

ICAP Journal Club

ICAP's Journal Club is designed to inform ICAP staff and colleagues of the latest scientific literature by providing a succinct summary and critical analysis of important studies, and by discussing the implications of the research on clinical work.

Article

Ngunjiri K, Ortblad KF, Mogere P, et al. **Efficiency of 6-month PrEP dispensing with HIV self-testing in Kenya: an open-label, randomised, non-inferiority, implementation trial.** *Lancet HIV.* 2022;9(7):e464-e473. [https://doi.org/10.1016/S2352-3018\(22\)00126-6](https://doi.org/10.1016/S2352-3018(22)00126-6)

Study Summary

The open-label, randomized, non-inferiority, implementation Jipime-JiPrEP trial compared HIV testing, drug refills and adherence outcomes among individuals receiving 6-month pre-exposure prophylaxis (PrEP) dispensing with HIV self-testing (HIVST) at home, to those receiving standard of care PrEP services.

Study Setting

- The Partners in Health and Research Development clinic, located in a peri-urban town in Kiambu County, Kenya.

Methods

- Adults (aged ≥ 18 years) were eligible to participate if they were HIV-negative; at risk of acquiring HIV; had started PrEP ≥ 1 month before enrollment and planned to continue PrEP; were not participating in another HIV prevention trial; were willing to be assigned to the HIVST group; and had no contraindications to taking PrEP drugs.
- Three types of populations at risk of acquiring HIV were recruited: 1) men in HIV serodifferent couples, 2) women in HIV serodifferent couples, and 3) women not in known HIV serodifferent couples (i.e. singly enrolled) and eligible for PrEP based on the national risk assessment tool.
- Participants were randomized (1:1:1) to receive either:
 - 6-month PrEP dispensing with biannual clinic visits plus interim blood-based HIVST,
 - 6-month PrEP dispensing with biannual clinic visits plus interim oral fluid-based HIVST, or
 - Standard of care PrEP delivery with 3-month PrEP dispensing and quarterly clinic visits.
- Participants in the 6-month PrEP dispensing groups received two HIV self-tests and were instructed to use one for interim 3-month HIV testing and the other as they wished (e.g., for additional testing, back-up testing, or testing for a sexual partner or friend). They were trained on how to use the self-tests at enrollment and all kits included a pictorial informational brochure in the local language. Participants also received a free 24-hour telephone number that they could call with any questions or if they tested positive.

- Participants in all groups were told they could contact or return to the clinic at any point between scheduled PrEP visits, and participants were reminded of their scheduled follow-up visits using standard clinical procedures in Kenya (a call 1 day after a missed visit and a second call 7 days later).
- Blood specimens for dried blood spot (DBS) testing were collected at the 6-month follow-up visit to measure PrEP adherence.
- The three co-primary outcomes assessed at the 6-month follow-up visit were:
 - The proportion of participants self-reporting any HIV testing (clinic-based or HIVST) after the enrollment visit and before the 6-month visit;
 - The proportion of participants who returned to the clinic to refill their PrEP medication, based on clinic records; and
 - The proportion of participants adherent to PrEP, defined as detectable tenofovir diphosphate concentrations in their DBS sample.
- The non-inferiority margin was set at -10% using a one-sided 95% confidence interval (CI) lower bound, and analyses were done using the intention-to-treat principle, with missing results classified as participants not achieving the study outcomes.
- The primary pre-specified comparison was 6-month PrEP dispensing plus interim HIVST (combined PrEP intervention groups) versus standard of care PrEP dispensing.
- Pre-specified subgroup analyses were conducted, including HIV serodifferent couples, all women (in HIV serodifferent couples and singly enrolled), and women singly enrolled. In addition, pre-planned superiority analyses were conducted for women who were singly enrolled.

Study Population and Follow-up

- Between May 2018 and February 2020, 527 individuals were screened and 495 were enrolled; 163 participants in the 6-month PrEP dispensing plus oral HIVST group, 166 in the 6-month PrEP dispensing plus blood-based HIVST group, and 166 in the standard of care group.
- Of those enrolled, 165 were men in HIV serodifferent couples, 130 were women in HIV serodifferent couples, and 200 were singly enrolled women.
- All participants were of Black African ethnicity, with a median age of 33 years (interquartile range [IQR] 27–40), and median duration of education of 9 years (IQR 8–12), and 77% were married (96% of members of serodifferent couples and 50% of singly enrolled women). Sociodemographic characteristics were similar across groups.
- All participants reported HIV risk behaviors according to the national PrEP screening tool, with 82% reporting inconsistent condom use in the past month, and 24% of singly enrolled women reported exchange of sex for money or goods in the past month.
- At 3 months, 89% of participants in the standard of care group returned for their scheduled follow-up visit, and 8% of participants in the combined 6-month PrEP dispensing group returned to the clinic for an unscheduled follow-up visit.
- At 6 months, 84% of participants in the standard of care group and 84% of participants in the combined 6-month PrEP dispensing group returned for follow-up (85% in the oral HIVST group and 83% in the blood-based HIVST group).

- No HIV seroconversions were observed during the study period.

Primary Outcomes

- Among participants in the combined 6-month PrEP dispensing group, 81% reported using at least one of the HIV self-tests and 42% reported using both.
- The median time between enrollment and completion of the first HIV self-test was 87 days (IQR 71–99) and 165 days (148–171) for the second self-test.
- All of the primary outcomes were non-inferior for the combined 6-month PrEP dispensing group when compared with the standard of care group:
 - 83% of participants in the combined 6-month PrEP dispensing group had tested for HIV in the previous 6 months compared with 84% of participants in the standard of care group (risk difference –1.15%; 95% CI lower bound –6.89)
 - 78% of participants in the combined 6-month PrEP dispensing group refilled PrEP at their 6-month visit compared with 81% in the standard of care group (risk difference –2.60%; 95% CI lower bound –8.88); and
 - 61% of participants in the combined 6-month PrEP dispensing group were adherent to PrEP compared with 57% in the standard of care group (risk difference 2.37%; 95% CI lower bound –5.05).
- All primary outcomes were non-inferior for participants randomly assigned to the oral HIVST group, when compared with the standard of care group.
- In the blood-based HIVST group, PrEP adherence was non-inferior compared with the standard of care group, but non-inferiority was not demonstrated for the HIV testing and PrEP refill outcomes.

Subgroup Analyses

- Among participants in HIV serodifferent couples, the only outcome that was non-inferior in the combined 6-month PrEP dispensing group was PrEP refills (79% vs. 80% in standard of care group; risk difference –1.19%, 95% CI lower bound –9.39). Non-inferiority was not demonstrated for the HIV testing outcomes (83% vs. 86%; risk difference –2.81%, 95% CI lower bound –10.04) or the PrEP adherence outcome (67% vs. 75%; risk difference –7.98%, 95% CI lower bound –16.95).
- Among all women, the study outcomes were non-inferior for the 6-month dispensing group compared with the standard of care.
- Among women who were singly enrolled, PrEP adherence was significantly higher in the combined 6-month PrEP dispensing group than the standard of care group (51% vs. 31%; risk difference 19.78%; 95% CI 5.80–33.77).
- Among participants aged ≥ 30 years, all outcomes in the combined 6-month PrEP dispensing group were non-inferior compared with the standard of care group, but non-inferiority was not established for the smaller subgroup of participants < 30 years old.

Critical Analysis

The open-label, randomized, non-inferiority, implementation Jipime-JiPrEP trial found that 6-month PrEP dispensing, supplemented with interim HIVST, was non-inferior to standard 3-month PrEP dispensing for HIV testing, PrEP refills, and PrEP adherence outcomes at 6 months. However, there were differences observed by subgroup, with less HIV testing and lower PrEP adherence among members of HIV serodifferent couples in the intervention groups, whereas PrEP adherence was greater among singly enrolled women receiving the intervention.

The following points should be considered when interpreting the study findings:

- Due to the nature of the intervention, participants and research staff were aware of treatment assignments. Additionally, HIVST was a self-reported outcome, which could be affected by social desirability bias in an unblinded study.
- The primary PrEP adherence outcome was any evidence of PrEP use in DBS samples. However, a sensitivity analysis using a protective concentration threshold of tenofovir diphosphate also established non-inferiority between the combined 6-month PrEP dispensing group and the standard of care group.
- The follow-up period for this study was 12 months and the outcomes were assessed after only one 6-month period. Therefore, the impact of this intervention over a longer time period is unknown.
- All primary outcome measurements were dependent on participants returning for their 6-month PrEP visit, therefore, the researchers used wide retention windows, from the day after enrollment until 2 weeks before the next scheduled visit (9-month visit for participants in the standard of care group and 12-month visit date for participants in the 6-month PrEP dispensing groups). This could lead to wide variability among participants in PrEP coverage over the follow-up period. However, the median time between enrollment and the 6-month follow-up visit suggests most visits occurred around the 6-month mark (178 days [IQR 168–181] for participants in the standard of care group and 178 days [IQR 168–183] for participants in the combined 6-month PrEP dispensing group).
- PrEP was delivered in accordance with Kenya national guidelines at the time, which recommended PrEP use in serodifferent partnerships until the partner with HIV achieves viral suppression. Therefore, participants in HIV serodifferent couples could discontinue PrEP if their partner had consistently been on treatment for 6 months and knowledge that PrEP was a short-term ‘bridge’ may have affected behaviors and outcomes in that subgroup.
- Among all women there was an indication that participants in the 6-month PrEP dispensing group had better PrEP adherence than those in the standard of care group (57% vs. 45%; risk difference 12.01%), but because this was an ad hoc analysis and not part of a pre-specified superiority analysis, the authors did not claim this result is evidence of superiority.
- The study was conducted at a single site and any missing results were classified as participants not achieving the study outcome. This conservative approach likely undercounts the number of participants achieving the primary outcomes, as it misses those seeking follow-up services elsewhere.

- The study was powered to observe differences between the combined groups receiving HIVST, making it difficult to interpret any differences found between those receiving blood-based HIVST and oral HIVST.

Implications

The open-label, randomized, non-inferiority, implementation Jipime-JiPrEP trial found that 6-month PrEP dispensing, supplemented with interim HIVST, did not adversely impact HIV testing, PrEP refills or PrEP adherence after 6 months, compared to standard PrEP care in Kenya. This model of PrEP service delivery halves the number of clinic visits, which could reduce costs and other burdens for clients, providers, and health systems. This study provides some of the first evidence on the use of HIVST to support PrEP continuation and informed a recent update by the World Health Organization, which permits HIVST use in PrEP programs.¹ Offering diverse PrEP service delivery models is a more person-centered approach and may help address some of the barriers to PrEP continuation.

References

- 1) World Health Organization. Differentiated and simplified pre-exposure prophylaxis for HIV prevention: update to WHO implementation guidance. Technical Brief. Geneva: World Health Organization; 2022

This article synopsis was written by Dr. Cassia Wells. Share your thoughts on this article or suggest an article for Journal Club by emailing her at caw2208@columbia.edu.