JAMA | Original Investigation

Association of Implementation of a Universal Testing and Treatment Intervention With HIV Diagnosis, Receipt of Antiretroviral Therapy, and Viral Suppression in East Africa

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IMPORTANCE Antiretroviral treatment (ART) is now recommended for all HIV-positive persons. UNAIDS has set global targets to diagnose 90% of HIV-positive individuals, treat 90% of diagnosed individuals with ART, and suppress viral replication among 90% of treated individuals, for a population-level target of 73% of all HIV-positive persons with HIV viral suppression.

OBJECTIVE To describe changes in the proportions of HIV-positive individuals with HIV viral suppression, HIV-positive individuals who had received a diagnosis, diagnosed individuals treated with ART, and treated individuals with HIV viral suppression, following implementation of a community-based testing and treatment program in rural East Africa.

DESIGN, SETTING, AND PARTICIPANTS Observational analysis based on interim data from 16 rural Kenyan (n = 6) and Ugandan (n = 10) intervention communities in the SEARCH Study, an ongoing cluster randomized trial. Community residents who were 15 years or older (N = 77 774) were followed up for 2 years (2013-2014 to 2015-2016). HIV serostatus and plasma HIV RNA level were measured annually at multidisease health campaigns followed by home-based testing for nonattendees. All HIV-positive individuals were offered ART using a streamlined delivery model designed to reduce structural barriers, improve patient-clinician relationships, and enhance patient knowledge and attitudes about HIV.

MAIN OUTCOMES AND MEASURES Primary outcome was viral suppression (plasma HIV RNA<500 copies/mL) among all HIV-positive individuals, assessed at baseline and after 1 and 2 years. Secondary outcomes included HIV diagnosis, ART among previously diagnosed individuals, and viral suppression among those who had initiated ART.

RESULTS Among 77 774 residents (male, 45.3%; age 15-24 years, 35.1%), baseline HIV prevalence was 10.3% (7108 of 69 283 residents). The proportion of HIV-positive individuals with HIV viral suppression at baseline was 44.7% (95% CI, 43.5%-45.9%; 3464 of 7745 residents) and after 2 years of intervention was 80.2% (95% CI, 79.1%-81.2%; 5666 of 7068 residents), an increase of 35.5 percentage points (95% CI, 34.4-36.6). After 2 years, 95.9% of HIV-positive individuals had been previously diagnosed (95% CI, 95.3%-96.5%; 6780 of 7068 residents); 93.4% of those previously diagnosed had received ART (95% CI, 92.8%-94.0%; 6334 of 6780 residents); and 89.5% of those treated had achieved HIV viral suppression (95% CI, 88.6%-90.3%; 5666 of 6334 residents).

CONCLUSIONS AND RELEVANCE Among individuals with HIV in rural Kenya and Uganda, implementation of community-based testing and treatment was associated with an increased proportion of HIV-positive adults who achieved viral suppression, along with increased HIV diagnosis and initiation of antiretroviral therapy. In these communities, the UNAIDS population-level viral suppression target was exceeded within 2 years after program implementation.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01864683

JAMA. 2017;317(21):2196-2206. doi:10.1001/jama.2017.5705

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Supplemental content

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Early antiretroviral therapy (ART) improves the health of individuals with human immunodeficiency virus (HIV) and reduces HIV transmission.[1-3] Mathematical models and observational analyses suggest that an intensive global investment to expand ART coverage could alter the epidemic trajectory and improve longevity, health, and economic productivity.[4-7] However, realizing this potential requires diagnosing HIV, initiating ART, and suppressing viral replication in most HIV-positive persons, a progression referred to as the HIV care cascade.

The global health community has responded with a mandate for action. In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) issued an ambitious worldwide target: by 2020, at least 90% of HIV-positive individuals will be diagnosed, at least 90% of those diagnosed will be receiving ART, and at least 90% of those receiving ART will have suppressed viral replication (known as the 90-90-90 target), for an overall target of 73% of all HIV-positive individuals with HIV viral suppression.[8] In 2015, the World Health Organization (WHO) recommended that all HIV-positive individuals initiate ART, irrespective of CD4 lymphocyte count.[9]

Apart from Botswana,[10] most nations in sub-Saharan Africa remain substantially below the UNAIDS target.[8,11-13] Furthermore, many nonsuppressed HIV-positive individuals are asymptomatic with high CD4 cell counts.[13] Such individuals may prove challenging to test, engage in care, and virally suppress.[14,15] Scalable strategies to effectively diagnose, treat, and achieve viral suppression among HIV-positive individuals in sub-Saharan Africa are needed.

The Sustainable East Africa Research in Community Health Study (SEARCH) is an ongoing cluster randomized trial in rural Kenya and Uganda evaluating the effect of a cascadewide test-and-treat strategy vs country-specific standard of care on HIV, health, and economic outcomes. The trial intervention integrates community-based multidisease testing, universal eligibility for ART for all HIV-positive individuals, and streamlined patient-centered ART delivery. In this descriptive study, interim data from the trial intervention communities were used to evaluate population-level HIV viral suppression and the HIV care cascade at study baseline and after 1 and 2 years of delivering the test-and-treat intervention.

Key Points

Question Was implementation of a human immunodeficiency virus (HIV) test-and-treat intervention in rural East Africa associated with increases in diagnosis, treatment, and viral suppression among individuals with HIV infection?

Findings In this study that included 77 774 residents of the intervention communities of an ongoing cluster randomized trial, the proportion of HIV-positive individuals with HIV viral suppression increased from 44.7% at baseline to 80.2% after 2 years, along with increases in HIV diagnosis and initiation of antiretroviral therapy.

Meaning Implementation of a community-based testing and treatment intervention in East Africa was associated with increased proportion of HIV-positive individuals who achieved viral suppression, along with increased HIV diagnosis and initiation of antiretroviral therapy.

Methods

Study Population

The SEARCH Study is a cluster randomized trial that enrolled 32 pair-matched rural communities, each with approximately 5000 residents. Between June 2013 and June 2014, all residents in each community were enrolled during a household census.[16] The study included data from residents (aged ≥15 years) of 10 Ugandan and 6 Kenyan intervention communities, each followed up for 2 years (until June 2015 to June 2016). The trial protocol is available in Supplement 1.

All participants provided verbal informed consent in their preferred language. The Makerere University School of Medicine Research and Ethics Committee (Uganda), the Ugandan National Council on Science and Technology (Uganda), the Kenya Medical Research Institute Ethical Review Committee (Kenya), and the University of California, San Francisco, Committee on Human Research (United States) approved the consent procedures and the study.

Intervention

Population-based HIV testing was conducted at baseline and annually thereafter using a hybrid model that combined multidisease community health campaigns (including diabetes and hypertension screening) with home-based testing for residents who did not attend the campaign.[16] All HIV-positive individuals were eligible for ART with efavirenz plus tenofovir disoproxil fumarate, co-formulated either with emtricitabine or with lamivudine, and were offered facilitated linkage to care consisting of (1) immediate appointments at government clinics, (2) personal introductions to clinic staff, (3) a clinician phone number, (4) a 1-time transport voucher, and (5) tracking of individuals who did not link to care.[17] Streamlined ART delivery included (1) a 3-month follow-up schedule for clinically stable patients, (2) flexible hours and a welcoming environment, (3) a clinician phone number, (4) text or telephone-based appointment reminders, and (5) HIV RNA measures, with structured discussion of results with patients to support visit and medication adherence.[18]

Measures

Demographic data were collected at the baseline census. Stable residence was defined as living in the community 6 or more months in the past year and nonstable residence was defined as living in the community less than 6 months in the past year. At baseline and after 1 and 2 years, HIV serostatus was measured at community health campaigns; adults who did not attend were subsequently tracked and offered home-based testing.[16] After baseline, individuals newly identified as community residents were classified as migrants into the community. Prior residents who were reported to no longer live in the community were classified as migrants out of the community.

Participants with a positive antibody test result, detectable HIV RNA, or a Ministry of Health record of prior HIV care

were considered HIV positive. Plasma HIV RNA was measured on all HIV-positive individuals annually during hybrid mobile testing (at the health campaign or subsequent tracking).[19] Viral suppression at baseline and after 1 and 2 years was defined as an HIV RNA measurement of less than 500 copies/mL, measured during that year's hybrid mobile testing. Prior diagnosis was defined as a prior positive HIV test or Ministry of Health record of HIV care; baseline self-reported diagnosis was included in sensitivity analysis. ART use was assessed with Ministry of Health records; HIV-positive individuals with suppressed HIV RNA were considered to have received ART.

Statistical Analyses

Power calculations and sample size were calculated for the primary randomized trial; this descriptive study was nested within the larger trial. The analysis was prespecified (Supplement 2).[20] The primary outcome was population-level viral suppression (plasma HIV RNA<500 copies/mL) among all HIV-positive residents. Secondary outcomes were HIV diagnosis, ART use among those diagnosed with HIV, and HIV viral suppression among those treated with ART. Primary and secondary outcomes were evaluated in an open cohort of HIV-positive community residents at 3 time points corresponding to the dates of annual community-wide testing at baseline and after 1 and 2 years of follow-up. Individuals entered the cohort at the first time point they were HIV infected, 15 years or older, and community residents. Individuals left the cohort when they died or migrated out of the community.

In this open cohort, we estimated the following proportions: (1) number of HIV-positive individuals with HIV viral suppression among all HIV-positive individuals (population-level suppression), (2) the number of individuals diagnosed with HIV prior to time of annual testing among all HIV-positive individuals, (3) number of individuals who had initiated ART prior to the time of annual testing among individuals diagnosed with HIV prior to time of annual testing, and (4) the number of individuals with HIV viral suppression among individuals who had initiated ART prior to the time of annual testing. Primary analysis was restricted to baseline stable residents (ie, those living in the community 6 months or more during the past year). Secondary analyses (1) stratified on sex, age, and country; and (2) included nonstable baseline residents (ie, those living in the community less than 6 months during the past year) and migrants into the community identified during postbaseline annual testing.

Because diagnosis, ART coverage, and HIV viral suppression in the open cohort of HIV-positive individuals depend not only on effective testing, treatment, and suppression but also on HIV incidence, population migration, and mortality, we also conducted longitudinal closed-cohort analyses. First, we estimated the proportion of stable residents diagnosed with HIV at or before study baseline who, after 1 and 2 years, had (1) never initiated ART, (2) initiated ART and had a plasma HIV RNA measurement of 500 copies/mL or more, (3) initiated ART and had a plasma HIV RNA measurement of less than 500 copies/mL, (4) died, and/or (5) migrated out of the community. Second, follow-up was censored at death or migration out of the community and the risk of and demographic factors associated with (1) never testing for HIV by 2 years (among residents without an HIV diagnosis prior to baseline), (2) never initiating ART by 2 years (among residents diagnosed with HIV at or before baseline), and (3) having an HIV RNA measurement of 500 copies/mL or more at 2 years (among residents diagnosed with HIV at or before baseline) were evaluated. Third, HIV viral suppression at 1 and 2 years, censoring at death or migration out of the community, was evaluated in the following subgroups of HIV-positive residents diagnosed at or before study baseline: (1) those who were newly diagnosed at baseline, (2) those who were previously diagnosed but ART naive at baseline, and (3) those who were currently or previously treated with ART at baseline (overall, and within baseline HIV viral suppression strata).

In primary analyses, targeted maximum likelihood estimation[21,22] was used to estimate (1) the number of HIV-positive individuals, adjusting for differences in baseline demographics and testing history between individuals with measured vs missing HIV serostatus (to account for possible overrepresentation or underrepresentation of HIV-positive individuals among those with HIV serostatus measured at annual testing), and (2) the number of HIV-positive individuals with HIV viral suppression, adjusting for differences in baseline demographics, testing, ART, and suppression history between individuals with measured vs missing HIV RNA (to account for possible overrepresentation or underrepresentation of individuals with HIV viral suppression among those with HIV RNA measured at annual testing). Unadjusted estimates were calculated as proportions among individuals seen at annual testing with known HIV serostatus and HIV RNA levels.

In secondary analyses, targeted maximum likelihood estimation was also used to adjust for censoring by death or migration out of the community and, in exploratory analysis, to evaluate demographic variables associated with failure to test, use ART, and suppress HIV replication. To minimize model misspecification bias, propensity score and outcome models were estimated using Super Learning,[22] a machine-learning method that used 5-fold cross-validation to combine general additive models, stepwise regression, and logistic regression. Analyses adjusted for community and used household as the independent unit in cross-validation and when calculating influence curve and nonparametric bootstrap-based standard errors. A 2-sided *P* value of less than 0.05 was considered significant. Analyses were conducted in R (R Foundation), version 3.3.2, using packages ltmle_0.9-8-4 and SuperLearner_2.0-21.[23-25]

Results

Study Population and Testing Coverage

There were 77 774 stable residents 15 years or older in the 16 intervention communities at baseline, of whom 45.3% were male and 35.1% were aged 15 to 24 years (**Table 1**). Baseline

Table 1. Characteristics of Baseline Stable Residents of 16 SEARCH Intervention Communities in Rural Uganda and Kenya[a]

	No. of Stable Residents (%)			
	Southwest Uganda (n = 25 014)	East Uganda (n = 25 120)	Kenya (n = 27 640)	Total (N = 77 774)
Known HIV status[b]	22 410 (89.6)	22 681 (90.3)	24 192 (87.5)	69 283 (89.1)
Residents with HIV[c]	1462 (6.5)	785 (3.5)	4861 (20.1)	7108 (10.3)
Male	11 687 (46.7)	11 394 (45.4)	12 165 (44.0)	35 246 (45.3)
Age, y				
15-24	8478 (33.9)	9582 (38.1)	9253 (33.5)	27 313 (35.1)
25-34	5732 (22.9)	5315 (21.2)	6688 (24.2)	17 735 (22.8)
35-44	4398 (17.6)	4007 (16.0)	4251 (15.4)	12 656 (16.3)
>44	6406 (25.6)	6216 (24.7)	7448 (26.9)	20 070 (25.8)
Not married[d]	7440 (29.7)	6924 (27.6)	7541 (27.3)	21 905 (28.2)
Education				
Less than primary[e]	4438 (17.7)	3871 (15.4)	2138 (7.7)	10 447 (13.4)
Primary	14 020 (56.0)	15 297 (60.9)	22 358 (80.9)	51 675 (66.4)
Secondary or higher	6556 (26.2)	5952 (23.7)	3144 (11.4)	15 652 (20.1)
Occupation				
Formal sector[f]	5280 (21.1)	5836 (23.2)	6626 (24.0)	17 742 (22.8)
High-risk informal sector[g]	657 (2.6)	399 (1.6)	2334 (8.4)	3390 (4.4)
Low-risk informal sector[h]	16 389 (65.5)	17 250 (68.7)	15 397 (55.7)	49 036 (63.0)
Other[i]	1550 (6.2)	880 (3.5)	1215 (4.4)	3645 (4.7)
No job or disabled	1138 (4.5)	755 (3.0)	2068 (7.5)	3961 (5.1)
Household wealth index quintile[j]				
First (least wealth)[k]	5301 (21.2)	4836 (19.3)	3041 (11.0)	13 178 (16.9)
Second	5218 (20.9)	5387 (21.4)	4492 (16.3)	15 097 (19.4)
Third	4740 (18.9)	5550 (22.1)	6557 (23.7)	16 847 (21.7)
Fourth	4442 (17.8)	5067 (20.2)	10 959 (39.6)	20 468 (26.3)
Fifth (most wealth)	5313 (21.2)	4280 (17.0)	2591 (9.4)	12 184 (15.7)
≥1 mo away from community in the past year[l]	3333 (13.3)	3045 (12.1)	1969 (7.1)	8347 (10.7)

Abbreviations: HIV, human immunodeficiency virus; SEARCH, Sustainable East Africa Research in Community Health Study.

[a] Stable residence indicates 6 mo or more of prior year living in the study community. Of the 16 SEARCH Intervention Communities, 10 were located in Uganda and 6 in Kenya.

[b] Tested HIV-positive or HIV-negative at baseline or with Ministry of Health record indicating prior HIV diagnosis.

[c] Tested HIV-positive at baseline or with Ministry of Health record indicating prior HIV diagnosis. Percent is among those with known HIV status.

[d] Missing data for 246 residents (0.3%).

[e] Missing data for 159 residents (0.2%).

[f] Formal sector occupation was defined as teacher, student, government worker, military worker, health worker, or factory worker.

[g] High-risk informal sector occupation was defined as fishmonger, fisherman, bar owner, bar worker, transport, or tourism.

[h] Low-risk informal sector occupation was defined as farmer, shopkeeper, market vendor, hotel worker, homemaker, household worker, construction worker, or mining.

[i] Missing data for 249 residents (0.3%).

[j] Quintiles were based on a principle components analysis of household wealth survey.

[k] Missing data for 249 residents (0.3%).

[l] Missing data for 4 residents (0.005%).

HIV prevalence was 10.3% (Southwest Uganda, 6.5% [1462 of 22 410 residents]; East Uganda, 3.5% [785 of 22 681 residents]; Kenya, 20.1% [4861 of 24 192 residents]). During 2 years of follow-up, 907 individuals died, 13 257 migrated out of a study community, and 9020 turned age 15 years (eFigure 1 in Supplement 3). Secondary analyses included an additional 11 851 nonstable residents and 6437 adult migrants into a study community (eFigure 2 in Supplement 3).

Annual HIV serostatus and RNA testing levels were high.[16] Of stable residents, 89.1% (69 283 of 77 774 residents) had known HIV status (tested at that year's annual campaign or had previously tested positive) at baseline; 89.4% (64 999 of 72 744 residents) had known HIV status at year 1; and 86.8% (63 045 of 72 630 residents) had known HIV status at year 2. Of those known to be HIV-positive, 70.1% (4983 of 7108 residents) had HIV RNA measured during hybrid mobile testing at baseline, 85.9% (6016 of 7003 residents) had HIV RNA measured at year 1, and 83.6% (5786 of 6925 residents) had HIV RNA measured at year 2. Missing HIV RNA levels were more common at baseline due to assay failures at early campaigns.[26]

Diagnosis, ART Use, and Suppression in an Open Cohort of HIV-Positive Individuals

At baseline, 44.7% of HIV-positive residents had achieved HIV viral suppression (95% CI, 43.5%-45.9%; 3464 of 7745

residents). Population-level suppression was 75.2% (95% CI, 74.1%-76.3%; 5399 of 7182 residents) after 1 year of intervention and 80.2% (95% CI, 79.1%-81.2%; 5666 of 7068 residents) after 2 years of intervention (**Figure 1**A; eTables 1-2 in Supplement 3). Over 2 years, population-level HIV viral suppression increased 35.5 percentage points (95% CI, 34.4-36.6; $P < .001$). At baseline, 64.9% of HIV-positive residents were previously diagnosed (95% CI, 63.8%-66.0%; 5028 of 7745 residents; 70.4% incorporating self-reported diagnosis [95% CI, 69.4%-71.5%], 5454 of 7745 residents), 80.3% of previously diagnosed HIV-positive residents had initiated ART (95% CI, 79.2%-81.4%; 4038 of 5028 residents), and 85.8% of HIV-positive residents with prior ART initiation had achieved HIV viral suppression (95% CI, 84.6%-87.0%; 3464 of 4038 residents). After 2 years, 95.9% of HIV-positive residents were previously diagnosed (95% CI, 95.3%-96.5%; 6780 of 7068 residents), 93.4% of previously diagnosed HIV-positive residents had initiated ART (95% CI, 92.8%-94.0%; 6334 of 6780 residents), and 89.5% of HIV-positive residents with prior ART initiation had achieved HIV viral suppression (95% CI, 88.6%-90.3%; 5666 of 6334 residents). Population-level HIV viral suppression at 2 years was similar when migrants into the community and nonstable residents were included (79.0% [95% CI, 78.0%-80.0%]; 6157 of 7792 HIV-positive residents) and was higher in unadjusted analyses (85.6% [95% CI, 84.6%-86.5%]; 4951 of 5786 residents) (eTables 2-3 in Supplement 3).

Among subgroups of the open cohort at baseline, a smaller proportion of HIV-positive males (55.9%) compared with females (69.7%) were previously diagnosed (difference, 13.8 percentage points [95% CI, 12.1-15.5]), and males were less likely to have achieved HIV viral suppression (39.1% among males vs 47.6% among females; difference, 8.5 percentage points [95% CI, 6.8-10.2]) (Figure 1B-G; eTable 2 in Supplement 3). At baseline, youth (aged 15 to 24 years) were less likely than older residents (aged >24 years) to have been previously diagnosed, treated once diagnosed, and suppressed once treated, and a lower proportion of HIV-positive youth (26.2%) compared with older adults (47.2%) had achieved HIV viral suppression (difference, 21.0 percentage points [95% CI, 18.5-23.5]). Age and sex disparities, although smaller, remained after 2 years. After 2 years, 76.2% of males vs 82.2% of females (difference, 6.0 percentage points [95% CI, 4.3-7.7), and 64.5% of youth vs 81.5% of older adults (difference, 17.0 percentage points [95% CI, 13.6-20.4]) had achieved HIV viral suppression.

ART Use and HIV Viral Suppression in a Closed Cohort of Baseline HIV-Positive Residents

Among a closed cohort of 7108 stable residents diagnosed with HIV at or before study baseline (**Figure 2**; eTable 4 in Supplement 3), 29.3% (n = 2080) were newly diagnosed and 13.9% (n = 990) were previously diagnosed but ART naive at baseline. Adjusting for missing HIV RNA measurements, an estimated 8.1% (n = 575) had initiated ART but had an HIV RNA measurement of 500 copies/mL or more and 48.7% (n = 3463) had an HIV RNA measurement of less than 500 copies/mL at baseline. In contrast, after 2 years, the estimated proportion of residents with HIV viral suppression was 73.4% (n = 5218), 1.9% (N = 136) had died, and 11.9% (N = 849) had migrated out of the community. Although initial disparities in suppression between ages and sexes declined over time (Figures 2B-G), by 2 years, 28.5% of youth (246 of 864 residents) had migrated out of the community and only 54.7% of youth (473 of 864 residents) were resident in the community with HIV viral suppression (vs 76.0% for age >24 years; 4748 of 6244 residents).

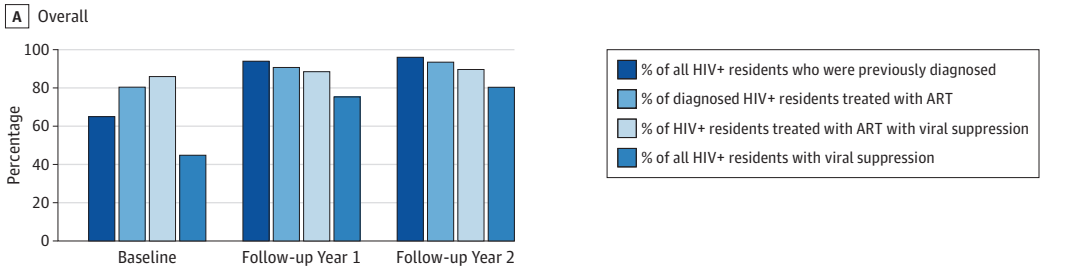
In longitudinal analysis in which follow-up was censored at death or migration out of the community with adjustment for potentially informative censoring and missing HIV RNA measurements, 79.7% (95% CI, 78.7%-80.8%) of the baseline HIV-positive cohort (n = 7108) had achieved HIV viral suppression after 1 year, increasing to 83.8% (95% CI, 82.8%-84.9%) after 2 years (**Table 2**). In the subgroup of individuals newly diagnosed at baseline (n = 2080), 62.8% (95% CI, 60.4%-65.2%) had achieved HIV viral suppression after 1 year, increasing to 68.8% (95% CI, 66.4%-71.2%) after 2 years. Individuals previously diagnosed but ART naive at baseline (n = 990) were more likely to have achieved HIV viral suppression (78.1% [95% CI, 75.3%-80.8%] at 1 year and 86.5% [95% CI, 84.2%-88.8%] at 2 years), whereas ART-experienced individuals with a baseline HIV RNA measurement of 500 copies/mL or more (n = 426) were less likely to have achieved HIV viral suppression (49.5% [95% CI, 44.2%-54.7%] at 1 year and 62.2% [95% CI, 57.2%-67.2%] at 2 years). Almost all individuals with a suppressed HIV RNA measurement at baseline (n = 2549) maintained a suppressed HIV RNA level 1 and 2 years later (96.3% [95% CI, 95.6%-97.1%] at 1 year and 96.8% [95% CI, 96.0%-97.6%] at 2 years).

Demographic Variables Associated With Testing, ART, and Suppression

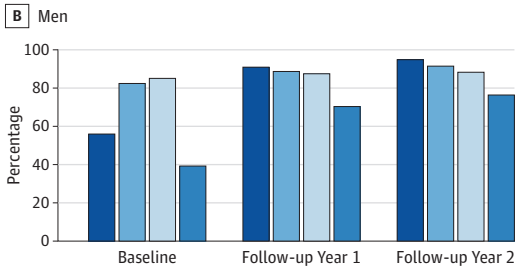
Associations between baseline demographics and failure to test for HIV, receive ART, and virally suppress were explored in closed cohort analyses, adjusting for censoring at death or migration out of the community and, for viral suppression outcomes, for missing HIV RNA measurements. Among 72 746 baseline stable residents not diagnosed with HIV before baseline, the probability of testing for HIV at least once over 2 years of follow-up was 96.8% (95% CI, 96.6%97.0%) (eTable 5 in Supplement 3). In multivariable analyses, residents who were male, never married, mobile (≥1 month in the past year away from community), aged 25-44 years (vs aged >44 years), and had less than primary education (vs primary) were at higher risk of never testing for HIV (eTable 6 in Supplement 3).

Among 7108 HIV-positive residents diagnosed at or before baseline, an estimated 93.8% (95% CI, 93.2%-94.4%) had ever used ART and 83.8% (95% CI, 82.8%-84.9%) had achieved HIV viral suppression at 2 years (Table 2; eTable 5 in Supplement 3). In multivariable analyses, residents who were male, younger, and had intermediate wealth were at higher risk of never receiving ART, whereas those who were male, younger, and not employed in the formal sector were at higher risk of nonsuppression (**Table 3**; eTable 7 in Supplement 3).

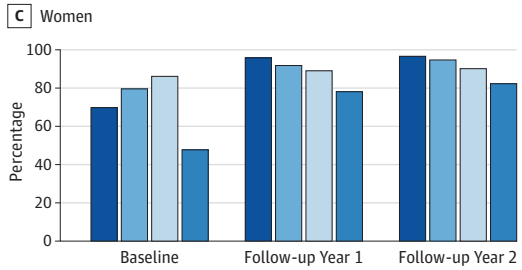
Figure 1. Prior Diagnosis, ART, and Viral Suppression Among HIV-Positive Stable Residents of 16 SEARCH Intervention Communities in Rural Uganda and Kenya (Open Cohort)



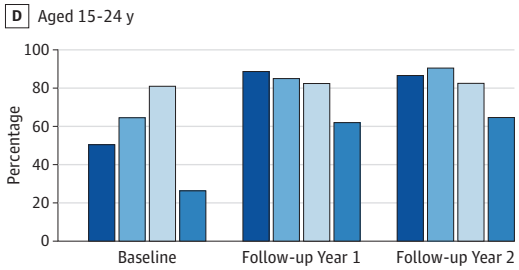
No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	5028/7745	6744/7182	6780/7068
Received ART/previously diagnosed	4038/5028	6110/6744	6334/6780
Viral suppression/received ART	3464/4038	5399/6110	5666/6334
Viral suppression/all HIV+	3464/7745	5399/7182	5666/7068



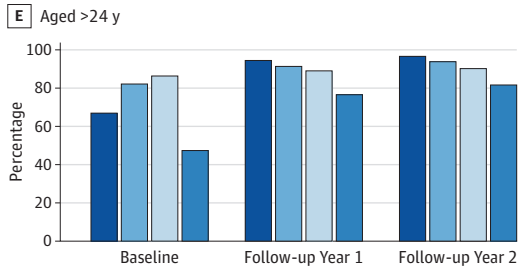
No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	1537/2749	2324/2559	2384/2517
Received ART/previously diagnosed	1265/1537	2057/2324	2176/2384
Viral suppression/received ART	1075/1265	1796/2057	1918/2176
Viral suppression/all HIV+	1075/2749	1796/2559	1918/2517



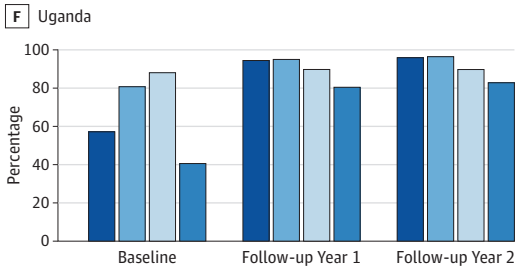
No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	3491/5011	4420/4621	4396/4550
Received ART/previously diagnosed	2773/3491	4053/4420	4158/4396
Viral suppression/received ART	2386/2773	3604/4053	3742/4158
Viral suppression/all HIV+	2386/5011	3604/4621	3742/4550



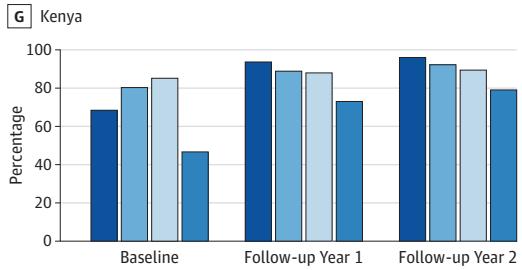
No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	472/938	603/680	542/626
Received ART/previously diagnosed	304/472	512/603	490/542
Viral suppression/received ART	246/304	421/512	404/490
Viral suppression/all HIV+	246/938	421/680	404/626



No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	4556/6818	6141/6513	6238/6463
Received ART/previously diagnosed	3734/4556	5598/6141	5844/6238
Viral suppression/received ART	3218/3734	4977/5598	5266/5844
Viral suppression/all HIV+	3218/6818	4977/6513	5266/6463



No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	1388/2431	2092/2217	2137/2232
Received ART/previously diagnosed	1120/1388	1985/2092	2058/2137
Viral suppression/received ART	985/1120	1779/1985	1845/2058
Viral suppression/all HIV+	985/2431	1779/2217	1845/2232

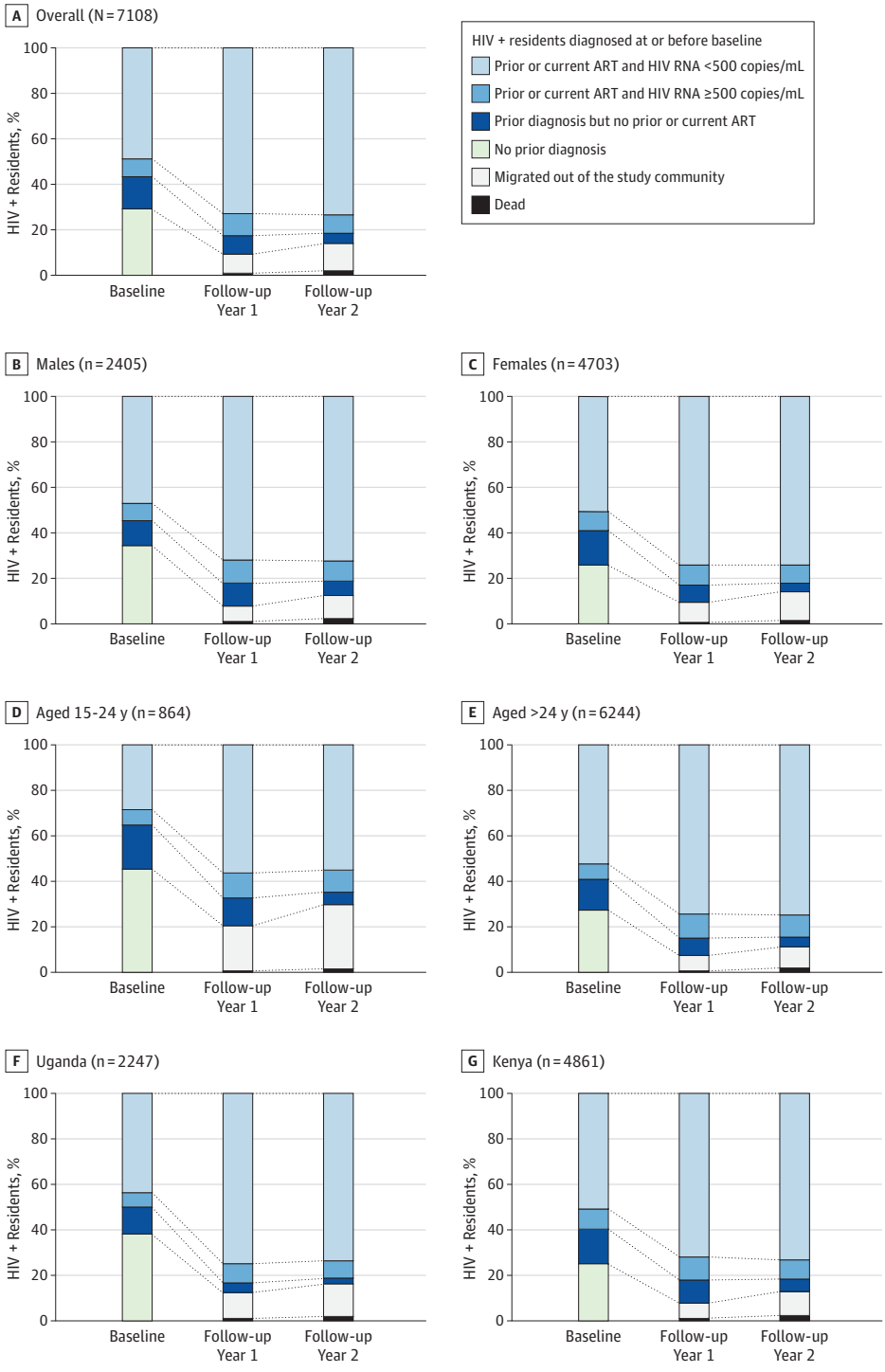


No. of residents/total No. of residents[a]	Baseline	Follow-up Year 1	Follow-up Year 2
Previously diagnosed/all HIV+	3640/5325	4652/4970	4643/4838
Received ART/previously diagnosed	2918/3640	4125/4652	4276/4643
Viral suppression/received ART	2480/2918	3621/4125	3818/4276
Viral suppression/all HIV+	2480/5325	3621/4970	3818/4838

ART indicates antiretroviral therapy; HIV, human immunodeficiency virus; SEARCH, Sustainable East Africa Research in Community Health Study. Stable residence was defined as living in the study community for 6 or more months in the past year. Viral suppression was defined as plasma HIV RNA measurement of less than 500 copies/mL.

[a] Estimates adjusted for incomplete HIV serostatus and HIV RNA measurement (eTables 1-2 in Supplement 3).

Figure 2. Prior Diagnosis, ART, Viral Suppression, Migration Out of the Community, and Death Among HIV-Positive Stable Residents of 16 SEARCH Intervention Communities in Rural Uganda and Kenya Who Were Diagnosed At or Before Baseline (Closed Cohort)[a]



ART indicates antiretroviral therapy; HIV, human immunodeficiency virus; SEARCH, Sustainable East Africa Research in Community Health Study. Stable residence was defined as living in the study community for 6 or more months in the past year. Viral suppression indicates residents who had less than 500 copies/mL of HIV RNA. Migration out of the study community indicates prior residents who were reported to no longer live in the community.

[a] Adjusted to account for incomplete plasma HIV RNA measurement (eTable 4 in Supplement 3).

Discussion

At baseline, 44.7% of HIV-positive residents had suppressed HIV viral replication. After 2 years of a community-based HIV test-and-treat intervention, 95.9% of HIV-positive individuals were previously diagnosed (prior to baseline or during the 2-year program), 93.4% of those had received ART, and 89.5% of those had achieved HIV viral suppression; overall, 80.2% of HIV-positive individuals had suppressed HIV viral replication.

Table 2. Postbaseline HIV Viral Suppression in a Closed Cohort of HIV-Positive Stable Residents of 16 SEARCH Intervention Communities in Rural Uganda and Kenya Who Were Diagnosed At or Before Baseline (n = 7108)[a]

Baseline Diagnosis, Treatment, and Suppression Status	No. of HIV-Positive Residents (%)[a]	Follow-up Year 1		Follow-up Year 2	
		No. of Residents With Viral Suppression/Total No. of Residents With Measured HIV RNA (%)[b]	Adjusted Proportion, % (95% CI)[c]	No. of Residents With Viral Suppression/Total No. of Residents With Measured HIV RNA (%)[d]	Adjusted Proportion, % (95% CI)[c]
Overall	7108 (100)	4682/5578 (83.9)	79.7 (78.7-80.8)	4602/5215 (88.2)	83.8 (82.8-84.9)
Newly diagnosed (HIV RNA≥500 copies/mL)	2080 (29.3)	963/1321 (72.9)	62.8 (60.4-65.2)	965/1205 (80.1)	68.8 (66.4-71.2)
Previously diagnosed with no ART (HIV RNA≥500 copies/mL)	990 (13.9)	649/812 (79.9)	78.1 (75.3-80.8)	685/778 (88.0)	86.5 (84.2-88.8)
Previous or current ART	4038 (56.8)	3070/3445 (89.1)	88.8 (87.7-89.9)	2952/3232 (91.3)	90.5 (89.4-91.6)
HIV RNA not measured	1063 (15.0)	732/846 (86.5)	86.6 (84.3-88.9)	685/779 (87.9)	87.2 (84.9-89.5)
HIV RNA≥500 copies/mL	426 (6.0)	175/355 (49.3)	49.5 (44.2-54.7)	204/325 (62.8)	62.2 (57.2-67.2)
HIV RNA<500 copies/mL	2549 (35.9)	2163/2244 (96.4)	96.3 (95.6-97.1)	2063/2128 (96.9)	96.8 (96.0-97.6)

Abbreviations: ART, antiretroviral treatment; HIV, human immunodeficiency virus; SEARCH, Sustainable East Africa Research in Community Health Study.

[a] Stable residence indicates 6 mo or more of prior year in the study community. Of the 16 SEARCH Intervention Communities, 10 were located in Uganda and 6 in Kenya. Viral suppression was defined as HIV RNA measurement of <500 copies/mL).

[b] Among 6460 baseline HIV-positive residents alive and not migrated out of the community by follow-up year 1.

[c] Among 7108 baseline stable HIV-positive residents. Estimated probability of viral suppression at the time of that year's annual testing, adjusted for censoring by death and migration out of the community and for missing HIV RNA measurements. Baseline adjustment variables included community, age, sex, occupation, mobility (≥1 mo away from the community in the past year), wealth, marital status, and education. Time-varying adjustment variables included prior health campaign or home-based contact, prior ART initiation (for subgroups that had not already initiated ART use at baseline), prior HIV RNA testing, and suppression history.

[d] Among 6123 baseline HIV-positive residents alive and not migrated out of the community by follow-up year 2.

The WHO global public health mandate to identify and offer ART to the 37 million persons living with HIV is a challenging goal—skepticism regarding the feasibility of reaching the UNAIDS 90-90-90 target by 2020 is legitimate. Globally, approximately half of persons living with HIV know their diagnosis,[8] many diagnosed persons do not link to care or drop out after starting ART,[27,28] HIV funding has not increased over the past 5 years,[29] and stigma remains a barrier, particularly in vulnerable populations.[30,31] The 2 most important findings of these analyses are (1) the 2015 WHO guidelines to treat persons regardless of CD4 cell count can be successfully implemented, and (2) the UNAIDS 90-90-90 target of 73% of HIV-positive persons with HIV viral suppression can be achieved and exceeded within a 2-year period in rural East Africa.

Few studies in sub-Saharan Africa have directly evaluated population-level HIV testing, treatment, and suppression of HIV viral replication to less than 500 copies/mL,[10,11,13,32-37] and even fewer have data after starting an HIV test-and-treat intervention.[38] Botswana—an upper-middle income country with a population of 2 million—is closest to achieving the UNAIDS 90-90-90 target.[10] Despite Botswana's policy to initiate ART at CD4 cell counts of less than 350 CD4 cells/mm^3, an estimated 70% of HIV-positive persons resident in Botswana have achieved HIV viral suppression, an achievement attributed to Botswana's political leadership, early adoption of HIV opt-out testing and ART, decentralization of HIV care, and access to HIV RNA monitoring.

This study demonstrates progress toward achieving the UNAIDS targets in rural Uganda and Kenya in regions with baseline HIV prevalence ranging from 3.5% to 20.1%. Furthermore, among populations in which less than half of HIV-positive adults had achieved HIV viral suppression at study baseline, an intervention that included treatment of adults with more than 350 CD4 cells/mm^3 using a streamlined HIV care delivery model integrated into government health clinics exceeded the UNAIDS overall population-level viral suppression target after 1 year.

HIV testing is one of the most challenging obstacles to achieving universal ART coverage. Before the testing intervention, 64.9% of HIV-positive community residents knew their status, less than the 83% with known status in Botswana,[10] but substantially more than the regional UNAIDS estimate of 56%.[8] Using an "out of facility" mobile testing strategy that combined multidisease testing at community health campaigns with home testing for nonattendees, the proportion of HIV-positive persons aware of their status increased to 95.9% after 2 years. Community engagement contributed to this success. Participation of men, whose knowledge of HIV status lagged that of women at study baseline, was enhanced by targeted outreach that included competitive sporting events, conveniently located testing services with evening hours, and non-HIV services including diabetes and hypertension screening and sexual health consultation.[16]

Poor retention in HIV care and adherence to ART, particularly among persons starting therapy with a high CD4 cell count, is a potential barrier to achieving the new WHO treatment guidelines.[9] A streamlined delivery model was used to enhance retention among patients initiating ART at all CD4 cell counts. This patient-centered model of care was designed to reduce structural barriers, improve patient-clinician relationships, and enhance patient knowledge and attitudes about HIV. It is an example of what is now called "differentiated" HIV care—a client-centered approach that adapts HIV services to reflect the preferences and expectations of people living with HIV.[39] There is increasing global consensus that successfully treating all persons living with

Table 3. Association Between Baseline Demographic Variables and HIV RNA ≥500 copies/mL at Follow-up Year 2 in a Closed Cohort of HIV-Positive Stable Residents of 16 SEARCH Intervention Communities in Rural Uganda and Kenya Who Were Diagnosed At or Before Baseline (n = 7108)[a]

	No. of Residents Without Viral Suppression/Total No. of Residents With HIV RNA Measured (%)[b]	Unadjusted Risk Difference, % (95% CI)	*P* Value	Adjusted Risk Difference, % (95% CI)[c]	*P* Value
Sex					
Male	228/1691 (13.5)	2.6 (0.7 to 4.4)	.006	6.0 (3.5 to 8.5)	<.001
Female	385/3524 (10.9)	Reference		Reference	
Age, y					
15-24	87/469 (18.6)	9.2 (3.6 to 14.9)	.001	15.3 (9.8 to 20.9)	<.001
25-34	224/1650 (13.6)	4.3 (1.5 to 7.0)	.002	8.8 (6.2 to 11.4)	<.001
35-44	163/1604 (10.2)	0.8 (−2.0 to 3.7)	.56	2.2 (−0.2 to 4.5)	.07
>44	139/1492 (9.3)	Reference		Reference	
Marital status					
Married, widowed, divorced, or separated	576/5003 (11.5)	Reference		Reference	
Never married	37/212 (17.5)	5.9 (2.7 to 9.1)	<.001	5.5 (−2.2 to 13.1)	.17
Education					
Less than primary	63/484 (13.0)	Reference		Reference	
Primary	484/4141 (11.7)	−1.3 (−3.2 to 0.5)	.16	−1.5 (−6.2 to 3.2)	.54
Secondary or higher	66/590 (11.2)	−1.8 (−12.1 to 8.5)	.73	−3.3 (−8.8 to 2.2)	.24
Occupation					
Formal sector[d]	18/211 (8.5)	Reference		Reference	
High-risk informal sector[e]	66/496 (13.3)	4.8 (−7.7 to 17.3)	.45	8.3 (3.3 to 13.4)	.001
Low-risk informal sector[f]	474/4087 (11.6)	3.1 (1.6 to 4.6)	<.001	6.3 (2.4 to 10.3)	.002
Other	28/197 (14.2)	5.7 (−7.9 to 19.3)	.41	10.2 (2.5 to 17.9)	.009
No job or disabled	27/224 (12.1)	3.5 (−10.0 to 17.0)	.61	11.4 (4.7 to 18.1)	<.001
Household wealth index quintile[g]					
First (least wealth)	88/813 (10.8)	−0.9 (−5.3 to 3.6)	.70	0.6 (−2.7 to 3.9)	.73
Second	129/989 (13.0)	1.4 (−3.6 to 6.3)	.59	2.1 (−1.2 to 5.4)	.21
Third	147/1177 (12.5)	0.8 (−3.3 to 4.9)	.70	2.8 (−0.3 to 6.0)	.08
Fourth	157/1449 (10.8)	−0.9 (−4.2 to 2.5)	.62	2.9 (−0.2 to 6.1)	.06
Fifth (most wealth)	92/787 (11.7)	Reference		Reference	
Mobility					
<1 mo away from community in the past year	562/4856 (11.6)	Reference		Reference	
≥1 mo away from community in the past year	51/359 (14.2)	2.6 (−0.6 to 5.9)	.11	2.5 (−1.2 to 6.2)	.19

Abbreviations: HIV, human immunodeficiency virus; SEARCH, Sustainable East Africa Research in Community Health Study.

[a] Stable residence indicates 6 mo or more of prior year in the study community. Of the 16 SEARCH Intervention Communities, 10 were located in Uganda and 6 in Kenya. Viral nonsuppression was defined as HIV RNA measurement of >500 copies/mL).

[b] Of the 7108 baseline HIV-positive individuals, 985 died or migrated out of the community by year 2. Of the remaining 6123 individuals, 5215 (85.2%) had HIV RNA measured at year 2 and contributed to the unadjusted analyses.

[c] All 7108 adults contributed to the adjusted analyses, which controlled for right-censoring by death and migration. Baseline adjustment variables included community, age, sex, occupation, mobility, wealth, marital status, and education. Time-varying adjustment variables (used in addition to baseline variables to adjust for censoring by death and migration and for missing HIV RNA measures) included prior health campaign and home-based contact, prior ART initiation, prior HIV RNA testing, and suppression history.

[d] Formal sector occupation was defined as teacher, student, government worker, military worker, health worker, or factory worker.

[e] High-risk informal sector occupation was defined as fishmonger, fisherman, bar owner, bar worker, transport, or tourism.

[f] Low-risk informal sector occupation was defined as farmer, shopkeeper, market vendor, hotel worker, homemaker, household worker, construction worker, or mining.

[g] Quintiles were based on a principle components analysis of household wealth survey.

HIV, as well as generating more efficient health systems, will require differentiated care approaches.

This study provides insight into 4 groups—youth, males, those newly diagnosed, and those without HIV viral suppression despite ART initiation—who are falling short of the UNAIDS 90-90-90 target. At baseline, only 50.3% of HIV-positive youth (15-24 years) were aware of their status. This increased to 86.5% after 2 years, suggesting that the testing strategy was reaching most youth. However, population-level HIV viral suppression at 2 years remained 64.5% in youth compared with 81.5% in older populations, due in part to the lower proportion of viral suppression (82.4%) among youth who had started therapy. Barriers faced by youth included stigma and logistics of HIV care for those in

boarding school. More research is needed to design age-specific solutions.

Among HIV-positive males at baseline, HIV testing and linkage for ART start were major barriers in the HIV care cascade. The testing intervention closed much of the sex gap in knowledge of HIV status over 2 years. However, after 2 years, HIV-positive males remained less likely to be diagnosed, treated, and virally suppressed on treatment, resulting in a persistent disparity in population-level suppression (82.2% among females vs 76.2% among males).

HIV-positive individuals who were newly diagnosed at baseline failed to achieve targets for ART initiation and viral suppression. In a closed-cohort analysis, only 68.8% had achieved HIV viral suppression after 2 years. This group will require new approaches to enhance linkage and adherence. Adults with an HIV RNA measurement of 500 copies/mL or more at baseline despite prior ART initiation also did not meet the target—only 62.2% had achieved HIV viral suppression after 2 years. Nonadherence, HIV drug resistance, and unmet structural barriers to care all likely contribute to poor suppression in this often vulnerable and difficult-to-reach population. Additional approaches, including improved implementation of second and third line ART treatment and possibly HIV resistance testing, should be evaluated.

This analysis did not address if HIV incidence decreased with the improvements observed in the care cascade. UNAIDS has already set a new target of 95-95-95 by 2030, recognizing that the current target alone is unlikely to eliminate the HIV epidemic.[40] Reaching the HIV-positive individuals who remain without HIV viral suppression is a priority, both for their own health and because of their potential contribution to ongoing HIV transmission.

Limitations

This analysis has several limitations. First, prior to trial completion, progress toward the UNAIDS target cannot be attributed to the intervention. Second, primary analysis focused on baseline stable community residents due to their full exposure to the intervention; however, these individuals may be easier to test, treat, and suppress than more mobile populations. Although sensitivity analyses including nonstable residents and migrants into the community yielded similar estimates, ascertainment of migrants into the community was not comprehensive. Cascade outcomes among individuals who left the community are also unknown, as is the contribution of migrants to ongoing HIV transmission.[38]

Conclusions

Among individuals with human immunodeficiency virus (HIV) in rural Kenya and Uganda, implementation of community-based testing and treatment was associated with an increased proportion of HIV-positive adults who achieved viral suppression, along with increased HIV diagnosis and initiation of antiretroviral therapy. In these communities, the UNAIDS population-level viral suppression target was exceeded within 2 years after program implementation.

ARTICLE INFORMATION

Accepted for Publication: May 3, 2017.

Author Contributions: Drs Petersen and Havlir had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Petersen, Balzer, Kwarsiima, Sang, Chamie, Kabami, Liegler, Kadede, Jain, van der Laan, Cohen, Charlebois, Kamya, Havlir.
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Supervision: Petersen, Kwarsiima, Lavoy, Bukusi, Cohen, Clark, Kamya.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This work was supported by grants UM1AI069502, U01AI099959 (both from Dr Havlir), and R01AI074345 (Dr van der Laan) from the National Institute of Allergy and Infectious Diseases at the National Institutes of Health and by the US President's Emergency Plan for AIDS Relief, the Office of the Global AIDS Coordinator, Gilead Sciences (Truvada donation), and the Office of AIDS Research. The University of California, San Francisco-Gladstone Institute of Virology and Immunology Center for Aids Research provided indirect funding through grant P30 AI027763 for laboratory infrastructure and Dr Liegler's support.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the residents of the SEARCH Study communities for their participation and the Uganda and Kenya Ministries of Health. They did not receive compensation for their contribution. We also thank the SEARCH Study Team.

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