



Published in final edited form as:

*J Acquir Immune Defic Syndr.* 2023 September 01; 94(1): 37–45. doi:10.1097/QAI.0000000000003226.

## Universal HIV Testing and Treatment with Patient-Centered Care Improves ART Uptake and Viral Suppression among Adults Reporting Hazardous Alcohol Use in Uganda and Kenya

Sarah B. Puryear, MD, MPH<sup>1</sup>, James Ayieko, MBChB, PhD<sup>2</sup>, Judith A. Hahn, PhD, MA<sup>1</sup>, Atukunda Mucunguzi, MBChB<sup>3</sup>, Asiphos Owaraganise, MBChB<sup>3</sup>, Joshua Schwab, MA<sup>4</sup>, Laura B. Balzer, PhD<sup>4</sup>, Dalsone Kwarisiima, MBChB, MPH<sup>3</sup>, Edwin D. Charlebois, PhD, MPH<sup>5</sup>, Craig R. Cohen, MD, MPH<sup>6</sup>, Elizabeth A. Bukusi, MBChB, PhD<sup>2</sup>, Maya L. Petersen, MD, PhD<sup>4</sup>, Diane V. Havlir, MD<sup>1</sup>, Moses R. Kanya, MBChB, MMed, MPH, PhD<sup>3,7</sup>, Gabriel Chamie, MD, MPH<sup>1</sup>

<sup>1</sup>Division of HIV, Infectious Diseases and Global Medicine, University of California, San Francisco, San Francisco, California, USA

<sup>2</sup>Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi, Kenya

<sup>3</sup>Infectious Diseases Research Collaboration, Kampala, Uganda

<sup>4</sup>Division of Biostatistics and Epidemiology, School of Public Health, University of California, Berkeley, California, USA

<sup>5</sup>Division of Prevention Sciences, Department of Medicine, University of California, San Francisco, San Francisco, California, USA

<sup>6</sup>Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, California, USA

<sup>7</sup>Department of Medicine, Makerere University, Kampala, Uganda

### Abstract

**Objective(s):** Determine if patient-centered, streamlined HIV care achieves higher ART uptake and viral suppression than the standard treatment model for people with HIV (PWH) reporting hazardous alcohol use.

**Design:** Community cluster-randomized trial

**Methods:** The SEARCH trial (NCT01864603) compared an intervention of annual population HIV testing, universal ART, and patient-centered care to a control of baseline population testing with ART by country standard in 32 Kenyan and Ugandan communities. Adults (> 15 years) completed a baseline Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) and were classified as no/non-hazardous (AUDIT-C 0–2 women/0–3 men) or hazardous alcohol use (> 3 women/ > 4 men). We compared year 3 ART uptake and viral suppression of PWH reporting

**Corresponding Author:** Sarah Puryear, MD, MPH, Division of HIV, ID, and Global Medicine, 995 Potrero Avenue, Ward 84, San Francisco, CA 94110, sarah.puryear@ucsf.edu, Telephone: +1-415-476-4082, ext. 445, Fax: +1-706-212-6511.

**Meetings at which data were presented in part at:** Conference on Retroviruses and Opportunistic Infections (CROI); Boston, Massachusetts, USA/Virtual; March 8-11, 2020

hazardous use between intervention and control arms. We compared alcohol use as a predictor of year 3 ART uptake and viral suppression among PWH, by arm.

**Results:** Of 11,070 PWH with AUDIT-C measured, 1723 (16%) reported any alcohol use; 893 (8%) reported hazardous use. Among PWH reporting hazardous use, the intervention arm had higher ART uptake (96%) and suppression (87%) compared to control (74%, aRR=1.28, 95%CI:1.19–1.38; and 72%, aRR=1.20, 95%CI:1.10–1.31, respectively). Within arm, hazardous alcohol use predicted lower ART uptake in control (aRR=0.86, 95%CI:0.78–0.96), but not intervention (aRR=1.02, 95%CI:1.00–1.04); use was not predictive of suppression in either arm.

**Conclusion:** The SEARCH intervention improved ART uptake and viral suppression among PWH reporting hazardous alcohol use and eliminated gaps in ART uptake between PWH with hazardous and no/non-hazardous use. Patient-centered HIV care may decrease barriers to HIV care for PWH with hazardous alcohol use.

### Keywords

HIV; Alcohol; AUDIT-C; Viral Suppression; ART Uptake; Sub-Saharan Africa

## INTRODUCTION

Hazardous alcohol use is an important predictor of poor HIV care outcomes.<sup>1</sup> Alcohol use among people with HIV (PWH) has been associated with lower antiretroviral therapy (ART) uptake,<sup>2,3</sup> decreased ART adherence,<sup>4</sup> reduced viral suppression,<sup>5–7</sup> and increased mortality.<sup>8,9</sup> Furthermore, alcohol use is prevalent among PWH, with an estimated 25% engaging in a range of alcohol use in low and middle income countries.<sup>10</sup> Interventions that improve ART uptake and viral suppression for this high-risk group are urgently needed, particularly in sub-Saharan Africa (SSA), where both HIV and alcohol misuse are common.

Hazardous alcohol use may negatively impact HIV care outcomes via several pathways. Alcohol use has known effects on memory, planning, and cognitive skills that may result in missed appointments and lapses in medication adherence,<sup>4</sup> leading to decreased viral suppression. Alcohol use can contribute to liver disease, diabetes, depression, and other comorbidities that impact individual morbidity and mortality in addition to HIV infection.<sup>8</sup> Moreover, patient and provider beliefs and knowledge gaps surrounding ART use while drinking may negatively impact care.<sup>11–13</sup> Several studies have shown that interactive toxicity beliefs regarding alcohol and ART are common and may lead to ART non-adherence.<sup>14–16</sup> Further, providers may withhold or delay ART for persons with hazardous alcohol use based on their opinions or misconceptions, despite universal treatment recommendations.<sup>2,3,12</sup> Alcohol-related stigma, both from providers and internalized by patients, may also adversely impact care engagement, adherence, and patient-provider relationships, contributing to lower viral suppression.<sup>14,17,18</sup>

To improve HIV outcomes among PWH engaged in hazardous alcohol use, interventions may target alcohol use reduction/cessation directly or take a harm reduction approach<sup>19</sup> through non-judgmental, low-barrier HIV care with or without directly intervening on alcohol use. Direct approaches target alcohol use as a modifiable risk factor via behavioral

or pharmacologic interventions. Counselling-based alcohol-reduction interventions among PWH have been shown to modestly increase ART adherence, improve viral suppression, and decrease risky sexual behaviors;<sup>20–22</sup> however, implementing and scaling up these interventions may be balanced against the opportunity costs of using resources for non-alcohol related interventions with broader potential benefits in resource-limited settings.<sup>23</sup> Harm reduction approaches using patient-centered care have been associated with improved health status, treatment adherence, and greater efficiency of care for general health problems,<sup>24,25</sup> but have not been systematically studied for PWH reporting alcohol use, particularly in SSA.

The Sustainable East Africa Research in Community Health (SEARCH) cluster-randomized trial examined the effect of an intervention of population-wide annual HIV testing and universal ART eligibility paired with streamlined, patient-centered care versus a control of baseline universal testing and ART eligibility and delivery by country standards from 2013–2017. The intervention resulted in significantly higher rates of viral suppression compared to the standard of care in a general population of PWH.<sup>26</sup> We previously reported that PWH reporting alcohol use had lower baseline ART uptake and viral suppression than non-drinkers when enrolling in the SEARCH trial.<sup>7</sup> Though the SEARCH HIV care model did not directly intervene on alcohol use, its focus on patient-centered care, improved patient-provider communication and relationships, and easier access to care, may have addressed multiple barriers commonly faced by PWH with hazardous alcohol use. In this secondary analysis, we sought to determine whether the SEARCH intervention improved ART uptake and viral suppression compared to control after 3 years among PWH reporting hazardous alcohol at baseline. We also sought to determine if gaps in ART uptake and viral suppression observed at baseline persisted between PWH with hazardous alcohol use and non-hazardous/non-use in either the intervention or control communities, separately.

## METHODS

### Study Design and Population

The SEARCH trial ([NCT01864603](#)) was a community cluster-randomized trial that compared an intervention of annual population-wide HIV testing and universal ART eligibility via streamlined, patient-centered care to a control of baseline population-wide testing with ART eligibility and delivery by evolving country standards. The trial included 32 communities in rural Kenya and Uganda over 3 years (2013–17). The trial methods and primary outcome results have been described previously.<sup>26</sup> Baseline (2013–2014) pair-matched randomization assigned 16 study communities to intervention and 16 to control. We conducted door-to-door census enumeration of community residents at baseline, followed by 2-week health fairs offering universal HIV testing integrated with multi-disease services and subsequent home-based testing for fair non-attendees.<sup>27</sup> In both study arms, individuals identified as HIV-positive (defined as confirmed HIV antibody test, detectable HIV RNA, or a Ministry of Health record of prior HIV care) received baseline CD4<sup>+</sup> cell count and HIV viral load testing, clinic appointments within one week (2 days if pregnant or CD4<sup>+</sup><200 cells/mm<sup>3</sup>), and one-time transportation vouchers for travel to clinic.

In intervention communities, health campaigns with HIV testing were conducted annually. All individuals identified as HIV-positive were offered ART regardless of CD4<sup>+</sup> count. All PWH received the SEARCH intervention of patient-centered streamlined care, which included 3-month visit intervals for stable patients, reduced wait times, friendly providers, welcoming staff, 24-hour mobile phone access to providers, appointment reminders, flexible schedules for accessing care, and graduated re-engagement efforts for missed appointments. The goal of the streamlined care intervention was to decrease barriers to engagement in care and viral suppression, improve relationships between patients and the clinic, and improve clinician and patient knowledge of HIV and ART, as previously described.<sup>28</sup> This approach did not include any specific alcohol interventions and providers did not receive alcohol related treatment training; however, individual providers may have addressed alcohol use with patients using their clinical judgement or skills gained from patient-centered care training received for the intervention, as previously described.<sup>28,29</sup> In control communities, health campaigns were held at baseline only and ART was offered according to country guidelines. ART eligibility rapidly expanded during the study the study, from CD4<sup>+</sup> 350 cells/mm<sup>3</sup> at baseline to <500 cells/mm<sup>3</sup> within 1 year, and subsequently to universal eligibility.<sup>26</sup> Participants in control communities received standard HIV care, with no specific alcohol interventions. After three years, campaigns were conducted in all communities for endpoint measurement, including viral load.

At community health campaigns, current alcohol use was measured by self-report (in response to the question “Do you drink alcohol?”). Those reporting use were asked questions that mapped onto the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), as previously described.<sup>7</sup> AUDIT-C scores range from 0 to 12; scores of at least 3 for women and 4 for men have optimal sensitivity and specificity for identifying hazardous alcohol use.<sup>30</sup> Individuals were categorized by AUDIT-C scores as “no alcohol use/non-hazardous use” (score 0–3 for men, 0–2 for women) and “hazardous use” (score 4–12 for men, 3–12 for women).

In this study, we conducted a secondary analysis of the SEARCH trial among adult community residents with HIV who completed an alcohol questionnaire at baseline. First, we sought to determine whether the SEARCH intervention resulted in increased prevalence of ART uptake and viral suppression compared with control among PWH who reported baseline hazardous alcohol use. Although all of these participants were aware of their status and ART eligible by trial close, we hypothesized that at year 3, ART uptake and viral suppression would be higher among intervention participants due to better care engagement, improved ART access, and access to streamlined care. Second, we sought to determine if hazardous alcohol use at baseline was associated with lower rates of ART uptake and viral suppression at 3 years versus no/non-hazardous use, within each trial arm. We hypothesized that hazardous alcohol use would be associated with worse outcomes in both intervention and control participants, but the disparity between those with and without hazardous alcohol use would be less in the intervention arm.

## Statistical Analysis

This was a secondary analysis of the SEARCH trial, whose sample size and power calculations have previously been described for the parent study's primary outcome: HIV incidence.<sup>26</sup>

**HIV Care Outcomes among PWH Reporting Hazardous Alcohol Use in Intervention versus Control Communities**—In this study, our primary outcome was the proportion of PWH reporting hazardous alcohol use at baseline who were virally suppressed (HIV RNA <500 copies/ml) at trial completion (year 3), with viral load measured during year 3 universal testing. We also assessed the proportion of PWH with hazardous use at baseline who had ART uptake by year 3. ART uptake was assessed by review of Ministry of Health records for evidence of either (1) ever being on ART prior to year 3 HIV testing or (2) a suppressed viral load at year 3.

First, we compared viral suppression at year 3 between PWH reporting hazardous alcohol use at baseline in intervention and control communities using a two-staged approach, accounting for clustering and the matched-pair design.<sup>31</sup> Our population included all adults (>15 years) residing in a study community, living with HIV, and self-reporting hazardous alcohol use at baseline. In stage one, we calculated the proportion of participants in each community with viral suppression, excluding persons who died, migrated away from the community, or otherwise did not undergo year 3 viral load measurement. In stage two, we compared viral suppression between study arms using community-level targeted maximum likelihood estimation (TMLE) with cross-validation to adaptively select from the candidate adjustment variables: baseline viral suppression prevalence, proportion of the community aged 15–24 years, or nothing (unadjusted).<sup>32</sup> An analogous analysis was done to compare ART uptake by year 3 between trial arms among PWH who reported hazardous alcohol use at baseline.

**Comparison of Baseline Hazardous Alcohol Use as a Predictor of Year 3 HIV Care Outcomes by Trial Arm**—To understand if the SEARCH intervention reduced previously observed disparities in HIV care outcomes between PWH with hazardous alcohol use versus PWH without hazardous use,<sup>7</sup> we assessed baseline hazardous alcohol use as an individual-level predictor of ART uptake and viral suppression among all PWH, within each trial arm separately. We used individual-level TMLE to estimate the relative risk of each outcome associated with hazardous alcohol use at baseline, after adjusting for sex, age, mobility, marital status, education level, occupation, and community. In these analyses, the household was treated as the conditionally independent unit.

## Ethics

All participants provided verbal informed consent in their preferred language. The study was approved by the Makerere University School of Medicine Research and Ethics Committee (Kampala, Uganda), Uganda National Council for Science and Technology (Kampala, Uganda), Kenya Medical Research Institute Scientific and Ethics Review Committee (Nairobi, Kenya), and the University of California, San Francisco Committee on Human Research (San Francisco, USA).

## RESULTS

### Study Population

Overall, there were 150,395 adult (> 15 years) residents in the 32 communities; 90% (135,484/150,395) had baseline HIV status measured (Figure 1). HIV prevalence was 10% (13,529/135,484). Among those identified as PWH at baseline, 11,070 (82%) completed baseline alcohol assessments and were included in this analysis: 83% (6,055/7,212) in intervention and 79% (5,015/6,317) in control communities.

Current alcohol use was reported by 16% (1723/11,070) of participants: 15% (880/6055) of participants in intervention and 17% (843/5015) in control communities. Among those with any alcohol use, hazardous use was reported by 51% (450/880) of intervention and 53% (443/843) of control participants.

### Characteristics of PWH reporting hazardous alcohol use

PWH reporting baseline hazardous alcohol use across both trial arms were 74% (663/893) male, 68% (609/893) married, 83% (738/893) employed in informal sector jobs (fishmonger, fisherman, bar owner, bar worker, transport, tourism, farmer, shopkeeper, market vendor, hotel worker, homemaker, household worker, construction, or mining), and 17% (154/893) were mobile (defined as living away from the study community for > 1 month in the past year). The median age (IQR) was 38 years (31–45); 31% (273/893) were resident in Eastern Uganda, 39% (349/893) in Western Uganda, and 31% (271/893) in Kenya.

Baseline characteristics of PWH reporting hazardous alcohol use were similar between intervention and control communities (Table 1).

### Characteristics of PWH reporting hazardous vs. no/non-hazardous alcohol use

At baseline, across both arms, PWH reporting hazardous alcohol use were older [median (IQR) 38 years (31–45)] than those with no/non-hazardous use [35 years (28–44)]. A higher proportion of PWH reporting hazardous alcohol use vs. no/non-hazardous use were Ugandan (70% vs. 37%), male (74% vs. 33%), single (10% vs. 7%), educated at a secondary level or higher (21% vs. 13%), in the lowest wealth quintile (26% vs. 19%), and mobile (17% vs. 10%). The mean CD4<sup>+</sup> count was lower among PWH with hazardous alcohol use than no/non-hazardous use (452 cells/μl, IQR 311–647 vs. 512 cells/μl, IQR 352–702) as were baseline viral suppression rates (32% vs. 50%).

### HIV Care Outcomes at year 3 among PWH Reporting Baseline Hazardous Alcohol Use in Intervention versus Control Communities

**ART Uptake by Year 3**—Among PWH reporting hazardous alcohol use at baseline, 382/443 (86%) of control participants and 385/450 (86%) of intervention participants were living in study communities at year 3; among these, measurement of ART uptake by year 3 was 100% in both arms. ART uptake at year 3 was higher among PWH reporting hazardous alcohol use at baseline in the intervention arm (96%, 95%CI: 93–98) versus the control arm (74%; 95%CI: 69–80). Intervention participants were 1.28 times as likely to be on ART



at year 3 compared to those in the control arm (adjusted risk ratio (aRR) 1.28, 95%CI 1.19–1.38;  $p < 0.001$ ) (Figure 2).

**Viral Suppression at Year 3**—Among PWH reporting hazardous alcohol use at baseline and residing in study communities at year 3, HIV viral loads at year 3 were measured in 291/382 (76%) control participants and 291/385 (76%) intervention participants. Viral suppression was 87% in the intervention arm (95% CI:83–90) and 72% in the control arm (95%CI: 67–78). At year 3, PWH with hazardous alcohol use were 1.2 times more likely to be virally suppressed in intervention compared to control (aRR 1.20, 95%CI 1.10–1.31,  $p < 0.001$ ) (Figure 2).

### Comparison of Hazardous Alcohol Use at Baseline as a Predictor of HIV Care Outcomes at Year 3 by Trial Arm

Within each trial arm we assessed whether baseline hazardous alcohol use remained a predictor of ART uptake and viral suppression at year 3, after adjusting for other known risk factors (Figure 3). In intervention communities, baseline hazardous alcohol use was not predictive of ART uptake (aRR 1.02, 95%CI 1.00–1.04,  $p = 0.12$ ) or viral suppression (aRR 0.94, 95%CI 0.88–1.01,  $p = 0.08$ ). However, in control communities, baseline hazardous alcohol use was strongly predictive of lower ART uptake (aRR 0.86 (95%CI: 0.78–0.95,  $p < 0.001$ ); there was no association with viral suppression (aRR 0.94, 95%CI 0.86–1.02,  $p = 0.15$ ) compared to no/non-hazardous use.

## DISCUSSION

The SEARCH intervention improved ART uptake and viral suppression after 3 years among PWH reporting hazardous alcohol use compared to the control. Our study demonstrates that universal HIV testing and treatment paired with a patient-centered, streamlined care intervention can achieve higher ART uptake and viral suppression for PWH reporting hazardous alcohol use than a control of baseline universal testing and standard HIV care, without including an intervention directly targeting alcohol reduction or cessation. PWH with baseline hazardous alcohol use had a 20% relative higher probability of viral suppression after 3 years in the streamlined care arm (viral suppression prevalence 87%) compared to the control (viral suppression prevalence 72%). In context, UNAIDS estimated viral suppression among all PWH in 2017—the year our primary outcomes were collected—to be 63% in Kenya and 56% in Uganda.<sup>33</sup> Our findings add to the evidence demonstrating that the population health benefits gained by the SEARCH intervention extend to PWH reporting hazardous alcohol use, adding to the previously identified groups at high risk for poor HIV care outcomes, including pregnant and postpartum women,<sup>34</sup> men with low CD4 counts,<sup>35</sup> and treatment experienced patients with viremia.<sup>29</sup>

There are several potential mechanisms for how the SEARCH intervention achieved a higher prevalence of ART uptake and viral suppression among PWH reporting hazardous alcohol use compared to control. First, and perhaps most importantly, patient-centered care focused on decreasing structural barriers, increasing care flexibility (i.e. allowing extended clinic hours, late arrivals, and appointment flexibility), improving patient-clinician relationships, and enhancing patient and physician HIV/ART knowledge, which have been

shown to predict retention in care.<sup>28</sup> For PWH engaged in hazardous alcohol use, this is particularly pertinent as gaps in provider knowledge on ART/alcohol interactions can result in withholding ART<sup>2,3,12</sup> and patient perceptions about drug interactions can reduce adherence.<sup>15,16,18</sup> Furthermore, long wait times, costs associated with seeking care, and inconvenience accessing care may be greater barriers for those with hazardous alcohol use, who may be balancing other priorities such as avoiding alcohol withdrawal symptoms or avoiding healthcare interactions while currently or recently intoxicated. Poor patient-provider relationships resulting from provider biases or internalized stigma by patients surrounding alcohol may also hinder care engagement. Second, universal ART eligibility from the trial outset may have increased ART uptake and subsequent viral suppression for intervention participants. Notably, near-universal ART eligibility was implemented for control participants one year after the trial start; however, this delay in ART eligibility for high CD4+ count participants in the control may have negatively impacted care engagement, patient-provider relationships, and ART uptake for a period beyond the changes in eligibility criteria. Third, enhanced linkage efforts including introductions by staff and access to a hotline may have increased ART uptake both by directly increasing linkage and by allaying fears of stigma from care providers for PWH reporting hazardous alcohol use.

Our results provide insight into the potential effects of universal testing and streamlined, patient-centered care on HIV care outcomes for persons with hazardous alcohol use in SSA. Other's findings suggest that alcohol use may negatively impact HIV elimination efforts in SSA, due to its negative effects on medication adherence, consequent risk of HIV drug resistance, and higher mortality and morbidity, leading to a call for integrated substance use prevention and treatment interventions with HIV care.<sup>17</sup> Published data on interventions to improve HIV treatment outcomes among persons reporting hazardous alcohol use in SSA have largely focused on behavioral alcohol reduction or cessation interventions, rather than harm reduction. In a recent meta-analysis of 21 behavioral interventions targeting alcohol use among PWH from an array of high, low, and middle income geographic regions, the authors found reductions in alcohol use, increases in ART adherence, and—in a subset of 7 studies—decreases in HIV viral loads.<sup>21</sup> A more recent systematic review did not find consistent effects,<sup>36</sup> and the findings from recent studies in SSA aiming to reduce alcohol use and/or risky sexual behavior and improve HIV associated outcomes have had mixed results.<sup>37–41</sup> There is a dearth of data on HIV outcomes among PWH reporting hazardous alcohol use following interventions aimed at non-alcohol use specific behaviors, such as ART uptake and adherence. In contrast with our findings within the intervention arm, the Botswana Combination Prevention Project (BCPP), a large universal HIV 'test and treat' (UTT) trial, found that the proportion of participants in the intervention arm who were not virally suppressed after 3 years of the UTT intervention was 1.36 times greater among those who used alcohol than those who did not.<sup>42</sup> The BCPP trial included universal HIV testing, mobile clinics, enhanced linkage to care and appointment reminders, and increased access to male circumcision.<sup>43</sup>

Our findings highlight the potential benefits of pairing patient-centered, streamlined care with universal HIV testing and treatment to improve outcomes and reduce gaps between those with and without hazardous alcohol use. While our results demonstrated that gaps in ART uptake and viral suppression between PWH with hazardous alcohol use and those with



no/non-use were not significant in the intervention arm but gaps in ART uptake remained significant in the control arm, hazardous alcohol use remains a risk factor for numerous comorbidities and all-cause mortality. Among PWH, reductions in heavy alcohol use have many potential health benefits beyond ART uptake and viral suppression, which were not assessed in this study. Patient-centered streamlined care alone is likely not enough to meet the care needs of PWH engaged in hazardous alcohol use. Further insights are needed into how to reduce hazardous alcohol use and its broader negative health effects. This group would likely benefit from specific, alcohol focused interventions in concert with harm reduction interventions to optimize outcomes.

Our study has limitations. First, alcohol use was assessed by self-report. This may have resulted in underreporting as a result of social desirability and recall biases, which has been shown when comparing self-report to alcohol biomarkers in a Ugandan cohort of PWH initiating ART.<sup>44</sup> However, alcohol use was measured at baseline, thus under-report was unlikely to be differential by study arm. Second, alcohol use was assessed at baseline and may not have represented alcohol use at the 3-year visit when we measured ART use and viral suppression. However, baseline alcohol reporting was used to define the sub-group prior to intervention activities in the randomized controlled trial. Lastly, the SEARCH intervention was delivered as a multicomponent package; so, we could not assess which components contributed most to the observed outcomes among those with alcohol use.

In conclusion, the SEARCH intervention achieved high prevalence of ART uptake and viral suppression regardless of baseline alcohol use and improved both outcomes after 3 years among PWH reporting hazardous alcohol use compared to control. The SEARCH intervention also reduced the gap in ART uptake and viral suppression between baseline hazardous drinkers and no/non-hazardous drinkers. These data suggest that the SEARCH intervention decreased barriers to HIV care and viral suppression for PWH reporting hazardous alcohol use. As countries move toward HIV elimination, reaching the hardest-to-reach-populations will be essential. For PWH reporting hazardous alcohol use, integrated patient-centered, streamlined HIV care with universal testing and treatment has the potential to close critical gaps in the HIV care cascade.

## ACKNOWLEDGEMENTS

The SEARCH project gratefully acknowledges the Ministries of Health of Uganda and Kenya, our research team, collaborators, and especially all communities and participants involved.

### Sources of Support:

Supported by the Division of AIDS, National Institute of Allergy and Infectious Diseases of the National Institutes of Health (NIH) (UM1AI068636 and U01AI099959, D.V.H.) and in part by the President's Emergency Plan For AIDS Relief and Gilead Sciences, which provided tenofovir–emtricitabine (Truvada) in kind. Additional funding by the National Institute on Alcohol Abuse and Alcoholism (K23 AA029045, SBP; K24 AA022586, J.A.H.) of the NIH.

### Conflicts of Interest and Sources of Funding:

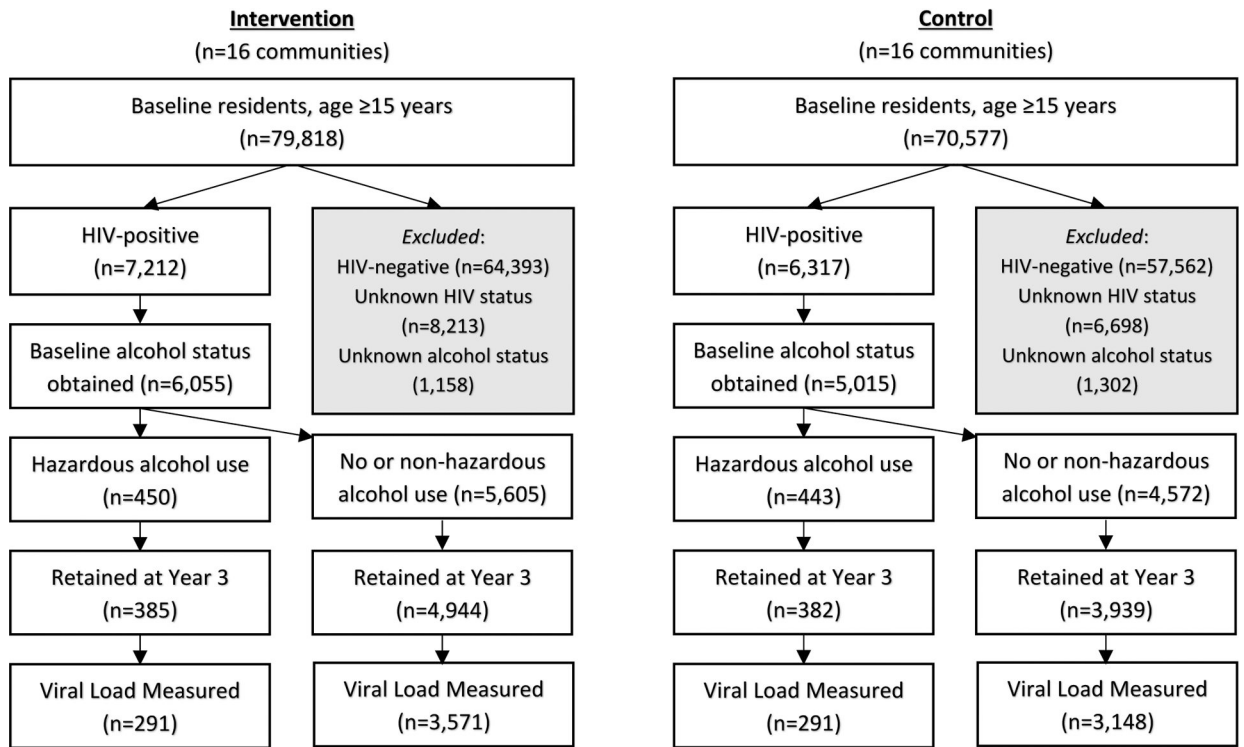
The authors have no conflicts of interest to disclose.

## REFERENCES

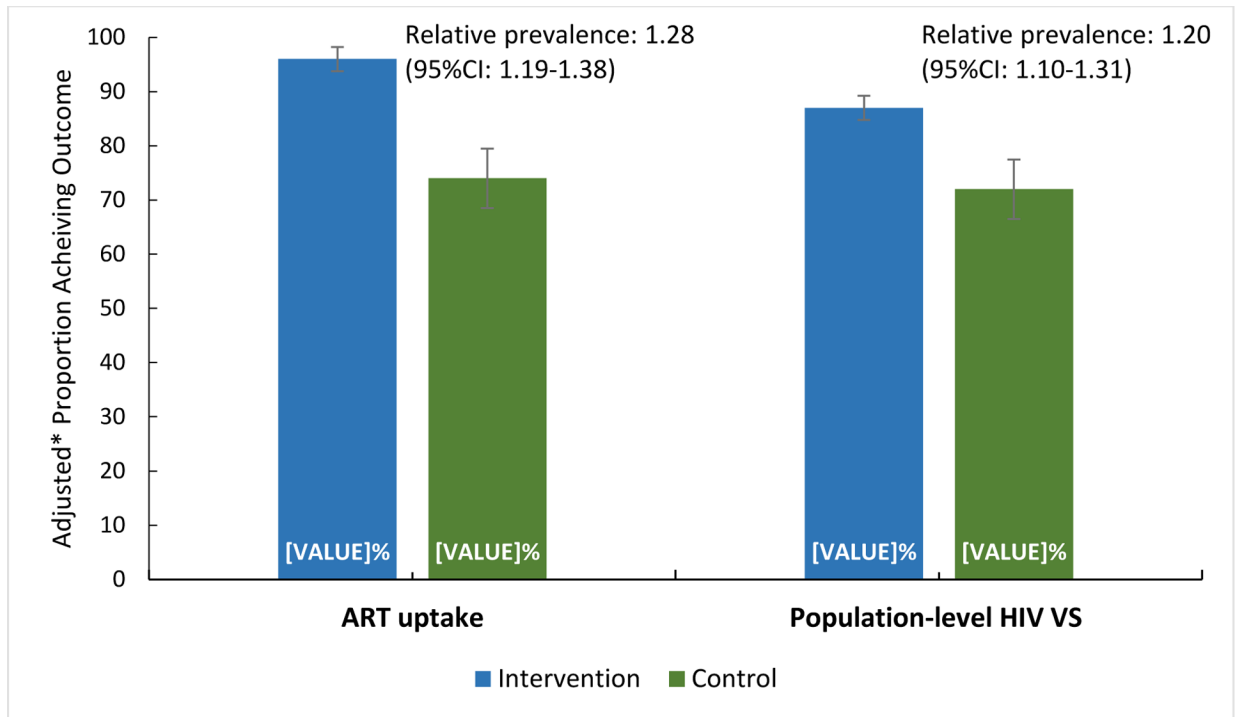
1. Hahn JA, Woolf-King SE, Muyindike W. Adding fuel to the fire: alcohol's effect on the HIV epidemic in Sub-Saharan Africa. *Curr HIV/AIDS Rep.* 2011;8(3):172–180. [PubMed: 21713433]
2. Patsis I, Goodrich S, Yiannoutsos CT, et al. Lower rates of ART initiation and decreased retention among ART-naïve patients who consume alcohol enrolling in HIV care and treatment programs in Kenya and Uganda. *PLoS One.* 2020;15(10):e0240654. [PubMed: 33095784]
3. Vagenas P, Azar MM, Copenhaver MM, Springer SA, Molina PE, Altice FL. The Impact of Alcohol Use and Related Disorders on the HIV Continuum of Care: a Systematic Review : Alcohol and the HIV Continuum of Care. *Curr HIV/AIDS Rep.* 2015;12(4):421–436. [PubMed: 26412084]
4. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: review and meta-analysis. *J Acquir Immune Defic Syndr.* 2009;52(2):180–202. [PubMed: 19668086]
5. Chander G, Lau B, Moore RD. Hazardous alcohol use: a risk factor for non-adherence and lack of suppression in HIV infection. *J Acquir Immune Defic Syndr.* 2006;43(4):411–417. [PubMed: 17099312]
6. Miller AP, Pitpitan EV, Kiene SM, et al. Alcohol use and alcohol-related consequences are associated with not being virally suppressed among persons living with HIV in the Rakai region of Uganda. *Drug Alcohol Depend.* 2021;228:109005. [PubMed: 34600249]
7. Puryear SB, Balzer LB, Ayieko J, et al. Associations between alcohol use and HIV care cascade outcomes among adults undergoing population-based HIV testing in East Africa. *AIDS (London, England).* 2019.
8. Justice AC, McGinnis KA, Tate JP, et al. Risk of mortality and physiologic injury evident with lower alcohol exposure among HIV infected compared with uninfected men. *Drug Alcohol Depend.* 2016;161:95–103. [PubMed: 26861883]
9. Neblett RC, Hutton HE, Lau B, McCaul ME, Moore RD, Chander G. Alcohol consumption among HIV-infected women: impact on time to antiretroviral therapy and survival. *J Womens Health (Larchmt).* 2011;20(2):279–286. [PubMed: 21281111]
10. Duko B, Ayalew M, Ayano G. The prevalence of alcohol use disorders among people living with HIV/AIDS: a systematic review and meta-analysis. *Subst Abuse Treat Prev Policy.* 2019;14(1):1–9. [PubMed: 30606266]
11. Kalichman S, Mathews C, Banas E, Kalichman M. Alcohol-related intentional nonadherence to antiretroviral therapy among people living with HIV, Cape Town, South Africa. *AIDS Care.* 2019:1–7.
12. Ferro EG, Culbert GJ, Wickersham JA, et al. Physician Decisions to Defer Antiretroviral Therapy in Key Populations: Implications for Reducing Human Immunodeficiency Virus Incidence and Mortality in Malaysia. *Open Forum Infect Dis.* 2017;4(1):ofw219. [PubMed: 28480230]
13. Campbell ANC, Wolff M, Weaver L, Jarlais DD, Tross S. “It’s Never Just About the HIV:” HIV Primary Care Providers’ Perception of Substance Use in the Era of “Universal” Antiretroviral Medication Treatment. *AIDS Behav.* 2018;22(3):1006–1017. [PubMed: 29264736]
14. Kalichman S, Banas E, Kalichman M, Mathews C. Stigmatisation of alcohol use among people receiving antiretroviral therapy for HIV infection, Cape Town, South Africa. *Global Public Health.* 2020;15(7):1040–1049. [PubMed: 32053472]
15. Pellowski JA, Kalichman SC, Kalichman MO, Cherry C. Alcohol-antiretroviral therapy interactive toxicity beliefs and daily medication adherence and alcohol use among people living with HIV. *AIDS Care.* 2016;28(8):963–970. [PubMed: 26964014]
16. Nkosi S, Rich EP, Kekwaletswe CT, Morojele NK. Experiences of alcohol consumption and taking antiretroviral medication among men living with HIV in Tshwane, South Africa. *Afr J AIDS Res.* 2016;15(4):367–376. [PubMed: 27974021]
17. Lancaster KE, Hetrick A, Jaquet A, et al. Substance use and universal access to HIV testing and treatment in sub-Saharan Africa: implications and research priorities. *J Virus Erad.* 2018;4(Suppl 2):26–32.

18. Kalichman S, Banas E, Kalichman M, Mathews C. Stigmatisation of alcohol use among people receiving antiretroviral therapy for HIV infection, Cape Town, South Africa. *Glob Public Health*. 2020;15(7):1040–1049. [PubMed: 32053472]
19. Marlatt GA, Witkiewitz K. Update on harm-reduction policy and intervention research. *Annu Rev Clin Psychol*. 2010;6:591–606. [PubMed: 20192791]
20. Satre DD, Sarovar V, Leyden W, et al. Changes in Days of Unhealthy Alcohol Use and Antiretroviral Therapy Adherence, HIV RNA Levels, and Condomless Sex: A Secondary Analysis of Clinical Trial Data. *AIDS Behav*. 2020;24(6):1784–1792. [PubMed: 31773444]
21. Scott-Sheldon LAJ, Carey KB, Johnson BT, Carey MP, Team MR. Behavioral Interventions Targeting Alcohol Use Among People Living with HIV/AIDS: A Systematic Review and Meta-Analysis. *AIDS Behav*. 2017;21(Suppl 2):126–143. [PubMed: 28831609]
22. Springer SA, Di Paola A, Barbour R, Azar MM, Altice FL. Extended-release Naltrexone Improves Viral Suppression Among Incarcerated Persons Living with HIV and Alcohol use Disorders Transitioning to the Community: Results From a Double-Blind, Placebo-Controlled Trial. *J Acquir Immune Defic Syndr*. 2018;79(1):92–100. [PubMed: 29781884]
23. Braithwaite RS, Nucifora KA, Kessler J, et al. How inexpensive does an alcohol intervention in Kenya need to be in order to deliver favorable value by reducing HIV-related morbidity and mortality? *J Acquir Immune Defic Syndr*. 2014;66(2):e54–58. [PubMed: 24828269]
24. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. *J Fam Pract*. 2000;49(9):796–804. [PubMed: 11032203]
25. Hawk M, Coulter RWS, Egan JE, et al. Harm reduction principles for healthcare settings. *Harm Reduction Journal*. 2017;14(1):70. [PubMed: 29065896]
26. Havlir DV, Balzer LB, Charlebois ED, et al. HIV Testing and Treatment with the Use of a Community Health Approach in Rural Africa. *N Engl J Med*. 2019;381(3):219–229. [PubMed: 31314966]
27. Chamie G, Clark TD, Kabami J, et al. A hybrid mobile approach for population-wide HIV testing in rural east Africa: an observational study. *Lancet HIV*. 2016;3(3):e111–119. [PubMed: 26939734]
28. Kwarisiima D, Kanya MR, Owaraganise A, et al. High rates of viral suppression in adults and children with high CD4+ counts using a streamlined ART delivery model in the SEARCH trial in rural Uganda and Kenya. *J Int AIDS Soc*. 2017;20(Suppl 4):21673. [PubMed: 28770596]
29. Hickey MD, Ayieko J, Kwarisiima D, et al. Improved Viral Suppression With Streamlined Care in the SEARCH Study. *J Acquir Immune Defic Syndr*. 2020;85(5):571–578. [PubMed: 32991337]
30. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcohol Clin Exp Res*. 2007;31(7):1208–1217. [PubMed: 17451397]
31. Balzer LB, van der Laan M, Ayieko J, et al. Two-Stage TMLE to reduce bias and improve efficiency in cluster randomized trials. *Biostatistics*. 2021.
32. Balzer LB, van der Laan MJ, Petersen ML. Adaptive pre-specification in randomized trials with and without pair-matching. *Stat Med*. 2016;35(25):4528–4545. [PubMed: 27436797]
33. UNAIDS. UNAIDS Data 2018. 2018.
34. Kabami J, Balzer LB, Saddiki H, et al. Population-level viral suppression among pregnant and postpartum women in a universal test and treat trial. *AIDS*. 2020;34(9):1407–1415. [PubMed: 32472768]
35. Kanya MR, Petersen ML, Kabami J, et al. SEARCH Human Immunodeficiency Virus (HIV) Streamlined Treatment Intervention Reduces Mortality at a Population Level in Men With Low CD4 Counts. *Clin Infect Dis*. 2021;73(7):e1938–e1945. [PubMed: 33783495]
36. Madhombiro M, Musekiwa A, January J, Chingono A, Abas M, Seedat S. Psychological interventions for alcohol use disorders in people living with HIV/AIDS: a systematic review. *Syst Rev*. 2019;8(1):244. [PubMed: 31661030]
37. Wandera B, Tumwesigye NM, Nankabirwa JI, et al. Efficacy of a Single, Brief Alcohol Reduction Intervention among Men and Women Living with HIV/AIDS and Using Alcohol in Kampala, Uganda: A Randomized Trial. *Journal of the International Association of Providers of AIDS Care*. 2017;16(3):276–285. [PubMed: 27215561]

38. Papas R, Gakinya B, Mwaniki M, et al. Successful treatment outcomes from a stage 2 randomized clinical trial of CBT to reduce alcohol use among HIV-infected outpatients in Western Kenya. Paper presented at: ALCOHOLISM-CLINICAL AND EXPERIMENTAL RESEARCH2017.
39. Huis in 't Veld D, Ensoy-Musoro C, Pengpid S, Peltzer K, Colebunders R. The efficacy of a brief intervention to reduce alcohol use in persons with HIV in South Africa, a randomized clinical trial. *PLoS One*. 2019;14(8):e0220799. [PubMed: 31430313]
40. Wechsberg WM, Browne FA, Ndirangu J, et al. Outcomes of Implementing in the Real World the Women's Health CoOp Intervention in Cape Town, South Africa. *AIDS Behav*. 2021;25(3):276–289. [PubMed: 33891233]
41. Papas RK, Gakinya BN, Mwaniki MM, et al. A randomized clinical trial of a group cognitive-behavioral therapy to reduce alcohol use among human immunodeficiency virus-infected outpatients in western Kenya. *Addiction*. 2021;116(2):305–318. [PubMed: 32422685]
42. Lebelonyane R, Bachanas P, Block L, et al. To achieve 95–95–95 targets we must reach men and youth: High level of knowledge of HIV status, ART coverage, and viral suppression in the Botswana Combination Prevention Project through universal test and treat approach. *PLoS One*. 2021;16(8):e0255227. [PubMed: 34375343]
43. Makhema J, Wirth KE, Pretorius Holme M, et al. Universal Testing, Expanded Treatment, and Incidence of HIV Infection in Botswana. *N Engl J Med*. 2019;381(3):230–242. [PubMed: 31314967]
44. Bajunirwe F, Haberer JE, Boum Y 2nd et al. Comparison of self-reported alcohol consumption to phosphatidylethanol measurement among HIV-infected patients initiating antiretroviral treatment in southwestern Uganda. *PLoS One*. 2014;9(12):e113152. [PubMed: 25436894]

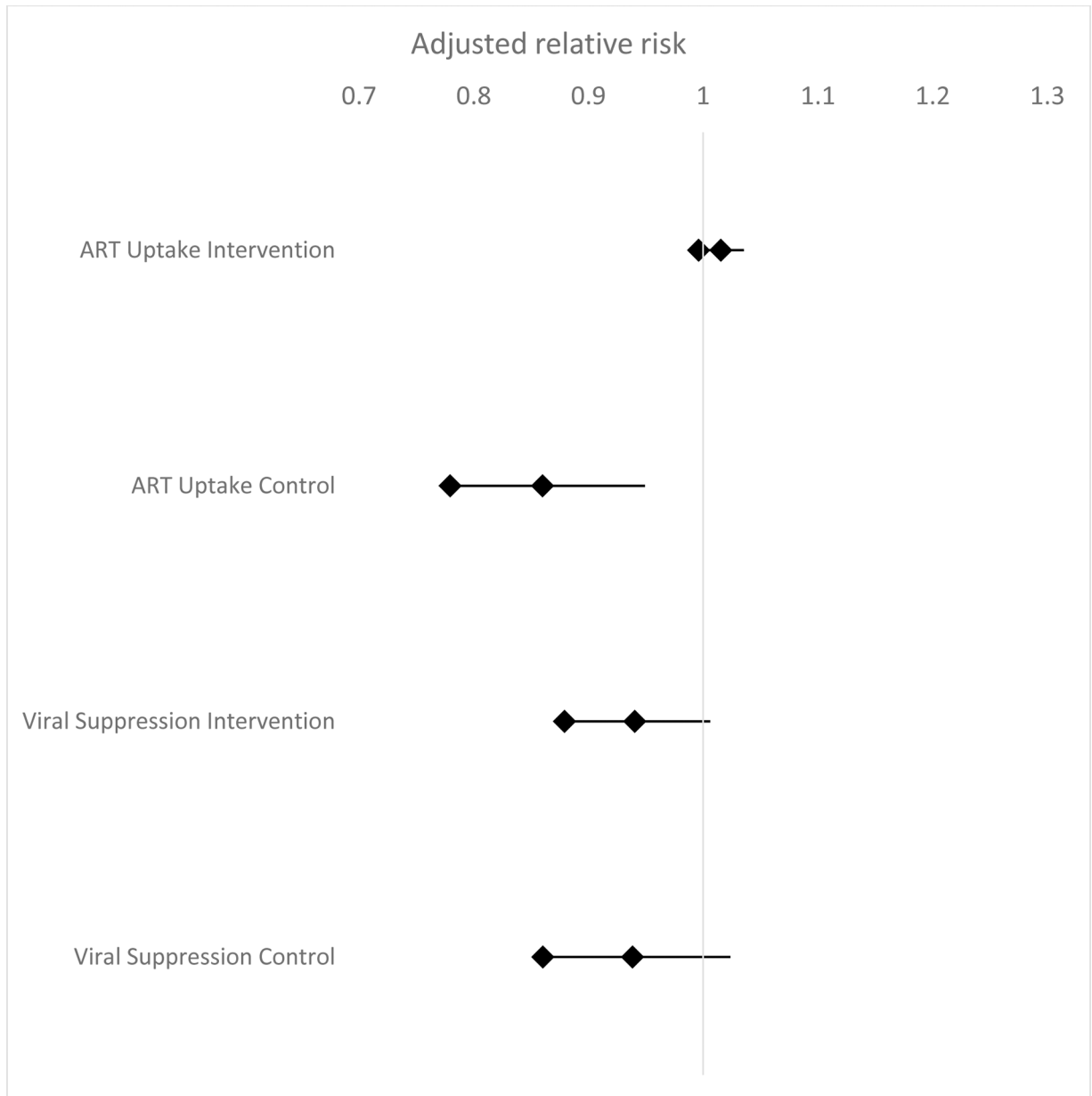


**Figure 1:**  
Participant Flow chart



**Figure 2:** Comparison of ART uptake and HIV viral suppression at Year 3 between SEARCH trial arms among PWH reporting hazardous alcohol use at baseline  
 \*Estimated within each community and compared at the community-level by arm with targeted maximum likelihood estimation (TMLE) . Black vertical lines indicated 95% confidence intervals.





**Figure 3:**

By SEARCH trial arm, hazardous alcohol use as a predictor of ART uptake and HIV viral suppression at year 3.

Adjusted relative risks estimated using individual-level TMLE.

Abbreviations: ART, antiretroviral therapy; TMLE, targeted maximum likelihood estimation

**Table 1:**

Baseline characteristics of adults (age ≥ 15 years) with HIV in rural Uganda and Kenya, stratified by SEARCH trial arm and self-reported level of baseline alcohol use (n=11,070)

Characteristic	INTERVENTION (n=6055)				CONTROL (n=5015)			
	Hazardous Alcohol Use		No/no-hazardous alcohol use		Hazardous Alcohol Use		No/non-hazardous alcohol use	
	n	%	n	%	n	%	n	%
Total	450	7.4	5,605	92.6	443	8.8	4,572	91.2
Country								
Kenya	132	29.3	3,692	65.9	139	31.4	2,715	59.4
Uganda	318	70.7	1,913	34.1	304	68.6	1,857	40.6
Age, y								
15–24	25	5.6	773	13.8	26	5.9	581	12.7
25–34	132	29.3	1,882	33.6	141	31.8	1,595	34.9
35–44	171	38.0	1,606	29.0	146	33.0	1,285	28.1
45	122	27.1	1,344	24.0	130	29.4	1,111	24.3
Sex								
Female	121	26.9	3,813	68.0	109	24.6	3,045	66.6
Male	329	73.1	1,792	32.0	334	75.4	1,527	33.4
Marital status								
Single	44	9.8	417	7.4	45	10.2	343	7.5
Married	306	68.0	3,846	68.6	303	68.4	3,142	68.7
Widowed, divorced, separated	100	22.2	1,335	23.8	94	21.2	1,082	23.7
Missing	-	-	7	0.1	1	0.2	5	0.1
Occupation								
Formal sector <sup>A</sup>	30	6.7	286	5.1	22	5.0	245	5.4
Informal sector <sup>B</sup>	370	82.2	4,708	84.0	368	83.1	3,838	84.0
Other	36	8.0	281	5.0	41	9.3	222	4.9
No job/disabled	14	3.1	325	5.8	11	2.5	262	5.7
Missing	-	-	5	0.1	1	0.2	5	0.1
Education								
Less than primary	274	60.9	4,191	74.8	307	69.3	3,368	73.67
Primary	60	13.3	666	11.9	66	14.9	572	12.51
Secondary or more	115	25.6	736	13.1	69	15.6	610	13.3
Missing	1	0.2	12	0.2	1	0.2	22	0.5
Wealth quintile categories <sup>C</sup>								
First, indicating least wealth	105	23.3	954	17.0	123	27.8	955	20.9
Second	83	18.4	980	17.5	90	20.3	751	16.4
Third	73	16.2	1,046	18.7	71	16.0	926	20.3

	INTERVENTION (n=6055)				CONTROL (n=5015)			
	Hazardous Alcohol Use		No/no-hazardous alcohol use		Hazardous Alcohol Use		No/non-hazardous alcohol use	
Characteristic	n	%	n	%	n	%	n	%
Fourth	101	22.4	1,208	21.6	70	15.8	969	21.2
Fifth, indicating most wealth	74	16.4	1,342	23.9	71	16.0	888	19.4
Missing	14	3.1	75	1.3	18	4.1	83	1.8
Mobile <sup>D</sup>	78	17.3	519	9.3	76	17.2	518	11.3
Alcohol use category <sup>E</sup>								
Non-use	-	-	5,175	92.3	-	-	4,172	91.3
Non-hazardous use	-	-	430	7.7	-	-	400	8.8
Hazardous use	450	100	-	-	443	100	-	-
On ART at baseline								
CD4+ at baseline	170	37.8	3,193	56.9	156	35.2	2,366	51.8
<200	45	10.0	382	6.8	42	9.5	345	7.6
200–350	90	20.0	z	15.4	83	18.7	700	15.3
351–500	101	22.4	1,217	21.7	102	23.0	947	20.7
>500	182	40.4	2,698	48.1	178	40.2	2,124	46.5
Missing	32	7.1	446	8.0	38	8.6	456	10.0
HIV RNA <500 copies/ml at baseline *	94/299	31.4	2,088/4,207	49.6	112/343	32.7	1,608/3,168	50.8

<sup>A</sup> **Formal sector** occupation defined as teacher, student, government worker, military worker, health worker, or factory worker.

<sup>B</sup> **Informal sector** occupation defined as fishmonger, fisherman, bar owner, bar worker, transport, tourism, farmer, shopkeeper, market vendor, hotel worker, homemaker, household worker, construction worker, or mining.

<sup>C</sup> **Wealth Quintile** calculated using principal component analysis of baseline household wealth survey. Calculated at the level of the household.

<sup>D</sup> **Mobility** defined as living away from the study community for more than 1 month in the past year.

<sup>E</sup> **Alcohol use category** defined by baseline AUDIT-C score as follows: “non-use” by AUDIT-C score 0, “non-hazardous use” by AUDIT-C score 1–3 for men, 1–2 for women, “hazardous use” by AUDIT-C score 4–12 for men, 3–12 for women.

\* Number participants in group with HIV plasma RNA <500 copies/ml at baseline/Number of participants with HIV plasma RNA measured at baseline