



Effects of Alcohol Use on Patient Retention in HIV Care in East Africa

Alexa Monroy¹ · Suzanne Goodrich² · Steven A. Brown³ · Theofanis Balanos³ · Giorgos Bakoyannis³ · Lameck Diero⁴ · Helen Byakwaga⁵ · Winnie Muyindike⁵ · Michael Kanyesigye⁵ · Maurice Aluda⁶ · Jayne Lewis-Kulzer⁷ · Constantin Yiannoutsos³ · Kara Wools-Kaloustian² on behalf of The East Africa International Epidemiologic Databases to Evaluate AIDS (EA-IeDEA) Consortium

Accepted: 24 August 2024
© The Author(s) 2024

Abstract

We sought to investigate the association between hazardous alcohol use and gaps in care for people living with HIV over a long-term follow-up period. Adults who had participated in our previously published Phase I study of hazardous alcohol use at HIV programs in Kenya and Uganda were eligible at their 42 to 48 month follow-up visit. Those who re-enrolled were followed for an additional ~12 months. Hazardous alcohol use behavior was measured using the Alcohol Use Disorders Identification Test (AUDIT) tool. Deidentified clinical data were used to assess gaps in care (defined as failure to return to clinic within 60 days after a missed visit). The proportion of patients experiencing a gap in care at a specific time point was based on a nonparametric moment-based estimator. A semiparametric Cox proportional hazard model was used to determine the association between hazardous alcohol use at enrollment in Phase I (AUDIT score ≥ 8) and gaps in care. Of the 731 study-eligible participants from Phase I, 5.5% had died, 10.1% were lost to follow-up, 39.5% transferred, 7.5% declined/not approached, and 37.3% were enrolled. Phase II participants were older, had less hazardous drinking and had a lower WHO clinical stage than those not re-enrolled. Hazardous drinking in the re-enrolled was associated with a Hazard Ratio (HR) of 1.88 [p-value = 0.016] for a gap in care. Thus, hazardous alcohol use at baseline was associated with an increased risk of experiencing a gap in care and presents an early target for intervention.

Keywords Gap in care · Alcohol · East Africa · HIV

✉ Alexa Monroy
alexam.monroy@gmail.com

¹ Division of Emergency Medicine, Department of Emergency and Transport Medicine, Children's Hospital Los Angeles, 4650 Sunset Blvd. MS # 113, Los Angeles, CA, USA

² Division of Infectious Diseases, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA

³ Department of Biostatistics and Health Data Science, Indiana University Fairbanks School of Public Health and School of Medicine, Indianapolis, IN, USA

⁴ Department of Medicine Moi, College of Health Sciences, Moi University, Eldoret, Kenya

⁵ Division of HIV Care, Mbarara University of Science and Technology/ Mbarara Regional Referral Hospital, Mbarara, Uganda

⁶ Centre for Microbiology Research, Kenya Medical Research Institute, Kisumu, Kenya

⁷ Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA, USA

Resumen

Buscamos investigar la asociación entre el uso riesgoso de alcohol y retención en programas de VIH a largo plazo. Todo adulto que participó en nuestro estudio previamente publicado sobre el uso riesgoso de alcohol en programas de VIH en Kenia y Uganda era elegible a los 42 a 48 meses de seguimiento. Los adultos reinscritos en la fueron seguidos por ~ 12 meses adicionales. Usamos el “Alcohol Use Disorders Identification Test” (AUDIT) para medir uso de alcohol. Usamos datos clínicos anonimizados para evaluar interrupciones en cuidado (definido como falta de regresar a clínica 60 días después de faltar a una cita). Basamos la proporción de pacientes con una interrupción en cuidado clínico en un estimador momentáneo y no-paramétrico. Determinamos la asociación entre el uso riesgoso de alcohol al inicio de la primera fase (puntuación AUDIT ≥ 8) con retención en servicios clínicos usando un modelo de riesgo Cox semiparamétrico. De los 731 participantes elegibles, 5.5% habían muerto, 10.1% fueron perdidos a seguimiento clínico, 39.5% se transfirieron a otro programa, 7.5% declinaron participación o no fueron reclutados y 37.3% fueron reinscritos en la segunda fase. Los participantes reinscritos eran mayores, tenían menos uso riesgoso de alcohol y tenían VIH menos avanzado. El uso peligroso del alcohol se vio asociado con el riesgo de tener una interrupción en cuidado clínico [Proporción de Riesgo (Hazard Ratio, HR) PR=1.88, valor-p = 0.016]. Por lo tanto, el uso peligroso del alcohol incrementa el riesgo de perder seguimiento clínico y presenta una oportunidad para intervención.

Introduction

Alcohol use is one of the top ten risk factors for overall global disease burden and precipitates mortality from both communicable and non-communicable diseases [1]. For people living with HIV (PLHIV), alcohol consumption exacerbates comorbidities and can disrupt the HIV care cascade at various points [1–7]. In the United States (U.S), 51–63% of PLHIV consume alcohol and 15–25% are “heavy drinkers”, consuming alcohol at twice the rate of the general population [8–10]. Studies from western and southern Africa have reported more variability in the prevalence of alcohol consumption among PLHIV, with rates ranging between 10–52% for any alcohol use and 2.6–30% for consumption above recommended limits (hazardous or disordered drinkers) [10–16]. Since alcohol use patterns vary greatly between countries and have important ramifications for HIV care provision, it is vital to understand the landscape of alcohol use in East Africa and characterize its impact on the HIV care cascade.

Alcohol consumption correlates with higher viral loads at enrollment, longer delays in antiretroviral treatment (ART) initiation and worse adherence to ART once engaged in care [6, 12, 14, 17]. The link between alcohol use and health care utilization, however, is less clear. In one study conducted in the U.S., heavy alcohol use had no impact on outpatient HIV care visits for a nationally representative sample of PLHIV. However, it was associated with fewer clinic visits for an at-risk cohort with a higher proportion of patients from minority groups with low socio-economic status, unemployment, homelessness, lack of insurance and illicit drug use [18]. Other studies conducted at HIV clinics in Nigeria and the U.S. have reported no significant association between heavy drinking and outpatient HIV clinic visit attendance [14, 19]. On the other hand, two

separate studies from South Africa and the U.S. found that heavy alcohol use at enrollment led to worse retention in HIV care at six and 12 months, respectively [9, 11]. In 2020, Patsis et al. published an observational study for our group of ART-naïve patients accessing care in Kenya and Uganda, in which 41.6% of the cohort consumed alcohol, 26.7% were hazardous drinkers (Alcohol Use Disorder Identification Test (AUDIT) score ≥ 8) and 16% were hyper drinkers (AUDIT score ≥ 16) [20]. In this cohort, any alcohol consumption was associated with a 25% lower likelihood of ART initiation in the pre-Treat All era, and a 77% higher risk of non-retention in care [20]. Thus, findings related to the impact of alcohol use on retention in the HIV care cascade vary across populations and settings. Our understanding of these relationships is limited by sparse data on the association between alcohol use and long-term retention in HIV care, especially in low- and middle-income countries (LMICs).

To better understand the long-term clinical impact of alcohol use patterns at time of enrollment into HIV care, we followed-up participants from the *Alcohol Use Assessment Sentinel Cohort* (AUAC) originally described by Patsis et al. [20]. The AUAC was a prospective study of adults (≥ 18 years) enrolling in HIV care at one of the five participating East Africa International Epidemiology Databases to Evaluate AIDS (EA-IeDEA) sites between January 25, 2013, and June 25, 2014 (Phase I). Baseline characteristics, recruitment details, and competing risk analysis for loss to follow-up and death were reported by Patsis et al. [20], and major findings are summarized in the paragraph above. In this study, we present results for Phase II of the same cohort. The primary outcome was likelihood of experiencing a gap in care at a median 48.7 months after enrollment in Phase II (range: 40.7 to 61.2 months). We also present the longitudinal analysis for Phase II of our study,

which includes clinical outcomes and risk of experiencing a gap in care at approximately 12 months after re-enrollment into the long-term portion of the study (median 11.5 months; range: 6.0 to 26.1 months). In addition, we present how alcohol use disorder patterns changed over this time by assessing change in AUDIT from enrollment in Phase I and throughout the Phase II follow-up period. Our results provide insight into factors present at enrollment that can affect the success of HIV care programs in the long-term.

Methods

Study Design

The original AUAC cohort was enrolled between January 25, 2013, and June 25, 2014 (Phase I) and short-term outcomes were described by Patsis et al. [20]. For the present study, the goal was to approach Phase I participants for re-enrollment in a second phase of the study approximately 42 to 48 months post-enrollment in Phase I and to follow them for an additional 12 months. However, due to delays in regulatory approval at some sites, there were staggered study initiation dates and a wide range of follow-up periods. In the end, participants were approached at a median of 48.7 months post-enrollment in Phase I for re-enrollment in Phase II (range 40.7–61.2 months). Participants opting into Phase II were followed for an additional median duration of 11.5 months from July 27, 2017 to July 5, 2018 (range 6.0–26.1 months). Data for Phase I participants who did not enroll into Phase II were reviewed at the initiation of Phase II to determine engagement status. For Phase II participants, our primary outcome was risk of experiencing a gap in care during the long-term follow-up period. Our primary exposure was the AUDIT questionnaire score at enrollment into Phase I (details of the questionnaire are described in further detail under Study Procedures). Only participants who consented to participation in both Phase I and Phase II were included in the longitudinal analysis. Our secondary outcome was change in AUDIT score at the time of enrollment in Phase II (median 48.7 months post enrollment in Phase I, range: 40.7–61.2 months).

The study was approved by the Indiana University Institutional Review Board and the ethical bodies affiliated with each participating site: The Academic Model Providing Access to Healthcare (AMPATH); Moi University College of Health Sciences and MOI Teaching and Referral Hospital's Institutional Research and Ethics Committee; Kenya Medical Research Institute (KEMRI) affiliated sites: KEMRI National Ethics Review Committee; Mbarara Immune Suppression Syndrome (ISS) Clinic; Mbarara University of Science & Technology Institutional Review Committee and Uganda National Council of Science and

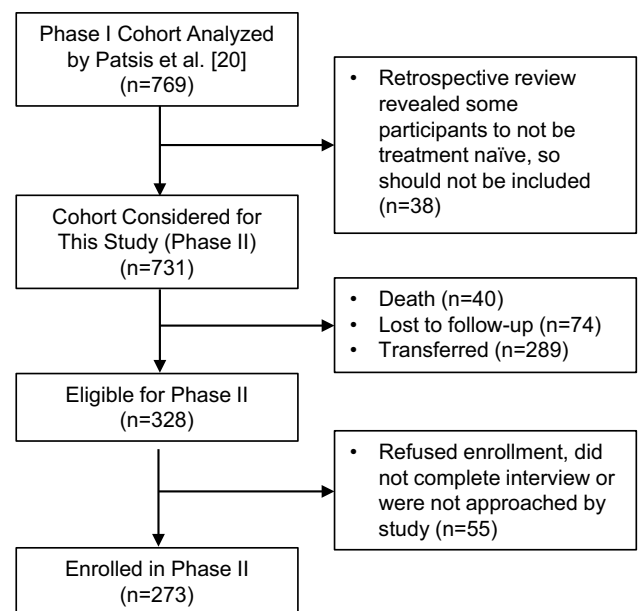


Fig. 1 Total enrollment numbers in phase II

Technology (UNCST). All participants were consented at enrollment and again before starting Phase II of the study.

Study Setting

Five clinics within the EA-IeDEA consortium participated in this study: Two KEMRI affiliated clinics (Kisumu and Homa Bay, Kenya); two AMPATH clinics (Eldoret, Kenya); and the ISS in Mbarara, Uganda. The sites in Eldoret and Kisumu are primarily urban. Suba District Hospital in Homa Bay is rural and Mbarara is semi-urban. All the clinics provide comprehensive HIV care according to their country's National Guidelines.

Study Population and Sample Size

All adult patients (≥ 18 years old) who were ART-naïve at the time of initial encounter and presented for HIV care at one of the above clinics were eligible for participation in Phase I of the study [20]. Patients were referred for enrollment by their clinician and consented for participation. All patients enrolled in Phase I were eligible for participation in Phase II except for 38 participants who were misclassified as ART-naïve in Phase I. A detailed flowchart for patient enrollment in both phases is included in Fig. 1.

Study Procedures

The initial phase of the study collected baseline characteristics, demographic information, and hazardous alcohol use behavior via the AUDIT questionnaire, which

was repeated at the Phase II visit [20, 21]. The AUDIT questionnaire was completed in English, Swahili, Luo or Rukiga/Runyankole, depending on a participant's preferred language.

Study Measures

The AUDIT is a 10-question instrument that asks about hazardous alcohol use patterns, with higher scores indicating a greater risk of having an alcohol use disorder [21]. The AUDIT questionnaire has been validated for our setting. The first three questions inquire about present alcohol use; if a patient scored 0 on these first three questions (no alcohol consumption), then subsequent questions were not asked. With a maximum total score of 40 points, a score ≥ 8 was classified as hazardous drinking, while a score ≥ 16 was classified as hyper drinking. These terms were defined in our prior paper and are used for ease of discussing individuals with AUDIT scores equal to or greater than 8 and 16, respectively [20]. All patients received a pamphlet on HIV and Alcohol Consumption after each administration of the AUDIT regardless of AUDIT score. AUDIT scores were also shared with clinical officers to inform clinical care.

Data Collection and Management

Study data were collected on paper Case Report Forms (CRFs) and then transferred to a password-protected REDCap database (developed by the East Africa IeDEA Regional Data Center [EA-RDC]) by the research assistants. Data collected as part of the routine clinic visit, such as demographic information, CD4 counts, viral loads, and WHO disease stage were extracted from the electronic medical record and entered into REDCap. All stored data were de-identified with CRFs using only study identification numbers (ID) for reference. The EA-RDC used separately stored study ID mapping files to confirm patient linkage. After data were linked, comprehensive data quality procedures were performed, including verification of value ranges, categorization of variables, and consistency checks across the data sources. All queries resulting from these procedures were investigated at each site and updated accordingly in the study database prior to analysis.

Statistical Analysis

Categorical variables were described using frequencies and proportions. Descriptions of the quantitative variables were based on the median and interquartile range (IQR). Two-sample comparisons of categorical variables were based on Pearson's chi-squared test. The nonparametric Mann–Whitney test was used to perform two-sample comparisons for the quantitative variables. The main

outcomes of interest were gaps in care after enrolling in Phase II. A gap in care was defined as no attendance for more than 60 days after a scheduled visit was missed. Because our clinic visits are associated with pharmacy refills, failure to return to clinic for more than 60 days after a missed appointment would be associated with a 60-day gap in access to ART [22, 23]. The conceptual multistate model of patient “churning” in and out of care has been described in previous manuscripts [24, 25]. This model captures the dynamic nature of the disengagement and re-engagement back in the care process. The goal of this analysis is to estimate the proportion of patients experiencing a gap in care at a specific point in time. The estimation of these quantities over time was based on a nonparametric moment-based estimator [26]. This estimator accounts for both the potential within-clinic correlation of patient outcomes and right censoring, defined as being alive by the end of the follow-up period. Unlike a traditional Kaplan–Meier survival curve which would depict the cumulative probability of just being gap-in-care-free, our approach provides an estimate of being in a gap in care at each timepoint throughout the entire follow-up period. This estimate incorporates all the gap in care events observed for each patient (not just the first one) and, also, the duration of each gap in care. Thus, it efficiently depicts the entire gap in care event history in our population. The probability of having a gap in care was statistically compared between those with and without hazardous drinking behavior at enrollment using a linear nonparametric two-sample test [27, 28]. To adjust for the lack of independence within clinics, variance estimation for the latter test statistic was performed using nonparametric cluster bootstrap at the clinic level, with 1000 replications [26]. To evaluate the effect of hazardous drinking on the rates of gap in care, while accounting for potential confounders, we fitted a semiparametric Cox proportional hazards model for recurrent events that incorporates all the gap in care events observed for each patient (and not just the first event). By analyzing all the observed gap in care events, we can obtain more precise effect estimates and achieve more powerful statistical hypothesis tests. The potential correlation of recurrent gaps in care for the same patient was taken into account using an appropriate sandwich-type variance estimator. Due to the small number of clinics, we accounted for the potential association between patients from the same clinic by incorporating clinic as a categorical covariate in the Cox model [29].

A secondary outcome was a change in alcohol consumption behavior between enrollment and the Phase II visit. We chose this outcome to explore whether engaging in the care continuum impacts alcohol use behavior. As in Phase I, patient AUDIT scores were classified into consumption categories, then designated by comparison to Phase I as “same”, “higher”, or “lower”. This categorical

change in alcohol consumption behavior was analyzed using multinomial logistic regression. Like the multivariable analyses of gaps in care, the potential within-clinic dependence was accounted for by incorporating clinic as a categorical covariate in the model.

Results

Patient Characteristics

Of the 731 Phase I participants identified as eligible for re-enrollment in Phase II, 40 (5.5%) had died, 74 (10.1%) were lost-to-follow-up (LTFU) and 289 (39.5%) had transferred to a non-study facility (Fig. 1). This resulted in a total of 328 patients being eligible for enrollment in Phase II, of whom 55 (7.5%) declined participation or were not approached. Participants were enrolled in Phase II at a median of 48.7 months (range 40.7–61.2 months) after enrollment in Phase I. The baseline characteristics of individuals enrolling in Phase II (N = 273), not enrolling (N = 458), and the total Phase I cohort (N = 731) are outlined in Table 1. Those enrolled versus not enrolled in Phase II were similar in terms of sex distribution, CD4 cell count, and HIV-disclosure status. However, Phase II participants were more likely to be older, have a lower AUDIT score and a lower enrollment WHO clinical stage and were less likely

to be enrolled at Mbarara, as compared to those participating in Phase I but not Phase II.

Most Phase II participants were female (65%) and the median age was 33.5 (IQR: 26.8, 41.7) years (Table 1). At baseline, the median CD4 cell count was 327 (IQR: 165, 511), most had a WHO Clinical Stage of 1 or 2 (86.4%) and most (60.2%) had not disclosed their HIV status. Participants were predominantly enrolled from KEMRI (39.9%) and AMPATH (38.8%) affiliated sites compared to Mbarara (21.2%). The baseline AUDIT for those enrolling in Phase II identified hazardous drinking behavior in 66 participants (24.2%; AUDIT score ≥ 8), moderate drinking in 35 participants (12.8%; AUDIT ≥ 1 and ≤ 7), and no alcohol use in 172 participants (63.0%). On repeat AUDIT hazardous drinking behavior was identified in 51 participants (18.7%), moderate drinking in 26 participants (9.5%), and no alcohol use in 196 participants (71.8%). The majority (61%) had no change in AUDIT score while 28% had a reduced score and 11% had a higher score.

Patient Churn and Retention in Care

For patients enrolled in Phase II, AUDIT score at time of enrollment in Phase I was used as the main predictor for experiencing a gap in care. The multistate churn model identified that the probability of a gap in care over time differs between those with and without a baseline AUDIT

Table 1 Characteristics of the phase I cohort and comparison of participants enrolled and not enrolled in phase II

	Overall N (%)	Enrolled in phase II N (%)	Not enrolled in phase II N (%)	Chi-Square	p-value
Sex				2.02	0.155
Female	447 (61.1)	176 (64.5)	271 (59.2)		
Male	284 (38.9)	97 (35.5)	187 (40.8)		
WHO stage at enrollment				8.78	0.032*
1	386 (57.3)	169 (64.3)	217 (52.8)		
2	179 (26.6)	58 (22.1)	121 (29.4)		
3	79 (11.7)	27 (10.3)	52 (12.7)		
4	30 (4.5)	9 (3.4)	21 (5.1)		
HIV status disclosed				2.30	0.129
No	265 (56.3)	124 (60.2)	141 (53.2)		
Yes	206 (43.7)	82 (39.8)	124 (46.8)		
East Africa IeDEA site				25.75	<0.001**
AMPATH	259 (35.4)	106 (38.8)	153 (33.4)		
KEMRI	236 (32.3)	109 (39.9)	127 (27.7)		
Mbarara	236 (32.3)	58 (21.2)	178 (38.9)		
				z	
Median age in years at enrollment (IQR)	30.9 (25.9, 39.6)	33.5 (26.8, 41.7)	30.6 (25.6, 37.1)	3.71	<0.001**
Median CD4 at enrollment (IQR)	327 (132, 511)	327 (165, 511)	320 (115, 513)	0.67	0.501
Median Phase I Audit-10 score (IQR)	0 (0, 9)	0 (0, 6)	0 (0, 10)	- 2.09	0.037*

* $p < .05$, ** $p < .01$

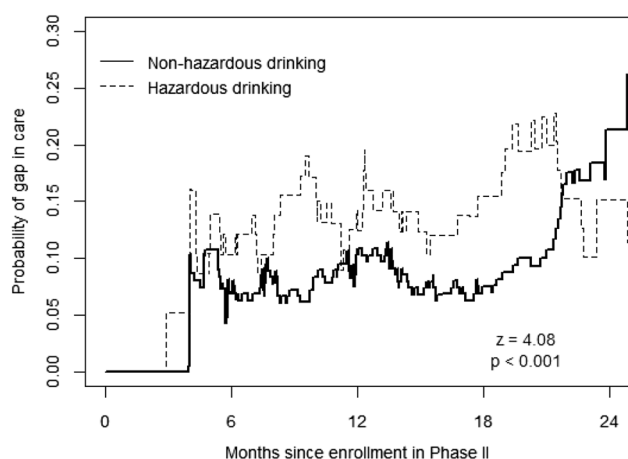


Fig. 2 Population-averaged probabilities of a gap in care by hazardous drinking status for participants enrolled in phase II. *Follow-up period for phase II was for approximately 12 months (median 11.5 months; IQR 6.9 months; minimum of 6.0 months; 26.1 months)

score indicating hazardous drinking (Fig. 2; $z = 4.08$, $p\text{-value} < 0.001$). In fact, without adjusting for potential confounders, those with hazardous drinking at enrollment in Phase I were more likely to have a gap in care at almost every time point during the long-term follow-up period.

The multivariable analysis of the hazard of a gap in care is presented in Table 2. Hazardous drinking at baseline remained associated with an increased hazard of a gap in care [Hazard Ratio (HR) = 1.88, $z = 2.415$, $p < 0.05$], after

Table 2 Multivariable analysis of the hazard of gap in care: results from a semiparametric cox proportional hazards model for recurrent events (incorporates all the gap in care events observed for each patient)

	HR	z	95% CI	p-value
Hazardous drinking				
No	1	–	–	–
Yes	1.882	2.415	(1.127, 3.143)	0.016*
Age				
Per 10 years increase	0.848	– 1.354	(0.668, 1.076)	0.176
Gender				
Female	1	–	–	–
Male	1.058	0.194	(0.601, 1.862)	0.846
HIV status disclosed				
No	1	–	–	–
Yes	1.168	0.445	(0.590, 2.314)	0.657
WHO stage				
1/2	1	–	–	–
3/4	0.725	– 0.871	(0.352, 1.494)	0.384

HR hazard ratio, 95% CI: 95% confidence interval,

*Estimates also adjusted for site, * $p < .05$, ** $p < .01$

accounting for age, gender, site, HIV status disclosure, and WHO stage at enrollment.

Change in AUDIT Score

Since hazardous alcohol use behavior was the main risk factor used for predicting the likelihood of a gap in care, change in AUDIT score throughout the study period was examined. Marginal multinomial logistic regression was used to evaluate qualitative changes in hazardous alcohol use (AUDIT score) between time of enrollment in Phase I and time of follow-up assessment during Phase II (median 11.5 months post enrollment in Phase II; range:

Table 3 Relative risk ratio of categorical change in AUDIT score between enrollment in phase I and follow-up assessment during phase II

	RRR	z	95% CI	p-value
Lower AUDIT score vs. no change in AUDIT score				
Age				
Per 10 years increase	1.352	1.62	(0.938, 1.949)	0.106
Sex				
Female	1	–	–	–
Male	1.959	1.79	(0.938, 4.091)	0.074
HIV status disclosed				
No	1	–	–	–
Yes	0.990	– 0.02	(0.423, 2.316)	0.981
WHO Stage				
1	1	–	–	–
2	1.520	0.99	(0.664, 3.481)	0.322
3	1.022	0.04	(0.351, 2.974)	0.968
4	0.972	– 0.03	(0.159, 5.943)	0.975
Higher AUDIT score vs. no change in AUDIT score				
Age				
Per 10 years increase	1.058	0.18	(0.560, 1.999)	0.860
Sex				
Female	1	–	–	–
Male	2.776	1.67	(0.836, 9.224)	0.096
HIV status disclosed				
No	1	–	–	–
Yes	4.190	2.16	(1.145, 15.34)	0.030*
WHO Stage				
1	1	–	–	–
2	2.199	1.35	(0.699, 6.951)	0.177
3	0.713	– 0.29	(0.070, 7.236)	0.775
4	6.203	1.58	(0.420, 59.87)	0.115

RRR relative risk ratio, 95% CI 95% confidence interval

*Estimates also adjusted for site; * $p < .05$, ** $p < .01$

6.0–26.1 months). Table 3 presents the results of the multivariable analysis of the categorical change in alcohol consumption. There appears to be a trend toward males being more likely to change their alcohol use behaviors relative to maintaining the same drinking behavior as compared to females, though results were not statistically significant. Participants with a disclosed HIV status at baseline were more likely to increase (RRR = 4.19, $z = 2.16$, $p < 0.05$) their alcohol use.

Discussion

Our study utilized the multi-state churn model to assess the risk of experiencing a gap in care for participants with and without hazardous drinking. Over the long-term follow-up period, participants with a history of hazardous drinking at baseline had nearly a 90% higher hazard of having a gap in care leading to a gap in ART. Consequences of such gaps in ART include viral rebound, viral resistance, and immune suppression [30]. As such, our findings provide a risk factor that is present at enrollment and could be a target for intervention to improve patient outcomes. Our findings expand on results for the same cohort that showed lower rates of ART initiation at diagnosis and worse retention at short-term follow-up for participants with any history of alcohol consumption [20]. Prior studies from care settings in various countries have demonstrated an association between alcohol use behavior and disengagement from care [11, 31, 32]. Fewer studies have examined missed appointments or gaps in care during a follow-up period, especially in Africa. Notably, a study by Monroe et al. at multiple sites in the U.S. found that alcohol use was associated with both long-term disengagement in care and with having more missed appointments [9]. Another study from Uganda demonstrated that individuals with higher AUDIT scores had a higher rate of missed appointments [33]. Thus, knowing a patient's alcohol use pattern at baseline can aid in developing a multi-component approach to avoiding gaps in care by prompting early referral to alcohol cessation services.

Interestingly, our study found that participants with a disclosed HIV status were more likely to have an increase in their AUDIT score over time, placing them at higher risk for experiencing a gap in care. HIV status disclosure is a necessary step to receive social support, but it also creates an avenue for discrimination and stigma [34]. It is possible that participants who disclose their HIV status experience more stigma, and thus increase maladaptive coping behaviors, such as alcohol use and appointment non-adherence. A study by Wardell et al. found that maladaptive coping is a mediator between perceived stigma and heavy alcohol use [35]. Alternatively, participants with hazardous alcohol use may simply be more likely to disclose their HIV status.

A study by Modi et al. found that participants who had accessed alcohol cessation services in the last six months had higher rates of broad disclosure of their HIV status [36]. Interventions to reduce gaps in care must consider a wide array of risk factors, including social support systems, experienced stigma, substance use and patient coping behaviors.

The main strength of our study is its long-term follow-up of a large cohort of participants from three programs in East Africa. Given the common mission of HIV care programs of retaining participants in care over their lifetime, this study adds valuable information about factors that may contribute to gaps in care. The limitations of our study center on the high number of participants who were LTFU or transferred to a different site prior to enrollment in Phase II, as the long-term outcomes of those participants could not be assessed. The sample in Phase II is biased toward individuals likely to remain in care due to the high LTFU rate prior to its initiation. As for the 40% of the Phase I cohort that transferred to a non-study facility before initiation of Phase II, it is difficult to predict how this may have impacted the results. It is worth noting that 83% of participants who were retained at their program of initial enrollment in Phase I re-enrolled in Phase II. However, the enrolled individuals in Phase II had lower mean baseline AUDIT scores than the non-enrolled individuals. As such, within this study we are likely underestimating the impact of hazardous alcohol use on engagement in care.

Conclusion

Our study found that hazardous alcohol use was associated with gaps in care at sites in East Africa, identifying it as an important indicator of participants who may benefit from additional interventions and social support. Integrating alcohol screening and subsequent protocols for referral to alcohol treatment programs is a key component to improving health outcomes for PLHIV and ensuring their continued connection to the care system.

Author Contributions Conceptualization: Alexa Monroy, Suzanne Goodrich, Beverly S. Musick, Kara K. Wools-Kaloustian. Data curation: Steven A. Brown. Formal analysis: Theofanis Balanos, Giorgos Bakoyannis. Funding acquisition: Kara K. Wools-Kaloustian, Constantin T. Yiannoutsos. Investigation: Suzanne Goodrich, Lameck Diero, Jayne L. Kulzer, Helen Byakwaga. Methodology: Giorgos Bakoyannis, Theofanis Balanos, Constantin T. Yiannoutsos. Project administration: Suzanne Goodrich. Resources: Lameck Diero, Jayne L. Kulzer, Helen Byakwaga, Patrick Oyaro, Kara K. Validation: Suzanne Goodrich, Jayne L. Kulzer, Helen Byakwaga, Kara K. Wools-Kaloustian. Writing—original draft: Alexa Monroy, Giorgos Bakoyannis, Theofanis Balanos. Suzanne Goodrich, Constantin T. Yiannoutsos, Beverly S. Musick, Kara K. Wools-Kaloustian.

Writing—review & editing: Alexa Monroy, Giorgos Bakoyannis, Theofanis Balanos, Suzanne Goodrich, Constantin T. Yiannoutsos, Steven A. Brown, Beverly S. Musick, Lameck Diero, Jayne L. Kulzer, Helen Byakwaga, Kara K. Wools-Kaloustian.

Funding Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), National Institute On Drug Abuse (NIDA), National Cancer Institute (NCI), and the National Institute of Mental Health (NIMH), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Fogarty International Center (FIC), National Heart, Lung, and Blood Institute (NHLBI), National Institute on Alcohol Abuse and Alcoholism (NIAAA), in accordance with the regulatory requirements of the National Institutes of Health under Award Number U01AI069911 East Africa IeDEA Consortium. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Declarations

Conflict of interest Alexa Monroy, Suzanne Goodrich, Kara Wools-Kaloustian, Giorgos Bakoyannis, Steven Brown, Theofanis Balanos, Lameck Diero, Helen Byakwaga, Winnie Muyindike, Michael Kanyesigye, Maurice Aluda, Jayne Lewis-Kulzer, Constantin Yiannoutsos have not disclosed any competing interests.

Ethical Approval This prospective observational study was approved by the Indiana University Institutional Review Board and the ethical bodies affiliated with each participating site: The Academic Model Providing Access to Healthcare (AMPATH): Moi University College of Health Sciences and MOI Teaching and Referral Hospital's Institutional Research and Ethics Committee; Family AIDS Care and Education Services (FACES): Kenya Medical Research Institute/ National Ethics Review Committee; Mbarara Immune Suppression Syndrome (ISS) Clinic: Mbarara University of Science & Technology Institutional Review Committee and Uganda National Council of Science and Technology (UNCST) Participant written informed consent was obtained at the time of enrollment into study.

Consent to Participant (Include Appropriate Consent Statements) Included in text.

Consent for Publication (Consent Statement Regarding Publishing an Individual's Data or Image) N/A

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

- DeLorenze GN, Weisner C, Tsai AL, Satre DD, Quesenberry CP Jr. Excess mortality among HIV-infected patients diagnosed with substance use dependence or abuse receiving care in a fully integrated medical care program. *Alcohol Clin Exp Res.* 2011;35(2):203–10. <https://doi.org/10.1111/j.1530-0277.2010.01335.x>.
- Baum MK, Rafie C, Lai S, Sales S, Page JB, Campa A. Alcohol use accelerates HIV disease progression. *AIDS Res Hum Retrovir.* 2010;26(5):511–8. <https://doi.org/10.1089/aid.2009.0211>.
- Anand P, Springer SA, Copenhaver MM, Altice FL. Neurocognitive impairment and HIV risk factors: a reciprocal relationship. *AIDS Behav.* 2010;14(6):1213–26. <https://doi.org/10.1007/s10461-010-9684-1>.
- Green JE, Saveanu RV, Bornstein RA. The effect of previous alcohol abuse on cognitive function in HIV infection. *Am J Psychiatry.* 2004;161(2):249–54. <https://doi.org/10.1176/appi.ajp.161.2.249>.
- Falang KD, Akubaka P, Jimam NS. Patient factors impacting antiretroviral drug adherence in a Nigerian tertiary hospital. *J Pharmacol Pharmacother.* 2012;3(2):138–42. <https://doi.org/10.4103/0976-500X.95511>.
- Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. *Drug Alcohol Depend.* 2010;112(3):178–93. <https://doi.org/10.1016/j.drugalcdep.2010.06.014>.
- 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):421–36. <https://doi.org/10.1007/s11904-015-0285-5>.
- Galvan FH, Bing EG, Fleishman JA, London AS, Caetano R, Burnam MA, Longshore D, Morton SC, Orlando M, Shapiro M. The prevalence of alcohol consumption and heavy drinking among people with HIV in the United States: results from the HIV cost and services utilization study. *J Stud Alcohol.* 2002;63(2):179–86. <https://doi.org/10.15288/jsa.2002.63.179>.
- Monroe AK, Lau B, Mugavero MJ, Mathews WC, Mayer KH, Napravnik S, Hutton HE, Kim HS, Jabour S, Moore RD, McCaul ME, Christopoulos KA, Crane HC, Chander G. Heavy alcohol use is associated with worse retention in HIV care. *J Acquir Immune Defic Syndr.* 2016;73(4):419–25. <https://doi.org/10.1097/QAI.0000000000001083>.
- Petry NM. Alcohol use in HIV patients: what we don't know may hurt us. *Int J STD AIDS.* 1999;10(9):561–70. <https://doi.org/10.1258/0956462991914654>.
- Cichowitz C, Maraba N, Hamilton R, Charalambous S, Hoffmann CJ. Depression and alcohol use disorder at antiretroviral therapy initiation led to disengagement from care in South Africa. *PLoS ONE.* 2017;12(12): e0189820. <https://doi.org/10.1371/journal.pone.0189820>.
- Jaquet A, Ekouevi DK, Bashi J, Aboubakrine M, Messou E, Maiga M, Traore HA, Zannou MD, Guehi C, Ba-Gomis FO, Minga A, Allou G, Eholie SP, Bissagnene E, Saso AJ, Dabis F. Alcohol use and non-adherence to antiretroviral therapy in HIV-infected patients in West Africa. *Addiction.* 2010;105(8):1416–21. <https://doi.org/10.1111/j.1360-0443.2010.02978.x>.
- Morojele NK, Kekwaletswe CT, Nkosi S. Associations between alcohol use, other psychosocial factors, structural factors and antiretroviral therapy (ART) adherence among South African ART recipients. *AIDS Behav.* 2014;18(3):519–24. <https://doi.org/10.1007/s10461-013-0583-0>.

14. Chime OH, Ndibuagu EO, Orji CJ. Rates and predictors of adherence and retention for antiretroviral therapy among HIV-positive adults in Enugu. *Nigeria Malawi Med J*. 2019;31(3):202–11. <https://doi.org/10.4314/mmj.v31i3.7>.
15. Magidson JF, Saal W, Nel A, Remmert JE, Kagee A. Relationship between depressive symptoms, alcohol use, and antiretroviral therapy adherence among HIV-infected, clinic-attending patients in South Africa. *J Health Psychol*. 2017;22(11):1426–33. <https://doi.org/10.1177/1359105316628743>.
16. Nakimuli-Mpungu E, Bass JK, Alexandre P, Mills EJ, Musisi S, Ram M, Katabira E, Nachega JB. Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: a systematic review. *AIDS Behav*. 2012;16(8):2101–18. <https://doi.org/10.1007/s10461-011-0087-8>.
17. Parry CD, Londani M, Shuper PA, Myers B, Kekwaletswe CT, Nkosi S, Morojele NK. Characteristics and drinking behaviour of patients on antiretroviral therapy who drink and attend HIV clinics in Tshwane, South Africa: implications for intervention. *S Afr Med J*. 2019;109(10):784–91. <https://doi.org/10.7196/SAMJ.2019.v109i10.13586>.
18. Cunningham WE, Sohler NL, Tobias C, Drainoni ML, Bradford J, Davis C, Cabral HJ, Cunningham CO, Eldred L, Wong MD. Health services utilization for people with HIV infection: comparison of a population targeted for outreach with the US population in care. *Med Care*. 2006;44(11):1038–47. <https://doi.org/10.1097/01.mlr.0000242942.17968.69>.
19. Cunningham CO, Sohler NL, Wong MD, Relf M, Cunningham WE, Drainoni ML, Bradford J, Pounds MB, Cabral HD. Utilization of health care services in hard-to-reach marginalized HIV-infected individuals. *AIDS Patient Care STDS*. 2007;21(3):177–86. <https://doi.org/10.1089/apc.2006.103>.
20. Patisis I, Goodrich S, Yiannoutsos CT, Brown SA, Musick BS, Diero L, Kulzer JL, Bwana MB, Oyaro P, Wools-Kaloustian KK. 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. <https://doi.org/10.1371/journal.pone.0240654>.
21. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. *AUDIT the alcohol use disorders identification test guidelines for use in primary care*. 2nd ed. Geneva: World Health Organization; 2001.
22. Enane LA, Apondi E, Aluoch J, Bakoyannis G, Lewis Kulzer J, Kwena Z, Kantor R, Chory A, Gardner A, Scanlon M, Goodrich S. Social, economic, and health effects of the COVID-19 pandemic on adolescents retained in or recently disengaged from HIV care in Kenya. *PLoS ONE*. 2021;16(9): e0257210.
23. Obua C, Kayiwa J, Waako P, Tomson G, Balidawa H, Chalker J, Ross-Degnan D, Wahlstrom R. Improving adherence to antiretroviral treatment in Uganda with a low-resource facility-based intervention. *Glob Health Action*. 2014;4(7):24198. <https://doi.org/10.3402/gha.v7.24198>.
24. Gill MJ, Krentz HB. Unappreciated epidemiology: the churn effect in a regional HIV care programme. *Int J STD AIDS*. 2009;20(8):540–4. <https://doi.org/10.1258/ijsa.2008.008422>.
25. Bakoyannis G, Diero L, Mwangi A, Wools-Kaloustian KK, Yiannoutsos CT. A semiparametric method for the analysis of outcomes during a gap in HIV care under incomplete outcome ascertainment. *Stat Commun Infect Dis*. 2020;12(Suppl 1):20190013. <https://doi.org/10.1515/scid-2019-0013>.
26. Bakoyannis G. Nonparametric analysis of nonhomogeneous multistate processes with clustered observations. *Biometrics*. 2021;77(2):533–46. <https://doi.org/10.1111/biom.13327>.
27. Bakoyannis G. Nonparametric tests for transition probabilities in nonhomogeneous Markov processes. *J Nonparametr Stat*. 2020;32(1):131–56. <https://doi.org/10.1080/10485252.2019.1705298>.
28. Bakoyannis G, Bandyopadhyay D. Nonparametric tests for multistate processes with clustered data. *Ann Inst Stat Math*. 2022;74(5):837–67. <https://doi.org/10.1007/s10463-021-00819-x>.
29. Spiekerman CF, Lin DY. Marginal regression models for multivariate failure time data. *J Am Stat Assoc*. 1998;93(443):1164–75. <https://doi.org/10.1080/01621459.1998.10473777>.
30. Strategies for Management of Antiretroviral Therapy (SMART) Study Group, El-Sadr WM, Lundgren J, Neaton JD, Gordin F, Abrams D, Arduino RC, Babiker A, Burman W, Clumeck N, Cohen CJ, Cohn D, Cooper D, Darbyshire J, Emery S, Fätkenheuer G, Gazzard B, Grund B, Hoy J, Klingman K, Losso M, Markowitz N, Neuhaus J, Phillips A, Rappoport C. CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med*. 2006;355(22):2283–96. <https://doi.org/10.1056/NEJMoA062360>.
31. Carlos S, Burgueño E, Ndarabu A, Reina G, Lopez-Del Burgo C, Osorio A, Makonda B, de Irala J. Predictors of retention in the prospective HIV prevention OKAPI cohort in Kinshasa. *Sci Rep*. 2021;11(1):5431. <https://doi.org/10.1038/s41598-021-84839-w>.
32. Koirala S, Deuba K, Nampaisan O, Marrone G, Ekström AM, CAT-S group. Facilitators and barriers for retention in HIV care between testing and treatment in Asia—a study in Bangladesh, Indonesia, Lao, Nepal, Pakistan Philippines and Vietnam. *PLoS ONE*. 2017;12(5):e0176914. <https://doi.org/10.1371/journal.pone.0176914>.
33. Sileo KM, Wanyenze RK, Kizito W, Reed E, Brodine SK, Chemusto H, Musoke W, Mukasa B, Kiene SM. Multi-level determinants of clinic attendance and antiretroviral treatment adherence among fishermen living with HIV/AIDS in communities on lake victoria. *Uganda AIDS Behav*. 2019;23(2):406–17. <https://doi.org/10.1007/s10461-018-2207-1>.
34. Derlega VJ, Winstead BA, Greene K, Serovich J, Elwood WN. Reasons for HIV disclosure/nondisclosure in close relationships: testing a model of HIV–disclosure decision making. *J Soc Clin Psychol*. 2004;23(6):747–67. <https://doi.org/10.1521/jscp.23.6.747.54804>.
35. Wardell JD, Shuper PA, Rourke SB, Hendershot CS. Stigma, coping, and alcohol use severity among people living with HIV: a prospective analysis of bidirectional and mediated associations. *Ann Behav Med*. 2018;52(9):762–72. <https://doi.org/10.1093/abm/kax050>.
36. Modi RA, McGwin GL Jr, Willig JH, Westfall AO, Griffin RL, Amico R, Martin KD, Raper JL, Keruly JC, Golin CE, Zinski A, Napravnik S, Crane HM, Mugavero MJ. Factors associated with HIV disclosure status among iENGAGE cohort of new to HIV care patients. *AIDS Patient Care STDS*. 2020;34(5):213–27. <https://doi.org/10.1089/apc.2019.0271>.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Terms and Conditions

Springer Nature journal content, brought to you courtesy of Springer Nature Customer Service Center GmbH (“Springer Nature”).

Springer Nature supports a reasonable amount of sharing of research papers by authors, subscribers and authorised users (“Users”), for small-scale personal, non-commercial use provided that all copyright, trade and service marks and other proprietary notices are maintained. By accessing, sharing, receiving or otherwise using the Springer Nature journal content you agree to these terms of use (“Terms”). For these purposes, Springer Nature considers academic use (by researchers and students) to be non-commercial.

These Terms are supplementary and will apply in addition to any applicable website terms and conditions, a relevant site licence or a personal subscription. These Terms will prevail over any conflict or ambiguity with regards to the relevant terms, a site licence or a personal subscription (to the extent of the conflict or ambiguity only). For Creative Commons-licensed articles, the terms of the Creative Commons license used will apply.

We collect and use personal data to provide access to the Springer Nature journal content. We may also use these personal data internally within ResearchGate and Springer Nature and as agreed share it, in an anonymised way, for purposes of tracking, analysis and reporting. We will not otherwise disclose your personal data outside the ResearchGate or the Springer Nature group of companies unless we have your permission as detailed in the Privacy Policy.

While Users may use the Springer Nature journal content for small scale, personal non-commercial use, it is important to note that Users may not:

1. use such content for the purpose of providing other users with access on a regular or large scale basis or as a means to circumvent access control;
2. use such content where to do so would be considered a criminal or statutory offence in any jurisdiction, or gives rise to civil liability, or is otherwise unlawful;
3. falsely or misleadingly imply or suggest endorsement, approval, sponsorship, or association unless explicitly agreed to by Springer Nature in writing;
4. use bots or other automated methods to access the content or redirect messages
5. override any security feature or exclusionary protocol; or
6. share the content in order to create substitute for Springer Nature products or services or a systematic database of Springer Nature journal content.

In line with the restriction against commercial use, Springer Nature does not permit the creation of a product or service that creates revenue, royalties, rent or income from our content or its inclusion as part of a paid for service or for other commercial gain. Springer Nature journal content cannot be used for inter-library loans and librarians may not upload Springer Nature journal content on a large scale into their, or any other, institutional repository.

These terms of use are reviewed regularly and may be amended at any time. Springer Nature is not obligated to publish any information or content on this website and may remove it or features or functionality at our sole discretion, at any time with or without notice. Springer Nature may revoke this licence to you at any time and remove access to any copies of the Springer Nature journal content which have been saved.

To the fullest extent permitted by law, Springer Nature makes no warranties, representations or guarantees to Users, either express or implied with respect to the Springer nature journal content and all parties disclaim and waive any implied warranties or warranties imposed by law, including merchantability or fitness for any particular purpose.

Please note that these rights do not automatically extend to content, data or other material published by Springer Nature that may be licensed from third parties.

If you would like to use or distribute our Springer Nature journal content to a wider audience or on a regular basis or in any other manner not expressly permitted by these Terms, please contact Springer Nature at

onlineservice@springernature.com