

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

Labhardt ND, Ringera I, Lejone TI, et al. **Effect of Offering Same-Day ART vs Usual Health Facility Referral During Home-Based HIV Testing on Linkage to Care and Viral Suppression Among Adults With HIV in Lesotho. The CASCADE Randomized Clinical Trial.** *JAMA*. Published online March 06, 2018. doi:10.1001/jama.2018.1818

## Study Summary

This open-label, randomized clinical trial examined the effect of offering same-day, home-based antiretroviral therapy (ART) initiation followed by less frequent clinic visits, compared to usual care with referral to the nearest health facility and monthly clinic visits, on linkage to care and viral suppression in individuals who test HIV-positive during home-based testing.

## Study Setting

- Rural villages and urban areas linked to six health care facilities in the Butha-Buthe district in northern Lesotho.

## Methods

- Teams consisting of a study nurse, team leader, and four lay counselors visited randomly selected villages and urban neighborhoods and offered HIV testing to all members of each household.
- Adults 18 years or older who tested HIV-positive were recruited to participate in the study.
- Exclusion criteria were: history of previous ART, pregnancy, breastfeeding, clinical WHO stage 4, on treatment for another chronic condition, positive cryptococcal antigen test, no domicile or employment in the region, or preference to seek care at a health facility other than those participating in the trial.
- Consenting eligible participants were randomized (1:1) into same-day ART or usual care groups.
- In the same-day ART group, participants received pre-ART counseling directly after testing, accompanied by a leaflet with information on ART adherence. If participants were ready to initiate ART, they were given a 30-day supply of medication and instructed to visit their health facility within two to four weeks.
- Once participants in the same-day ART group linked to care at the health facility, they received regular care, except with longer intervals between follow-up visits (1.5, 3, 6, 9 and 12 months after ART initiation) than the usual monthly interval.
- In the usual care group, participants received post-test counseling in the home and an appointment at the nearest health facility within 28 days.

- Once participants in the usual care group linked to care, they underwent two pre-ART health facility visits for bloodwork, pre-ART counseling, and a readiness assessment by health facility staff. After ART initiation, participants had monthly follow-up visits at the health facility.
- In both groups, blood was drawn in the home on the day of testing for point-of-care CD4 cell count, creatinine, and hemoglobin tests; however, participants in the usual care group did not receive their results.
- The study had two co-primary outcomes: 1) three-month linkage to care, defined as attending the health facility within 90 days of the home-based HIV test; and 2) 12-month viral suppression, defined as viral load <100 copies/milliliter from 11 through 14 months after study enrollment. Those who did not attend the health facility or have blood drawn during this interval were considered not to have achieved viral suppression.
- Pre-specified secondary outcomes included viral suppression at six months and 12-month mortality.
- Post hoc analyses included ART initiation at three months, 12-month retention in care (defined as the patient or treatment buddy picking up a refill at the health facility between 11 and 14 months), viral suppression at 12 months among those with a documented viral load result, median time between visits, and number of visits attended according to study protocol.
- A lay counselor contacted participants who did not link to care within three months and who were not retained in care at 12 months to ascertain their outcome. If the lay counselor could not reach the participant by telephone, the lay counselor asked a village health worker to visit the participant's home.
- Data were collected through a short questionnaire administered to participants upon enrollment, and through reviewing health facility records every two months.
- All analyses were by intention-to-treat.

### Study Population

- From February to July 2016, study teams visited 6,655 households in 60 rural villages and 17 urban areas, and reached 13,586 household members with unknown HIV status. Of these, 11,590 agreed to home-based testing and 441 individuals from 420 households tested HIV-positive.
- Of those who tested positive, 278 participants from 268 households fulfilled inclusion criteria. The most common reasons for exclusion were wanting to attend a non-study health facility (n=71), being in care for another chronic medical condition (n=43), age <18 years (n=25), not living or working in the area (n=19), and being pregnant (n=16).
- The final analysis included 137 participants from 132 households in the usual care group and 137 participants from 132 households in the same-day ART group.
- Median age was 39 years (interquartile range [IQR], 28–52 years).
- The majority were women (65.7%), married or living with a partner (65.1%), without regular income (77%), with clinical WHO stage 1 (78.1%), and having a CD4 cell count of  $\geq 350$  cells/cubic millimeter (55.6%).
- In the same-day ART group, 134 (97.8%) were ready to start treatment that day and two (1.5%) within the next few days. A one-month supply of ART was given to each of these 136 participants.

### Primary Outcomes

- Linkage to care within three months was 68.6% in the same-day ART group vs. 43.1% in the usual care group ( $p < 0.001$ ).
- Viral suppression at 12 months was achieved in 50.4% in the same-day ART group vs. 34.3% in the usual care group ( $p < 0.007$ ).

### Secondary Outcomes and Post Hoc Analyses

- At six months, viral suppression was documented in 37.2% of participants in the same-day ART group vs. 26.3% in the usual care group ( $p = 0.05$ ).
- At 12 months, 63.5% of participants in the same-day ART group vs 48.2% in the usual care group were retained in care at the six participating health facilities ( $p = 0.01$ ). The most frequent reported reasons for not remaining in care were being treated at another facility (29.4%), refusing to attend (24.4%), and having no time to attend (19.3%).
- At 12 months, there were two deaths in the same-day ART group and none in the usual care group.
- Among all participants who linked to care within three months ( $n = 153$ ), retention in care was higher in the same-day ART group vs. the usual care group (log-rank  $p = 0.02$ ). However, there was no significant difference in retention in care when considering all participants who linked to care during the entire study period, including 30 participants who linked after three months (log-rank  $p = 0.17$ ).
- ART initiation (in addition to linkage to care) occurred for 68.6% of participants in the same-day ART group and 32.1% of participants in the usual care group within three months of enrollment ( $p < 0.001$ ).
- Among those with a documented viral load result in the 11–14-month window after enrollment, viral suppression was not significantly different (94.5% in same-day ART group vs. 90.4% in the usual care group,  $p = 0.38$ ).
- The median time span between all health facility visits was 59 days (IQR, 52–70 days) in the same-day ART group and 40 days (IQR, 32–58 days) in the usual care group ( $p < 0.001$ ).
- The number of visits attended according to the study protocol was 17.0% in the same-day ART group and 17.7% in the usual care group ( $p = 0.91$ ), although 73% of participants in the same-day ART group had more visits than expected and 77% of participants in the usual care group had fewer visits than expected ( $p < 0.001$ ).

### **Critical Analysis**

This study found that home-based, same-day initiation of ART following a positive HIV test increased linkage to care after three months and viral suppression after 12 months compared to standard health facility referral. This is the first randomized study that demonstrates the feasibility of same-day ART initiation outside of a health facility, and the first to show improved clinical and linkage outcomes with same-day initiation in the era of treatment for all people living with HIV.

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

- Linkage to care and viral suppression rates were relatively low in the same-day ART group, suggesting that further interventions are needed to achieve UNAIDS 90-90-90 targets.
- Participants in the same-day ART group were given three-month follow-up intervals between health facility appointments, whereas the usual care group were required to return to the facility every month. Given that the median travel time to the health facility for both groups was 60 minutes, this component of the intervention likely contributed to the 12-month outcomes.
- Participants who transferred care to another health facility were considered as being not retained in care and as having unsuppressed viral load. Therefore, these findings likely underestimate overall retention in care and viral suppression.
- Viral suppression in this study was defined as <100 copies/milliliter, which is more conservative than the WHO and PEPFAR definition of <1000 copies/milliliter.
- Viral suppression in those with documented 12-month viral load was similar between the groups and  $\geq 90\%$ , suggesting that additional interventions should focus on improving linkage and retention in care.
- This study excluded pregnant and breastfeeding women, those with chronic disease, including tuberculosis, and those with advanced disease, which are groups who may benefit from rapid ART initiation the most.
- The study only included people who lived or worked in the area, and who were willing to seek care at pre-specified health facilities; therefore, these findings may not be generalizable to populations who are more mobile.
- This study was conducted in a predominantly rural population, so the benefits of home-based services that were found may not be generalizable to more urban settings.
- This study was also relatively small, and was conducted in a single district in Lesotho, which further limits generalizability.

## Implications

This open-label, randomized clinical trial in rural Lesotho found that same-day ART initiation after home-based HIV testing improved linkage to care and viral suppression at 12 months. This study also demonstrated that home-based ART initiation was generally accepted by participants and was feasible with a trained nurse and the use of point-of-care laboratory testing. As country programs work toward achieving the goal of 90% of people living with HIV knowing their status, more HIV testing is occurring outside of health facilities. Consequently, efforts to improve linkage to care following a positive test result in the community are increasingly important. This study provides evidence that offering same-day ART in the community can be a strategy to improve linkage and clinical outcomes in similar populations. However, overall viral suppression remained low, suggesting additional interventions will be necessary to ensure 90% of those on treatment are virally suppressed.

*This article synopsis was written by Cassia Wells. Share your thoughts on this article or suggest an article for Journal Club by emailing her at [can2208@columbia.edu](mailto:can2208@columbia.edu).*

