# Evidence of HIV infection prior to rapid antibody test positivity in PrEP breakthrough infections

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## BACKGROUND

- Exposure to antiretrovirals in PrEP users with breakthrough infection can suppress viral replication early after HIV acquisition, leading to **delayed or inconclusive seroconversion.**
- **Limitations in HIV diagnostic accuracy** in this context are higher for assays with lower sensitivity, such as point-of-care antibody-only rapid tests (RT).

## METHODS

- We obtained plasma samples from **visits prior to the first positive RT** from **251 participants with incident HIV during randomized PrEP trials** (iPrEx and Partners PrEP – Figure 1), which used antibody-only RT (state-of-the-art for HIV diagnosis at the time).
- Samples were categorized into **time intervals** and analyzed using higher performance tests (Abbott Alinity s HIV Ag/Ab Combo, Roche Elecsys HIV Duo, and Ortho VITROS HIV Combo for antigen/antibodies detection; Roche cobas MPX for RNA detection) to **address positivity comparing participants assigned to active PrEP (N=101) to those assigned to placebo (N=150)**

## RESULTS

- A **large percentage of samples** had **positive results** in higher performance tests **before infection detection by RT** (Figure 2).
- **Rates were consistently higher for participants assigned to active PrEP compared to placebo**, with statistical significance for the <8 weeks timepoint in 2 of 4 assays.
- The combination of RNA and antigen/antibody tests further increased overall positivity, although not reaching statistical significance when compared to antigen/antibodies tests alone.
- We also analyzed signal-to-cutoff/cutoff index results in antigen/antibodies tests over time prior to the first positive RT, by treatment assignment; levels were somewhat higher, and positivity was identified earlier in participants assigned to active PrEP, **suggesting longer duration of infection prior to the first positive RT.**

Using samples from PrEP trials and lab-based serologic and nucleic acid detection assays, we found evidence that **exposure to PrEP** increases the likelihood of **falsely negative rapid diagnostic tests**

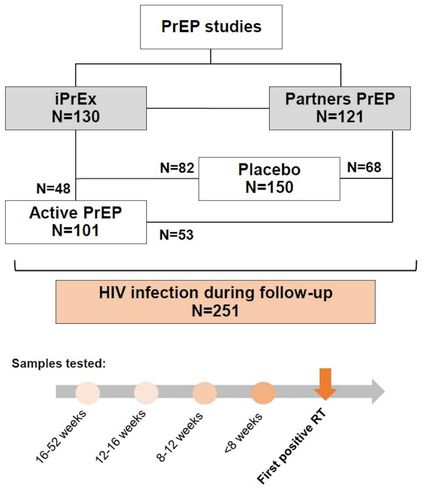


**Figure 1:** Participants and samples included in the study

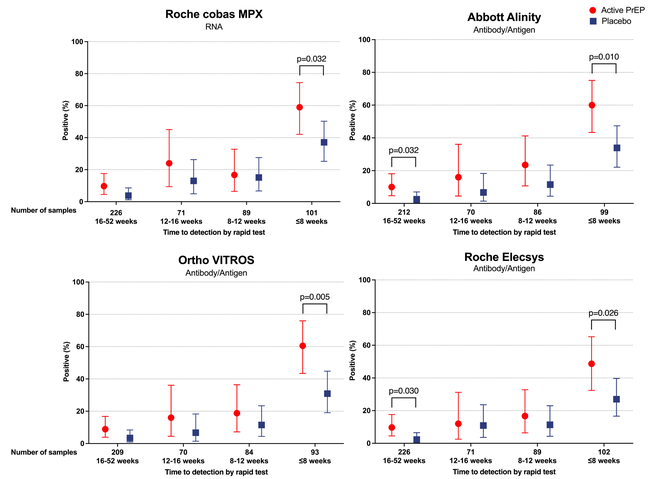


**Figure 2:** Percentages and 95% confidence intervals of participants with evidence of infection prior to detection by rapid tests, according to PrEP treatment assignment.

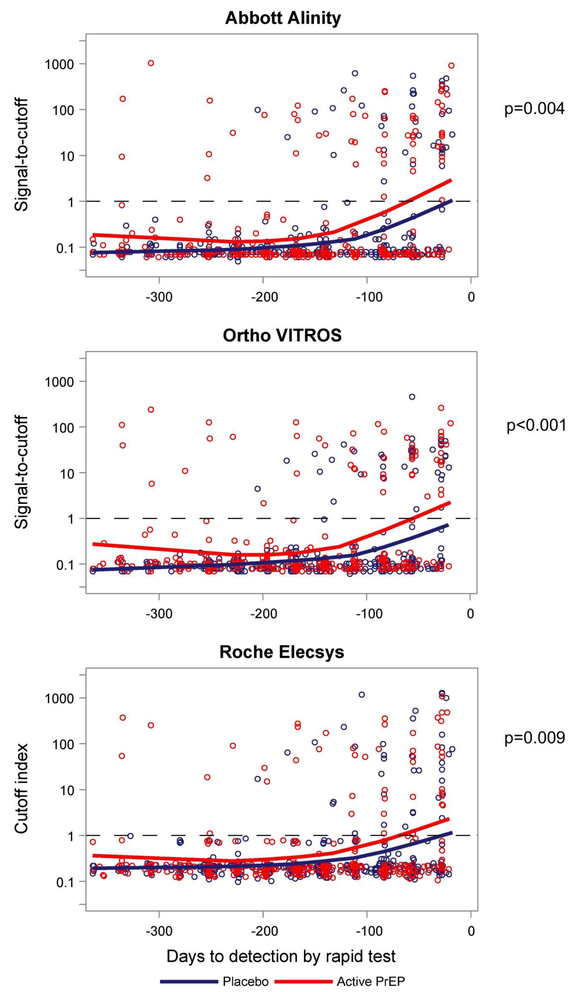


**Figure 3:** Ab signals and smoothed splines in samples collected prior to detection by rapid test in PrEP trials. P-values calculated using repeated measures spline regressions.

## CONCLUSIONS

- Compared to antibody-only RT, higher sensitivity lab-based serologic and nucleic acid detection assays can **enhance the identification of breakthrough HIV infections in PrEP users.**
- Our findings suggest consideration of adopting higher sensitivity tests in PrEP programs that rely exclusively on point-of-care 3rd generation RT for follow-up.
- For blood donor centers, our results reinforce that screening with parallel lab-based serologic and RNA tests should be ensured.
- Study limitations include sample storage beyond the manufacturers' labeled claims and possible laboratory errors.

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