer

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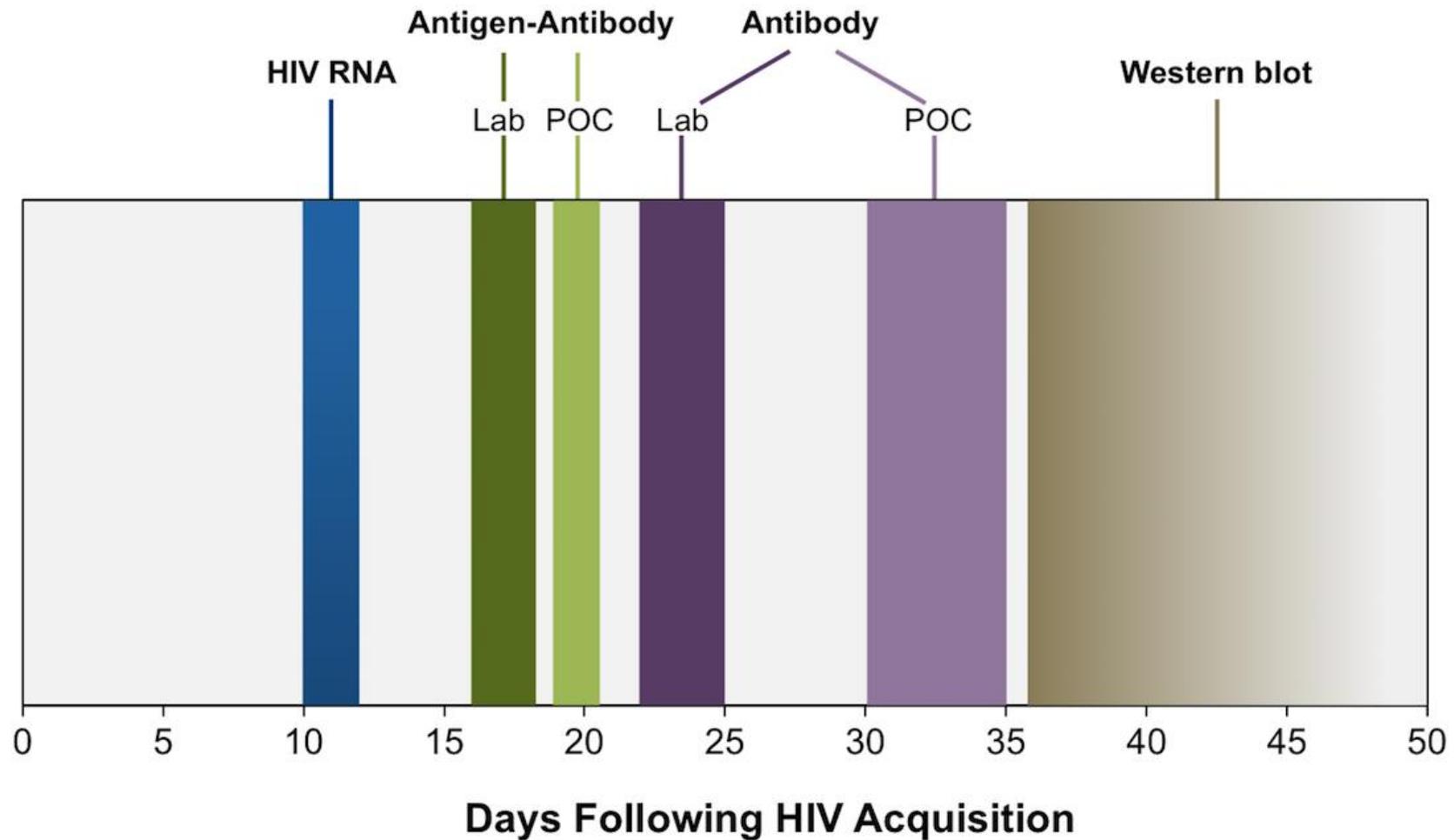
Daily oral PrEP (2021 CDC/HHS Guidelines)

| | Sexually-Active Adults and Adolescents ¹ | Persons Who Inject Drug ² |
|---|--|--|
| Identifying substantial risk of acquiring HIV infection | <p>Anal or vaginal sex in past 6 months AND any of the following:</p> <ul style="list-style-type: none"> • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months³ • History of inconsistent or no condom use with sexual partner(s) | <p>HIV-positive injecting partner OR Sharing injection equipment</p> |
| Clinically eligible → | <p><u>ALL OF THE FOLLOWING CONDITIONS ARE MET:</u></p> <ul style="list-style-type: none"> • Documented negative HIV Ag/Ab test result within 1 week before initially prescribing PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥ 30 ml/min⁴ • No contraindicated medications | |
| Dosage | <ul style="list-style-type: none"> • Daily, continuing, oral doses of F/TDF (Truvada®), ≤ 90-day supply OR • For men [redacted] at risk for sexual acquisition of HIV; daily, continuing, oral doses of F/TAF (Descovy®), ≤ 90-day supply | |
| Follow-up care → | <p><u>Follow-up visits at least every 3 months to provide the following:</u></p> <ul style="list-style-type: none"> • HIV Ag/Ab test and HIV-1 RNA assay, medication adherence and behavioral risk reduction support • Bacterial STI screening for MSM [redacted] – oral, rectal, urine, blood • Access to clean needles/syringes and drug treatment services for PWID <p><u>Follow-up visits every 6 months to provide the following:</u></p> <ul style="list-style-type: none"> • Assess renal function for patients aged ≥ 50 years or who have an eCrCl < 90 ml/min at PrEP initiation • Bacterial STI screening for all sexually-active patients³ – [vaginal, oral, rectal, urine- as indicated], blood <p><u>Follow-up visits every 12 months to provide the following:</u></p> <ul style="list-style-type: none"> • Assess renal function for all patients • Chlamydia screening for heterosexually active women and men – vaginal, urine • For patients on F/TAF, assess weight, triglyceride and cholesterol levels | |

Timeline: Recommendations for Routine HIV NAT in PrEP

- 2021 CDC/HHS: oral PrEP follow-up, CAB baseline and follow-up
- 2021 CAB package insert: CAB baseline and follow-up
- 2022 IAS/USA: CAB baseline and follow-up
- 2024 IAS/USA: oral PrEP/CAB baseline, not at follow-up for either
- 2025 LEN package insert: at baseline
- 2025 CDC MMWR (LEN): NAT or repeat Ag/Ab at 4 weeks
unless switching from other regimen - then not needed

Window periods of different HIV tests



Delayed detection of HIV infection in oral PrEP

PrEP may lead to delayed seroconversion and false-negative tests, particularly with oral fluid tests

Curlin et al CID 2017; 64(12): 1663-69

- Delayed diagnosis occurred in 80 of 287 seroconverting individuals
- OFOQ conversion delay: median 98.5, range 14.5-547.5 days
- Delay was associated with low plasma RNA level

Donnell et al AIDS 2017; 31(14): 2007-16

- PrEP was associated with more frequent delayed diagnosis >100 days by POC Ab testing (17% v 6%)

Rationale for NAT in oral PrEP

Delayed detection of HIV infection in HPTN 083 (n=42)

| | Baseline (n=3) | Incident infections (n=39) |
|--|-----------------|----------------------------|
| Median delay 1 st pos (range) | 34 (14-36) days | 31* (7-68 days*) |
| Median log VL at 1 st pos visit | 3.3 (2.1-4.7) | 4.1 (NQ-4.3)** |
| | 3/3 detectable | 6/7 detectable |

*excluding case with visit interval 372 days

**for the 6 participants with detectable VL

4 participants continued to receive oral PrEP

5 M184V/I, 1 K65R

PrEP USE DURING ACUTE HIV INFECTION IN A COMMUNITY SETTING COMPROMISES HIV DIAGNOSIS

Table: Clinical and diagnostic test results from 6 Thai MSM who started PrEP during acute HIV infection. xG=x generation HIV antibody test, Gn= Geenius, =nonreactive, =reactive, ND=not done

| Partici- -pant | # days on PrEP | HIV diagnosis | Pre-PrEP VL (cps/mL) | Pre-ART VL (cps/mL) | Pre-ART CD4 (cells/ μ L) | Week 0 | | | Week 24 | | | Week 48 | | | |
|-------------------|-------------------|------------------|-------------------------|---------------------------|------------------------------------|-------------------------------------|-------------------------------------|--------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--------------------------|--------------------------|-------------------------------------|--------------------------|
| | | | | | | 2G | 3G | 4G | 2G | 3G | 4G | 2G | 3G | 4G | Gn |
| 3145 | 7 | NAAT | 16,780 | 216 | 685 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | ND | ND | <input type="checkbox"/> | <input type="checkbox"/> |
| 4634 | 2 | NAAT | 219 | 2,317 | 528 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | ND | <input type="checkbox"/> | <input type="checkbox"/> |
| 5803 | 29 | Ab | 58 | 37,222 | 302 | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | ND | ND | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| 6313 | 91 | Ab | 223,361 | 389 | 690 | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input type="checkbox"/> | ND | ND | <input type="checkbox"/> | <input type="checkbox"/> |
| 6934 | 2 | NAAT | 32 | 276 | 739 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 7167 | 15 | NAAT | 317 | 8,802 | 521 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> | ND | ND | ND | <input type="checkbox"/> |

WB = Indeterminate or NEG at all time points in all participants

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Delayed detection of HIV infection in CAB-LA PrEP (n=11)

| | Baseline | Incident infection |
|--|-----------------|--------------------|
| Median delay 1 st pos (range) | 62 (28-72) days | 98 (35-185 days) |
| Median log VL at 1 st pos visit | 4.4 (3.1-4.7) | 2.1 (ND-2.9) |
| | | 5 of 7 detectable |
| Received CAB p infection | 4/4 | 6/7 |

5 of these participants acquired INSTI resistance.

These 11 are 0.2% of the 4570 participants in the study.

Real issue: cost and back of envelope cost-effectiveness

- Some payers refuse to cover screening with HIV NAT in PrEP.
- CAB \$164/test, 2283 participants
 - Baseline testing = $2283 \times \$164 / 4$ participants = additional ~\$95,000 per AHI identified
 - Followup = 9 NAT (Q2 months over 17 months) = \$3,369,708
 - With 5 of 11 participants acquiring INSTI resistance = ~\$700,000/case identified
 - And it is unclear if these cases of resistance could have been prevented.
- FTC/TDF, 2287 participants
 - Follow-up (Q3mo) = $2287 \times \$164 \times 5$ tests = \$1,875,340
 - With 5 M184V/I = additional ~\$375,000/case identified

Is routine HIV NAT cost-effective?

DISCOVER OLE (Wohl et al, Lancet HIV 2024)

23 (85%) of 27 persons diagnosed with HIV had stored plasma specimens.

4 (17%) of 23 participants had detectable HIV RNA at the visit before dx.

Median delay 10 weeks (5, 8, 11, 14 weeks)

Median HIV RNA 741 copies (257, 332, 1150, 220k)

19,468 routine RNA tests to detect one case sooner in setting of oral PrEP.

Clinical Infectious Diseases

MAJOR ARTICLE



OXFORD

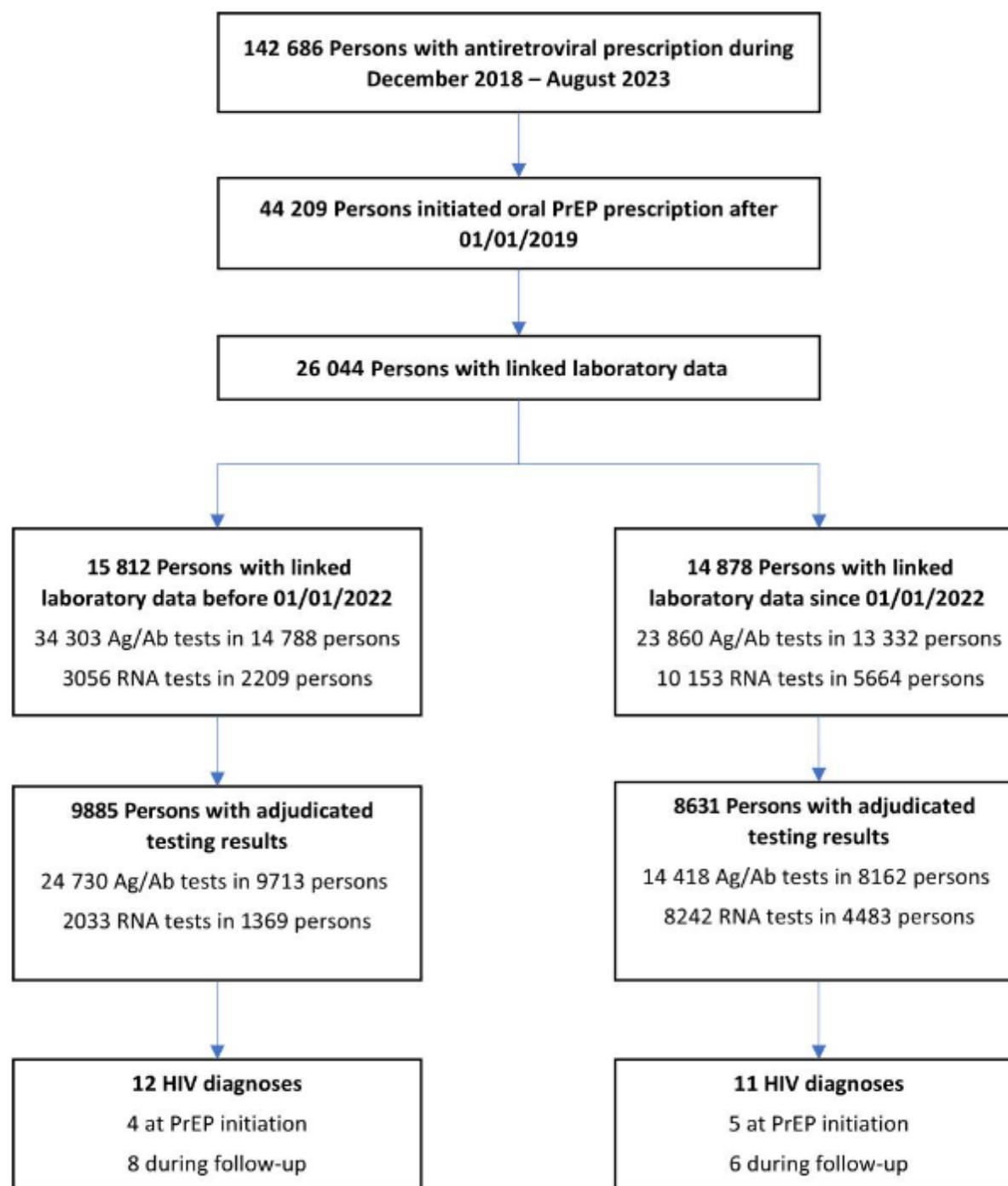
Limited Utility of HIV RNA Testing to Monitor Oral Preexposure Prophylaxis Use: A Real-World Cohort Study—United States, 2019–2023

Weiming Zhu,[□] Kevin P. Delaney,[□] Ya-lin A. Huang,[□] Rupa R. Patel,[□] Athena P. Kourtis,[□] and Karen W. Hoover[□]

HIV Research Branch, Division of HIV Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Limited Utility of HIV RNA Testing to Monitor Oral PrEP

- HealthVerity HIV cohort (insurance claims, EMRs, labs, pharmacy records)
- Two periods: 2019-2021, 2022-Aug 2023
- PrEP initiation testing = first FTC/TDF or FTC/TAF +/- 14 days
- PrEP follow-up testing = >15 days



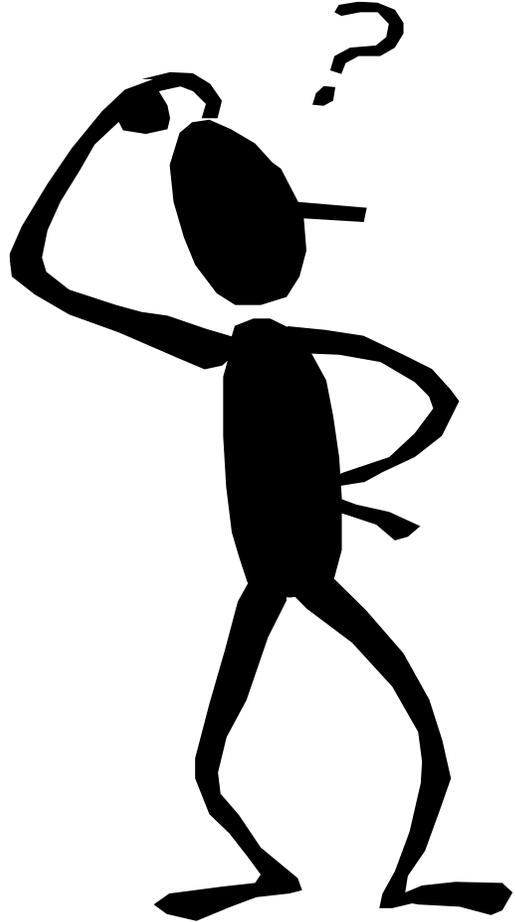
Limited Utility of HIV RNA Testing to Monitor Oral PrEP

- HIV RNA increased post-2021
 - 14% of PrEP users (2209 of 15812) v 38% (5664 of 14878) had at least one RNA.
- 23 adjudicated HIV diagnoses, 17 with both Ag/Ab + RNA
 - In 16/17 the RNA test result was concurrent or later than Ag/Ab.
 - In 1/17 the RNA was earlier than positive Ag/Ab test - among 8226 RNA tests conducted during PrEP follow-up.
- 8226-9900 tests needed for 1 HIV diagnosis earlier than Ag/Ab testing alone.

Conclusions

- Routine HIV NAT is of limited utility and is not cost-effective in monitoring during oral PrEP.
- HIV NAT is still recommended at baseline in setting of recent exposure or symptoms of acute HIV infection at PrEP initiation.
- Package inserts for both formulations of injectable PrEP specify routine HIV NAT at initiation.
- Package insert for injectable CAB specifies routine HIV NAT at follow-up, though RCT data suggests it will also be of limited utility and not cost-effective, although real-world data are not yet available.

Questions?



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