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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

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IMPORTANCE Home-based HIV testing is a frequently used strategy to increase awareness of HIV status in sub-Saharan Africa. However, with referral to health facilities, less than half of those who test HIV positive link to care and initiate antiretroviral therapy (ART).

OBJECTIVE To determine whether offering same-day home-based ART to patients with HIV improves linkage to care and viral suppression in a rural, high-prevalence setting in sub-Saharan Africa.

DESIGN, SETTING, AND PARTICIPANTS Open-label, 2-group, randomized clinical trial (February 22, 2016-September 17, 2017), involving 6 health care facilities in northern Lesotho. During home-based HIV testing in 6655 households from 60 rural villages and 17 urban areas, 278 individuals aged 18 years or older who tested HIV positive and were ART naive from 268 households consented and enrolled. Individuals from the same household were randomized into the same group.

INTERVENTIONS Participants were randomly assigned to be offered same-day home-based ART initiation (n = 138) and subsequent follow-up intervals of 1.5, 3, 6, 9, and 12 months after treatment initiation at the health facility or to receive usual care (n = 140) with referral to the nearest health facility for preparatory counseling followed by ART initiation and monthly follow-up visits thereafter.

MAIN OUTCOMES AND MEASURES Primary end points were rates of linkage to care within 3 months (presenting at the health facility within 90 days after the home visit) and viral suppression at 12 months, defined as a viral load of less than 100 copies/mL from 11 through 14 months after enrollment.

RESULTS Among 278 randomized individuals (median age, 39 years [interquartile range, 28.0-52.0]; 180 women [65.7%]), 274 (98.6%) were included in the analysis (137 in the same-day group and 137 in the usual care group). In the same-day group, 134 (97.8%) indicated readiness to start ART that day and 2 (1.5%) within the next few days and were given a 1-month supply of ART. At 3 months, 68.6% (94) in same-day group vs 43.1% (59) in usual care group had linked to care (absolute difference, 25.6%; 95% CI, 13.8% to 36.3%; $P < .001$). At 12 months, 50.4% (69) in the same-day group vs 34.3% (47) in usual care group achieved viral suppression (absolute difference, 16.0%; 4.4%-27.2%; $P = .007$). Two deaths (1.5%) were reported in the same-day group, none in usual care group.

CONCLUSIONS AND RELEVANCE Among adults in rural Lesotho, a setting of high HIV prevalence, offering same-day home-based ART initiation to individuals who tested positive during home-based HIV testing, compared with usual care and standard clinic referral, significantly increased linkage to care at 3 months and HIV viral suppression at 12 months. These findings support the practice of offering same-day ART initiation during home-based HIV testing.

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With the 90-90-90 targets, the global strategy to end AIDS focuses on treatment as prevention and early initiation of antiretroviral therapy (ART).[1] The 90-90-90 targets refer to 90% of people living with HIV being aware of their status, 90% of those receiving ART, and 90% of those achieving viral suppression.[2]

One strategy to achieving a 90% rate of individuals knowing their HIV status is to conduct testing at people's homes rather than in clinics, a method used in many countries and endorsed by the World Health Organization (WHO).[3] However, if individuals are found HIV positive during home-based testing, less than half of those patients link to care to initiate ART.[4,5] The 2017 consolidated WHO guidelines recommend that ART initiation should be offered on the same day to everyone who is ready to start,[6] and UNAIDS stated that the adoption of same-day initiation was one of the most crucial cornerstones in successfully achieving the 90-90-90 targets.[7] Yet evidence for this statement remains limited.[8] Three recent trials specifically addressed same-day ART initiation: 2 in South Africa[9,10] and 1 in Haiti.[11] However, all 3 trials enrolled individuals who tested HIV positive at the health facility and had low CD4 cell counts. To our knowledge, neither evidence on same-day ART initiation as a test-and-treat approach independent of CD4 cell count nor evidence on same-day ART start outside the health facility has been published.

The CASCADE trial was designed to respond to this evidence gap. The trial was conducted in Lesotho, a high-prevalence setting in southern Africa, where home-based HIV testing has been shown to have acceptance rates of more than 90% but linkage to care rates of only 25%.[12] This open-label, randomized clinical trial examined the effect of offering same-day, home-based, ART initiation on linkage to care and viral suppression in individuals who tested HIV positive during a home-based HIV testing program.

Key Points

Question Does offering antiretroviral therapy (ART) to sub-Saharan African residents the same day they tested positive for HIV in a home-based testing program improve linkage to care and viral suppression?

Findings In this randomized clinical trial involving 278 adults in rural Lesotho, offering home-based HIV testing and immediate ART initiation, compared with usual care and standard clinic referral, resulted in significantly higher rates of linkage to care at 3 months (68.6% vs 43.1%), and higher rates of HIV viral suppression at 12 months (50.4% vs 34.3%).

Meaning Offering same-day ART initiation to individuals who test HIV positive during a home-based testing program improved rates of linkage to care and viral suppression.

Methods

Ethics

The trial protocol was approved by the ethical board in Switzerland and the National Health Research and Ethics Committee of the Ministry of Health of Lesotho (Supplement 1). During home-based HIV testing for recruitment, 3 levels of written consent were obtained: consent from the head of the household for the study team to enter the household, consent from the household member to be tested, and consent from the eligible household member to participate in the trial. Illiterate participants provided their thumb-print, and a witness (independent of the trial and >21 years), chosen by the participant, cosigned the form. During the consent process, individuals were informed that this study assesses different ways of initiating ART, either at home or at the clinic. The trial participation information emphasized that participants in each group had the option of starting or not starting ART.

Trial Design

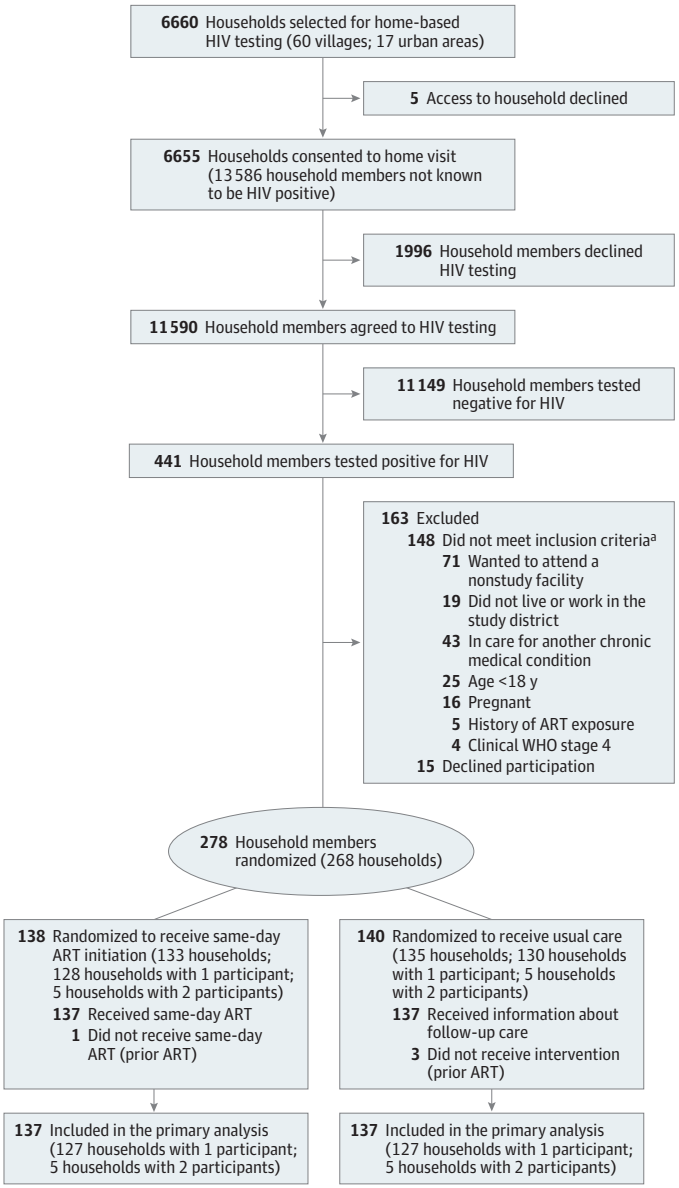
The study protocol has been published[13] and the full protocol is available in Supplement 1. This multicenter, 2-group, open-label, randomized clinical trial recruited participants who tested positive during home-based HIV testing and were randomly assigned (1:1 allocation) into same-day or usual care treatment groups. Participants randomized to the same-day group were offered home-based ART initiation the same day. Specifically, they were given a 1-month drug-supply and instructed to visit their health facility within 2 to 4 weeks for their first check-up and drug-refill. Subsequent visits to the health facility were scheduled at intervals of 1.5, 3, 6, 9, and 12 months after ART initiation. Usual care in Lesotho at the time involved monthly clinic visits, during which patients underwent a minimum of 2 pre-ART counseling sessions at the health facility with a subsequent offer to start ART, followed by monthly visits after ART initiation. In both groups, the quantity of the drug supply that a participant received during the clinic visit depended on the scheduled next visit (ie, 1 box if the next visit was scheduled in a month, 3 boxes if in 3 months).

Participants, Setting, and Recruitment

Consenting adults (≥18 years) found to be HIV positive and ART naive were eligible (**Figure 1**). Exclusion criteria were history of previous combination ART exposure, pregnancy, breastfeeding, clinical WHO stage 4,[14] already being treated for any chronic condition (ie, tuberculosis or diabetes), a positive cryptococcal antigen test, no domicile or employment in the region where the trial was conducted, or the wish to seek care at a health facility other than the 6 health facilities participating in the study. Participants were enrolled before they were asked about their readiness for same-day ART initiation. Readiness to start ART was not an eligibility criterion.

The trial was conducted in the Butha-Buthe district in rural northern Lesotho. Six facilities in the district, 4 public nurse-led health centers plus the public hospital and the missionary hospital participated in the trial. During the recruitment period, 3 teams, each consisting of a study nurse, a team-leader, and 4 lay counselors, visited randomly selected villages or urban neighborhoods in Butha-Butha town. Once there, teams visited each household and proposed HIV testing to all household members. Testing for HIV followed the

Figure 1. Patient Flow Through the CASCADE Trial



ART indicates antiretroviral therapy; WHO, World Health Organization.

[a] Participants could have had more than 1 reason for exclusion.

national testing algorithm, using 2 different third-generation serology point-of-care tests in a serial algorithm recommended by WHO.[15,16]

Randomization

For each rural health facility, equal numbers of villages in the catchment area were randomly selected from a list of all eligible villages (1 village consisted of 40-80 households). For the health facility in an urban setting, neighborhoods in the catchment area were randomly selected for inclusion.

A computer-generated randomization list was generated in block sizes of 4. A separate person, not involved in the trial, prepared the sealed, sequentially numbered, opaque envelopes. The study nurse allocated participants to a group by opening the next sealed envelope in the sequence. Households with more than 1 eligible individual were automatically allocated to the same group to reduce contamination between the groups.

Interventions

Participants randomized to the usual care group followed the usual care provided in Lesotho, which is similar to most settings in southern Africa. They received posttest counseling in the home and an appointment at their nearest health facility within the next 28 days. Once linked to care, they had to undergo at least 2 pre-ART health facility visits. During the first health facility visit, blood was drawn for baseline laboratory work and a first pre-ART counseling session was conducted. At the second health facility visit, laboratory results were communicated and the patient's readiness to

start ART was assessed. Depending on the judgment of the health facility staff, the participant was offered to start ART. Once ART was started, the participants were given monthly follow-up and drug refill dates.

In the same-day group, participants were offered same-day ART initiation. Participants received pre-ART counseling directly after testing, accompanied by a leaflet that summarized the key points of ART adherence. If they agreed to start therapy within the upcoming days, the study nurse left a 30-day supply of ART. Once participants linked to care at the health facility and had their first health facility visit (including ART dispensing), they followed the usual care for ART patients with the exception of longer intervals between follow-up visits (1.5, 3, 6, 9, and 12 months after ART start).

In both groups blood was drawn for point-of-care laboratory assessment including CD4 cell counts (PIMA, Alere), creatinine levels (StatSensor Creat, Nova Biomedical), and hemoglobin (Hemocue, HB301). Results from baseline tests were only disclosed to patients in the same-day group because patients in the usual care group had to attend the clinic to do a baseline laboratory work-up. In both groups, medical care at the health facility was provided by facility-employed ART nurses and followed national and WHO guidelines.[15,16] Study personnel were involved in recruitment and data collection but not in clinical management.

Outcomes

The trial had 2 coprimary end points, 3-month linkage to care and 12-month viral suppression. The rationale for choosing these 2 primary end points was that to be considered beneficial, same-day ART initiation should lead not only to the short-term effect of higher linkage to care but also to a higher proportion in care and achievement of viral suppression. For the first primary end point, 3-month linkage to care, a participant was considered to have linked to care if he/she attended the health facility at least once within 90 days after having been found HIV positive during the home-based visit. For the second primary end point, viral suppression at 12 months was defined as viral load of less than 100 copies/mL from 11 through 14 months after enrollment. Those who did not attend the health facility or had no blood drawn during this interval were considered not to have achieved viral suppression.

Prespecified secondary outcomes were viral suppression at 6 months (range, 5-7 months) after enrollment, 12-month to follow-up, and 12-month mortality (died <1 year after enrollment). Patients who did not attend the clinic in the 11 through 14 months after enrollment and could not be reached by telephone or by the village health worker were defined as lost to follow-up. A participant was categorized as dead if there was a death certificate or if the village chief or a close family member confirmed the death of the participant to the lay counselor. Additional prespecified secondary end points assessed among patients who remained in care at the 12-month follow-up were changes in CD4 cell count, hemoglobin level, body weight, and occurrence of a new clinical WHO stage 3 or 4 event. However, due to a long-lasting national shortage of reagents for CD4 cell count, only 14 participants had full documentation of CD4 cell counts. As a result, this secondary end point is not reported.

We further conducted a post hoc analysis of 1-year retention in care that was defined as either the patient or his/her treatment buddy going to the health facility to get a drug-refill during the 11 through 14 months after enrollment. It is part of usual care in Lesotho for patients to send a friend or a relative to pick-up their drugs if they cannot attend personally. Participants who died or were lost from care, or were transferred to another health facility were considered as not retained in care. Because ascertainment of transfer is not always possible in this setting, patients not attending the health facility and thereafter self-reporting transfer to another clinic were conservatively considered as not retained.

Additional post hoc outcomes included rates of ART initiation at 3 months, viral suppression at 12 months among participants with a documented viral load result during the 11 through 14 months after enrollment, and median time between visits and number of visits attended according to the study protocol (monthly for usual care and 1.5, 3, 6, 9, and 12 months for same-day). If a participant attended a visit within 7 days of their expected visit schedule (ie, monthly for usual care and 1.5, 3, 6, and 9 for same-day), he/she was considered to have attended the visit according to protocol.

Participants who did not link to care within 3 months and participants who were not retained in care at 12 months were contacted by a lay counselor to ascertain their outcome. If a participant could not be reached by telephone, the lay counselor asked a village health worker to visit the participant's home.

Data Collection, Processing, and Monitoring

At enrollment, the study nurses collected baseline sociodemographic variables using a short structured questionnaire. Follow-up data were collected by study nurses who visited the 6 participating health facilities every second month. Data closure was September 17, 2017 (14 months after last participant enrolled). Data were recorded on paper-based case reporting forms that were scanned in Lesotho and subsequently processed with Data-Scan 5.7.7 (Neoptec) for electronic data capture. To optimize data quality, all handwritten digits were counterchecked by a data clerk. The trial underwent independent external monitoring, including 3 study site visits from an independent trial monitor and a distance monitoring review, to independently check completeness and accuracy of scanned informed consent and case-reporting forms and consistency between paper-based and digitalized data.

Sample Size

Based on routinely collected data from home-based testing campaigns regularly conducted in Lesotho, 3-month linkage to care rates of 40% in the usual care group were expected. Based on available data on clinic-based same-day ART initiation[17] and older studies using other methods to facilitate linkage,[4] we assumed that same-day ART initiation would achieve a 20% higher linkage rate than usual care. A total of 260 households with at least 1 participant who was HIV positive were required to detect a 20% increase in linkage to care

assuming a type I error rate of 5% and a power of 90%. Because those not linking to care were considered not to have achieved viral suppression, we expected viral suppression rates of 25% in the usual care group and 45% in the same-day group. With 130 individuals per group, there was a 93% power to detect a difference of 20% in viral suppression rates.

Statistical Analysis

Patients were analyzed according to their randomization group following an intention-to-treat protocol (Figure 1). No patient withdrew consent during the trial. The proportion linked to care, virally suppressed, retention in care, rates of ART initiation, lost to follow-up, and mortality were compared using χ^2 tests with absolute differences; 95% CIs were estimated using the Newcombe-Wilson score method.[18] The planned mixed-effects analysis to adjust for clustering at the household level did not produce stable results due to an insufficient number of households (n = 10) with more than 1 eligible individual. Differences in medians of body weight and hemoglobin levels were compared using the Wilcoxon rank sum test. Formal comparison of differences in new WHO clinical stage 3 or 4 events and mortality were not possible due to low number of events. Retention in care was also analyzed using Kaplan-Meier survival curves and compared using the log-rank test. The proportional hazards assumption was checked with tests based on Schoenfeld residuals. Individuals who had not visited during the 11- through 14-month window were censored at the time of their last health facility visit. The median time between visits was compared using the Wilcoxon rank sum test of medians.

Three sensitivity analyses were performed: assessment of linkage to care among all those linked during the study period regardless of timing; analyses accounting for potential clustering effects at the household, village, and facility levels for primary outcomes (the χ^2 test statistic and the *P* value from the likelihood ratio test of the correlation from the random effect is presented); and post hoc sensitivity analysis of retention in care considering those who did not visit during the 11- through 14-month window but did visit after 14 months to be retained in care. All analyses were performed using Stata (StataCorp) software version 14. All tests were 2-sided with a significance level set at .05.

Patients with missing data for the primary end point, viral suppression, were considered as having unsuppressed viral load. For other outcomes (weight and hemoglobin level), missing data were not imputed because the missing data mechanism was considered to be not at random and therefore not ignorable. Analyses of the secondary outcomes were not adjusted for multiple comparisons, so the interpretation should be considered exploratory.

Results

From February 22 to July 17, 2016, study team members visited 6655 households in 60 rural villages and 17 urban areas in Butha-Buthe. A total of 441 individuals from 420 households tested HIV positive and were screened for eligibility. Of these, 278 participants from 268 households fulfilled inclusion criteria and were randomized (Figure 1). After randomization, 4 of 278 participants (1.4%) found to be ART experienced after randomization were excluded from the study. A total of 137 patients from 132 households were analyzed in the usual care group and 137 from 132 households in the same-day group. Five households in each group had 2 participants.

Baseline characteristics were well balanced (**Table 1**). Participants were a median age of 39 years (interquartile range [IQR], 28.0-52.0 years). The majority were women (65.7%), married or living with a partner (65.1%), without regular income (77%), presenting with a clinical WHO stage 1 (78.1%), and had a CD4 cell count of 350 cells/μL or higher (55.6%). One hundred thirty-six participants (99.3%) in the same-day group indicated that they understood the implications of starting lifelong ART, and 134 (97.8%) were ready to start treatment that day and 2 (1.5%) within the next few days. A 1-month supply of ART was given to each of these 136 participants.

Primary End Points

Linkage to Care

Linkage to care within 90 days after enrollment was 68.6% (94 of 137) in the same-day group vs 43.1% (59 of 137) in the usual care group (absolute difference, 25.6%; 95% CI, 13.8%-36.3%; *P* < .001; **Table 2**). Patient-reported reasons for not linking to care are listed in **Table 3**.

Viral Suppression

Overall, 42.3% (116 of 274) participants achieved documented viral suppression (<100 copies/mL) from 11 through 14 months after enrollment: 50.4% (69 of 137) in the same-day group vs 34.3% (47 of 137) in the usual care group (absolute difference, 16.0%; 95% CI, 4.4%-27.2%; *P* < .007; Table 2). In each group, 10.2% (14 of 137) had no documented viral load result despite having attended the health facility within the predefined 11- through 14-month window (22, no blood drawn; 6, technical error at the laboratory). The remaining did not attend the health facility within that time frame (Table 2).

Secondary End Points

Overall, 31.8% (87 of 274) participants had documented viral suppression (<100 copies/mL) 6 months after enrollment, 37.2% (51 of 137) in same-day group vs 26.3% (36 of 137) in the usual care group (absolute difference, 11.0%; 95% CI, −0.1% to 21.6%, *P* = .05). Loss to follow-up at 12 months was 8.8% (12 of 137) in the same-day group vs 7.3% (10 of 137) in the usual care group (absolute difference, 1.5%, 95% CI, −5.2% to 8.2%; *P*=.66). At 12 months, there were 2 deaths in the same-day group and none in the usual care group.

There were no significant differences in changes in hemoglobin levels and body weight among patients who were retained in care at 12 months between groups (Table 2).

Two cases of pulmonary tuberculosis were diagnosed during follow-up; both occurred in the usual care group. Otherwise, there were no reported new clinical WHO stage 3 or 4 events in either group. Supplement 2 provides information on reported deaths and on adverse events in participants who had initiated ART.

Table 1. Baseline Characteristics of Participants

	No. (%) of Participants	
	Same-Day ART (n=137)	Usual Care (n=137)
Age, median (IQR), y	41.0 (31.0-53.0)	38.0 (28.0-50.0)
Women	90 (65.7)	90 (65.7)
Marital status[a]		
Single	16 (11.7)	19 (14.1)
Married/lives with partner	86 (62.8)	91 (67.4)
Widowed	35 (25.5)	25 (18.5)
No. of children, median (IQR)	1.0 (0.0-3.0)	2.0 (0.0-3.0)
Completed years of school, y		
<6	71 (51.8)	61 (44.5)
6-9	57 (41.6)	63 (46.0)
>9	9 (6.6)	13 (9.5)
Employment		
In Lesotho with regular income	21 (15.3)	33 (24.1)
Outside Lesotho	4 (2.9)	5 (3.6)
No regular income	112 (81.8)	99 (72.3)
Newly diagnosed HIV	105 (76.6)	98 (71.5)
HIV status of partner		
No partner	51 (37.2)	48 (35.0)
Positive, taking ART	13 (9.5)	17 (12.4)
Positive, not taking ART	2 (1.5)	11 (8.0)
Positive, ART status unknown	0	3 (2.2)
Negative, recently tested	17 (12.4)	15 (10.9)
Partner with unknown status	54 (39.4)	43 (31.4)
Plan to disclose to someone[b]		
Yes	120 (88.2)	115 (87.8)
No, not for the moment	11 (8.1)	8 (6.1)
I don't know yet	5 (3.7)	8 (6.1)
Travel method to health facility		
Horse or donkey	2 (1.5)	1 (0.7)
Taxi or own car	65 (47.4)	71 (51.8)
Walk	70 (51.1)	65 (47.4)
Travel time to health facility, median (IQR), min[c]	60.0 (30.0-90.0)	60.0 (30.0-60.0)
Last visit to a health facility[d]		
<4 weeks	17 (12.4)	17 (12.4)
1-12 mo	50 (36.5)	68 (49.6)
≥1 y	70 (51.1)	52 (38.0)
WHO stage, No. (%)[e]		
1 (asymptomatic)	102 (75.0)	109 (81.3)
2 (oligosymptomatic)	27 (19.9)	21 (15.7)
3 (advanced)	7 (5.1)	4 (3.0)
BMI, median (IQR)[f]	22.5 (20.2-27.5)	23.4 (21.2-26.6)
<18.5	14 (10.3)	6 (4.4)
18.5-30	103 (75.7)	111 (82.2)
>30	19 (14.0)	18 (13.3)
CD4 cell count[g]		
Median (IQR), cells/μL	346.0 (243.5-497.0)	417.5 (255.0-558.0)
CD cell count levels, cells/μL		
<200	22 (16.2)	22 (16.4)
200-349	46 (33.8)	30 (22.4)
≥350	68 (50.0)	82 (61.2)

Abbreviations: ART, antiretroviral therapy; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared, IQR, interquartile range; WHO, World Health Organization.

[a] Marital status is missing for 2 participants in the usual care group.

[b] Responses from 7 participants were missing.

[c] Participants' estimation of travel time using 15-minute intervals.

[d] Self-reported.

[e] No participant was staged with clinical WHO stage 4; detailed definition of clinical stages may be found in the WHO guidelines 2013[14] as reported by participant. Responses from 4 participants were missing.

[f] Data from 3 participants were missing.

[g] Data from 4 participants were missing.

Table 2. Primary and Secondary End Points of the Trial and Post Hoc Analyses

	No. (%) of Participants			
	Same-Day ART (n = 137)	Usual Care (n = 137)	Absolute Difference, % (95% CI)	*P* Value
Primary Outcomes				
Linkage to care at 90 d after enrollment	94 (68.6)	59 (43.1)	25.6 (13.8 to 36.3)	<.001
Viral load <100 copies/mL, 11-14 mo after enrollment[a]	69 (50.4)	47 (34.3)	16.0 (4.4 to 27.2)	.007
Secondary Outcomes and Post Hoc Analyses				
Viral load <100 copies/mL 6 mo after enrollment	51 (37.2)	36 (26.3)	11.0 (−0.1 to 21.6)	.05
12-Month outcomes				
Lost to follow-up	12 (8.8)	10 (7.3)	1.5 (−5.2 to 8.2)	.66
Died[b]	2 (1.5)	0		
Physiological changes, median (IQR)				
Body weight, kg (n = 90)[c]	−1 (−5 to 1.5)	−1.5 (−5 to 2)		.84
Hemoglobin, g/dL (n = 78)[c]	1.4 (0.4 to 2.3)	0.8 (−0.2 to 2.1)		.14
New WHO stage 3 or 4 event (n = 156)[b,d]	0	2 (2.9)		
Attended care				
11-14 mo after enrollment	87 (63.5)	66 (48.2)	15.3 (3.6 to 26.5)	.01
At any point >11 mo after enrollment	88 (64.2)	68 (49.6)	14.6 (2.9 to 25.8)	.02

Abbreviations: ART, antiretroviral therapy; IQR, interquartile range; WHO, World Health Organization.

[a] In each group, 10.2% (14/137) had no documented viral load result despite having attended the health facility within the predefined 11- through 14-month window (22 no blood drawn, 6 technical error at laboratory).

[b] Formal comparisons are not warranted due to small numbers.

[c] Includes only participants retained in care with reported data 11-14 mo after enrollment.

[d] Includes only participants attending ART follow-up at the health facility. A detailed definition of clinical stages may be found in the WHO guidelines 2013.[14]

Table 3. Main Reported Reasons for Not Linking to Care Within 3 Months After Enrollment

	No. (%) of Participants		
Main Reported Reason	Same-Day ART (n = 43)	Usual Care (n = 78)	Total (n = 121)
Too busy to attend care	13 (30.2)	21 (26.9)	34 (28.1)
Refused to attend care	6 (13.9)	11 (13.1)	17 (14.1)
Transfer out (self-reported)	4 (9.3)	9 (11.5)	13 (10.7)
Did not understand that he/she should attend care	4 (9.3)	8 (10.3)	12 (9.9)
No money for transport	2 (4.7)	5 (6.4)	7 (5.8)
Died	2 (4.7)	0	2 (1.7)
Lost to follow-up[a]	11 (25.6)	24 (30.8)	35 (28.9)

[a] Patients who could not be reached by the lay counselor or found at home by the village health worker.

Sensitivity Analysis

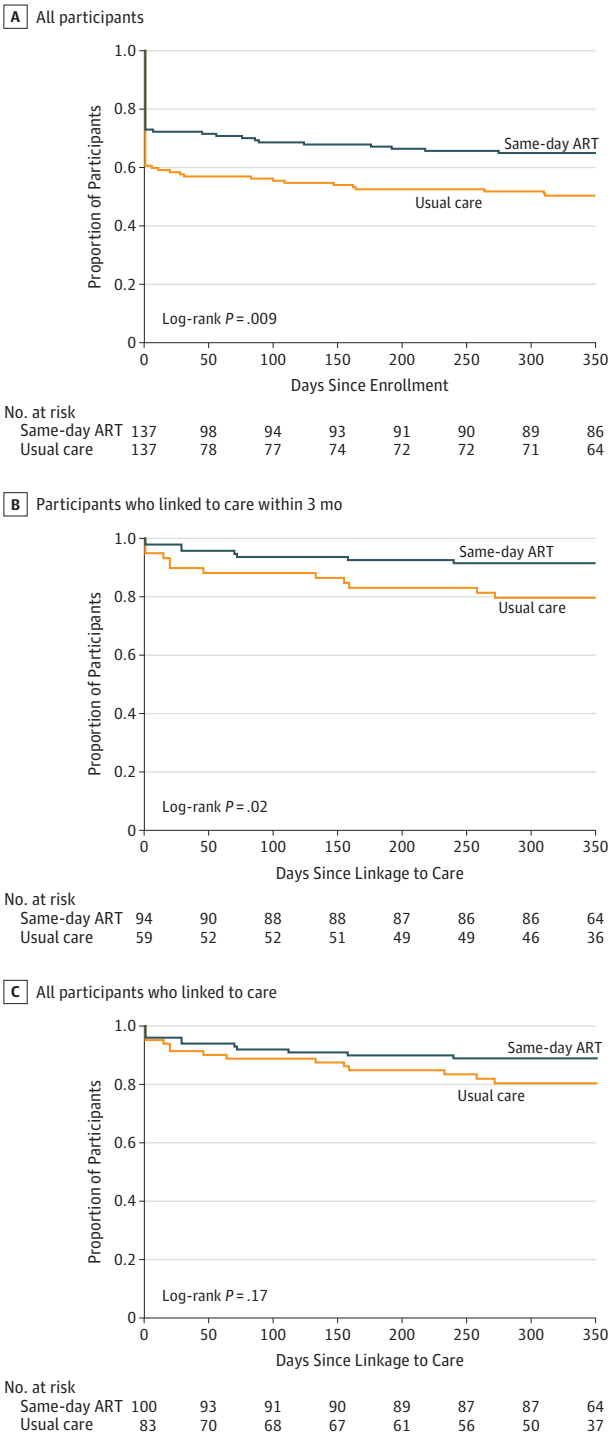
An additional 30 patients (6, same-day; 24, usual care) linked to care after the 90-day end point definition. Allowing for linkage after 90 days, linkage rates were still higher in the same-day group (same-day group, 100 of 137 vs usual care group, 83 of 137, absolute difference, 12.4%; 95% CI, 1.3%-23.2%; $P = .03$).

Ten households included 2 participants in the study, 5 in the same-day group and 5 in the usual care group. Within all 10 households, the outcomes among the 2 participants were the same. Given the small number of households with more than 1 participant, adjusting for clustering at the household level did not produce stable results. In sensitivity analyses, 1 of the 2 participants were excluded, which did not affect the results or conclusions (linkage to care at 3 months: absolute difference, 24.8%; 95% CI, 13.1%-35.6%; $P < .001$); viral suppression: absolute difference, 15.3%; 95% CI, 3.7%-26.4%; $P < .009$). Mixed-effects logistic regression models of the primary end points with the respective study group included as a fixed effect and village or health facility as a random effect did not find a significant clustering effect (the *P* values from the likelihood ratio test of the correlation from the random effect were for linkage to care at 3 months: village, $P > .99$; facility, $P = .30$; for viral suppression: village, $P > .99$; facility, $P = .50$).

Post Hoc Analysis

Eighty-seven of 137 participants (63.5%) in the same-day vs 66 of 137 participants (48.2%) in the usual care group remained in care at 1 year (absolute difference, 15.3%; 95% CI, 3.6-26.5; $P = .01$). **Figure 2** shows Kaplan-Meier estimates for retention in care. Retention in care since enrollment was significantly higher in the same-day group ($P=.009$, based on the log-rank tests; corresponding $\chi^2 = 6.84$); Figure 2A, proportionality hazard assumption met; $P = .48$). eTable 1 displays tracing information from the 118 participants not active in care for more than 11 months after enrollment (Supplement 2). Overall, the most frequent reported reasons for not remaining in care included being treated at another facility (29.4%), refusing to attend (24.4%), and having no time to attend (19.3%; eTable 1 in Supplement 2). Neither the lay

Figure 2. Kaplan-Meier Curves for Retention in Care



The curves were compared using log-rank tests. A, Kaplan-Meier estimates for all participants enrolled (n = 274); the median follow-up days for the same-day group was 370 (IQR, 1-393) and for the usual care group, 338 (IQR, 1-381). B, From the day of linkage to the facility. It includes participants who linked to care within 3 months (n = 153); the median follow-up days for the same-day group was 365 (IQR, 344-390) and for the usual care group, 357 (IQR, 327-382). C, Those who linked to care after 3 months (n = 183); median follow-up days for the same-day group was 364 (IQR, 337-385.5) and for the usual care group, 344 (IQR, 170-367).

counselor nor the village health worker could contact 19.3% of participants, who as a result were considered lost to follow-up. Retention in care was significantly higher in the same-day group among the 153 individuals who had linked within 3 months (P = .02; χ^2 = 6.22; Figure 2B); however, there was no significant difference in retention in care when considering the 183 individuals who ever linked to care during the entire study period, including 30 participants who linked after 3 months (P = .17; χ^2=1.9; Figure 2C).

ART initiation (in addition to linkage to care) occurred for 94 of 137 participants (68.6%) in the same-day group and 44 of 137 (32.1%) in the usual care group 3 months after enrollment for an absolute difference of 36.5% (95% CI, 24.9%-46.7%; P < .001). Information on ART usage was available from 21 of the 43 participants (48.8%) in the same-day group who did not link within 3 months, and 81% of these reported having started ART. Among those with a documented viral load result in the 11- through 14-month window after enrollment, viral suppression was not significantly different: 69 of 73 participants (94.5%) in same-day group vs 47 of 52 (90.4%) in the usual care group, for an absolute difference of 4.1% (95% CI, −5.4% to 15.6%; P = .38).

The median time span between all health facility visits was 59 days (IQR, 52-70 days) in the same-day group and 40 days (IQR, 32-58 days) in the usual care group (P < .001). The number of visits attended according to the study protocol was 17.0% in the same-day group and 17.7% in the usual care group (P = .91), although 73% of participants in the same-day group had more visits and 77% of participants in the usual care group had fewer visits than expected (P < .001).

Discussion

This trial found that participants who were HIV positive and ART naive during home-based HIV testing and were randomized to same-day home-based ART initiation were more likely to link to the health facility for follow-up at 3 months and to be active in care with a suppressed viral load 12 months after enrollment than were patients who were referred according to the standard health facility referral practice. Two previous clinical trials showed that same-day ART initiation improved retention in care and viral suppression among persons who tested HIV positive at the clinic.[9,10] To our knowledge, this trial is the first to assess same-day ART initiation as a strategy for patients tested at home. Moreover, it is the first trial testing same-day ART initiation for all individuals found HIV infected, irrespective of CD4 cell count.

Without specific interventions, less than a third of those who test HIV positive during home-based HIV testing link to care.[4,5,19] The few studies from sub-Saharan Africa having achieved linkage rates after home-based testing of more than 50% were those that used facilitated linkage strategies, ie, counselors revisiting persons who tested HIV positive at home, transport vouchers, telephone messaging, or tracing of persons who did not link.[20-25] Recently, the SEARCH (Sustainable East African Research in Community Health)[26] project conducted in Uganda and Kenya, reported

observational data with high linkage and viral suppression rates for individuals testing HIV positive at their home, using facilitated linkage and streamlined ART delivery at facilities in a test-and-treat setting. Whereas these studies indicate that facilitated linkage, streamlined ART delivery and repeated support through counselors are effective, many of these interventions require additional resources. There is a possibility that such models work as pilot projects with external support but are not sustainable as part of routine care in resource-limited settings. In contrast, it is possible that the option of same-day ART initiation can be integrated into HIV testing campaigns with fewer resources than required by facilitated linkage. Because the nurse is already in the village when testing takes place, he/she is in a position to assess individuals who tested positive during home-based HIV testing and leave a box with antiretroviral drugs to begin treatment in the household.

In both groups of our study, participants who linked to care and continued treatment achieved rates of viral suppression of more than 90%. Other studies assessing viral suppression among individuals recruited during community-based HIV testing also found high rates of viral suppression among those who were taking ART.[23,24,26] Similarly, recent population-based studies conducted in South-Eastern Africa show that if patients continue ART, rates of viral suppression are close to 90%.[27] These data suggest that to achieve UNAIDS 90-90-90 targets in remote areas, the main emphasis should be placed on HIV testing and subsequent linkage to care.

Limitations

This study has several limitations. First, the generalizability could be an issue. The study was conducted in 6 facilities of 1 district in Lesotho, a typical rural high-prevalence setting and solely enrolled individuals consenting to home-based HIV testing. The consent rates in this setting have, however, been shown to be high.[12] Second, no information about the outcomes of patients who transferred to another health facility during the trial is available. To be conservative, they were considered not retained in care. Third, we have no information about whether participants in the same-day group who started ART at home and subsequently did not link to care developed therapy resistance as a result of an unstructured treatment interruption. Fourth, there were no corrections for multiple comparisons, and the results of the secondary outcomes should be considered exploratory.

Conclusions

Among adults in rural Lesotho, a setting of high HIV prevalence, offering same-day home-based ART initiation to individuals who tested positive during home-based HIV testing, compared with usual care and standard clinic referral, significantly increased linkage to care at 3 months and HIV viral suppression at 12 months. These findings support the practice of offering same-day ART initiation during home-based HIV testing.

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Concept and design: Labhardt, Ringera, Lejone, Glass.
Acquisition, analysis, or interpretation of data: Labhardt, Ringera, Lejone, Klimkait, Amstutz, Glass.
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