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Alcohol and falls among people with HIV infection: A view from Russia and the United States

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Abstract

Background: Both HIV and alcohol use predispose to autonomic/sensory neuropathy, imbalance symptoms, and cognitive impairment - conditions associated with a greater risk of falls - yet it is not clear how to identify people with HIV (PWH) whose drinking is associated with falls. Research on alcohol and falls using the same instruments in different countries would be helpful in substantiating the level of alcohol associated with fall risk. We examined whether a consumption-based measure (Alcohol Use Disorders Identification Test-Consumption [AUDIT-C])

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and/or a symptom-based measure (DSM-5 criteria for alcohol use disorder [AUD]) is associated with sustaining a fall among PWH in St. Petersburg, Russia and Boston, United States.

Methods: Separate multivariate logistic regressions were used for each cohort to examine cross-sectional associations for each alcohol measure predicting fall. Potential confounders included physical functioning, depressive symptoms, and other substance use (Addiction Severity Index).

Results: A fall was reported by 35% (87/251) of the sample in Boston and 12% (46/400) in St. Petersburg. Each additional AUD criteria - but not higher AUDIT-C score - was significantly associated with a fall in both Boston (odds ratio [OR] =1.10; 95% confidence interval [CI] 1.02, 1.18) and St. Petersburg (adjusted OR AOR=1.10; 95%CI 1.02, 1.18). Heavy alcohol use (>6 drinks/occasion, any vs none) was associated with more than twice the odds of a fall (AOR=2.24; 95%CI 1.21, 4.13) in Boston.

Conclusions: These findings suggest that while fall risk may vary by setting and population, heavy alcohol use and AUD symptom severity are potential targets for fall prevention interventions. Studies in diverse global settings advance understanding the relationship between alcohol and falls in PWH.

Keywords

Alcohol; falls; screening; prevention; HIV

INTRODUCTION

Falls are the most common cause of injury among older adults both in the U.S. (Moreland, et al., 2020) and globally (Clausen et al., 2015). Recent estimates indicate 27% of adults over the age of 65 in the U.S. have had at least one fall in the past year with 10% sustaining a fall-related injury (Moreland, et al., 2020). Among people with HIV (PWH), falls are prevalent even at younger ages with fall estimates that range between 16–41% in the past year (Berner et al., 2019; Erlandson et al., 2019; Kim et al., 2018; Sharma et al., 2020; Womack et al., 2019) including 16% sustaining a fall that required medical attention (Kim et al., 2018). What is known about falls in PWH is largely from high-income countries with very limited research in lower-middle-income countries (Berner et al., 2019; Charumbira et al., 2020). Falls are particularly consequential for PWH given their elevated risk of low bone density (Brown et al., 2004; Erlandson et al., 2018) and fracture (Sharma et al., 2015). A recent study demonstrated an association between incident fracture and all-cause mortality in a national cohort of PWH in care (Battalora et al., 2021). Even falls that do not result in injury can have devastating impact on ambulation due to “fear of falling” contributing to subsequent falls. For PWH, who are less likely to maintain functional abilities with aging (Fazeli et al., 2020), falls are an important concern (Greene et al., 2018) and often viewed as heralding a process of declining independence (Womack et al., 2018).

A broad array of social, biological, and environmental factors contributes to fall risk. One factor, alcohol consumption, has been understudied despite the high prevalence of unhealthy alcohol consumption in PWH (Williams et al., 2016). Alcohol can increase fall risk for PWH in several ways. Both HIV and alcohol use predispose to autonomic/sensory neuropathy, imbalance symptoms, and cognitive impairment (M Elicer et al., 2018; Malvar et al., 2015;

Robinson-Papp and Sharma, 2013), all of which are associated with a greater risk of falls (Erlandson et al., 2016; Sharma et al., 2020). Even with viral suppression and immune reconstitution, PWH are also vulnerable to developing sarcopenia, a condition characterized by low muscle mass and function, increasing the risk of falls and fracture (Hawkins et al., 2018). Sarcopenia - with an estimated prevalence of 24% of PWH - can also be the result of heavy alcohol consumption (McClain et al., 2021) and associated with chronic immune activation, declining physical function, and frailty (Brañas et al., 2017; Hawkins et al., 2018; Oliveira et al., 2020), another risk factor for falls (Tassiopoulos et al., 2017). Lifetime alcohol consumption contributes to frailty among PWH (Maffei et al., 2020). Besides direct effects of HIV and/or alcohol, common comorbidities such as chronic pain and depression can lead to prescription of sedating medications (i.e., polypharmacy), less physical activity, and in turn, a higher risk of falls (Erlandson et al., 2019; Kim et al., 2018; Womack et al., 2019).

Despite the potential for alcohol use to contribute to the risk of falls in PWH, the research on the impact of alcohol on falls among PWH has been limited and yielded inconsistent results (Erlandson et al., 2019; Tassiopoulos et al., 2017; Womack et al., 2019). This research has used a wide array of measures to assess alcohol exposure and lacks validated tools to assess alcohol consumption and fall history. In addition, patterns of drinking, which may be more important than overall alcohol consumption, have not been well-delineated. As a result, alcohol use has largely been neglected in fall prevention recommendations, standard risk assessment tools, and patient education. This lack of attention to alcohol includes the most widely recommended fall risk assessment for older general populations: the Centers for Disease Control Stopping Elderly Accidents, Deaths, and Injuries (STEADI) program (Ganz and Latham, 2020; Sarmiento and Lee, 2017).

Although health care providers should screen for falls and determine fall risk for PWH (Ganz and Latham, 2020), it is not clear how best to identify patients whose drinking confers risk for falls. Should a consumption-based measure be used to identify PWH at risk of falls and at what level of alcohol? One possible measure is the widely used consumption-based survey, the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) (Bush et al., 1998), which is well-validated (Bradley et al., 2007) and predictive of other clinically relevant risks, such as perioperative mortality and medication non-adherence (Bradley et al., 2011b; Bryson et al., 2008). Another way to assess alcohol exposure is with Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnostic criteria for alcohol use disorder (AUD), which are based upon symptoms (e.g., craving) and functioning (e.g., drinking despite failure to fulfill certain role activities) with no reference to amount or pattern of drinking (American Psychiatric Association, 2013).

Lack of data on diverse global settings is another gap in the literature given the wide spectrum of environmental, social, and individual factors that contribute to fall risk. This gap is particularly pronounced for PWH in lower-middle-income countries where at-risk alcohol consumption may be common (Nouaman et al., 2018). There is a growing interest in the impact of HIV on functional outcomes such as disability in PWH who are on long-term antiretroviral medication (Hanass-Hancock et al., 2015). Research on alcohol and falls using the same instruments in different countries would be helpful in substantiating

thresholds or cut points to identify those whose drinking is associated with greater risk of falls. Rather than extrapolating study findings in higher-income countries to those in lower-middle-income countries, developing appropriate fall prevention interventions requires an understanding of globally relevant determinants of falls (Charumbira et al., 2020).

This study's objective was to describe the incidence of falls in two cohorts of PWH - one in St. Petersburg (Russia) and the other in Boston (USA) and to ascertain the severity of alcohol use associated with a fall using the AUDIT-C questionnaire and a symptom-based measure, DSM-5 criteria for AUD (American Psychiatric Association, 2013).

MATERIALS AND METHODS

Study design

This study used data from the Uganda Russia Boston Alcohol Network for Alcohol Research Collaboration on HIV/AIDS (URBAN ARCH) consortium: Russia ARCH in St. Petersburg, Russia and Boston ARCH in Boston, USA. The overall objective of the URBAN ARCH consortium is to research the impact of alcohol on PWH and develop interventions to reduce alcohol-related consequences.

Russia ARCH cohort: The Russia ARCH cohort (n=400) was comprised of PWH enrolled in a 12-month randomized trial of varenicline, cytisine, and nicotine replacement therapy for heavy alcohol consumption and tobacco use (the St. PETER HIV [Studying Partial agonists for Ethanol and Tobacco Elimination in Russians with HIV] study). The study design, recruitment, and eligibility have been described (Tindle et al., 2020). Briefly, eligible participants were age 18–70 years old, HIV positive, who reported daily tobacco use, ≥5 heavy drinking days (i.e., National Institute on Alcohol Abuse and Alcoholism definition for at-risk drinking) within the past 30 days, interest in reducing alcohol or tobacco use, and stable address (within 100 km of St. Petersburg). Recruitment occurred between 2017 and 2019. Study activities were conducted at Pavlov University in St. Petersburg, Russia. All participants enrolled in the St. PETER study were included in the current study's analyses. The St. PETER study was approved by the Institutional Review Boards (IRB) of Pavlov University, Boston Medical Center / Boston University Medical Campus, and Vanderbilt University Medical Center.

Boston ARCH cohort: The Boston ARCH participants (n=251) were enrolled in a prospective study on alcohol consumption, falls, and frailty. Eligible participants were English-speaking PWH over the age of 18 years; willing to provide information for at least one alternate contact; who reported any illicit drug use in the past 12 months (Tobacco, Alcohol, Prescription Medication and Other Substances Tool), positive AUDIT-C score (≥3 for women, ≥4 for men), or enrollment in a previous Boston ARCH study (Kim et al., 2018). Participants were recruited from adult primary care and HIV clinics at BMC between 2018 and 2020. The study was approved by the BMC/BUMC IRB. All participants in the Boston ARCH cohort were included in the current study.

Data collection

Trained research associates administered standardized research interviews at baseline and 12-month follow-up assessments in each of the cohorts. The AUDIT-C questionnaire was only administered at baseline in the Boston cohort. In addition to standardized interviews, CD4 count and HIV viral load were collected by electronic health record review in Boston and phlebotomy in St. Petersburg.

Outcome

We used the AIDS Clinical Trials Group (ACTG) A5322 fall history questionnaire (Tassiopoulos et al., 2017) to assess the study outcome, a fall in the past 6 months, in both cohorts: “I am now going to ask you some questions about falls that may have happened during your usual daily activities. A ‘fall’ or ‘falling’ is an unexpected event, including a slip or trip, in which you lost your balance and landed on the floor, ground or lower level, or hit an object like a table or chair.” Falls from a major medical event (for example, a stroke or seizure) or an overwhelming external hazard (for example, hit by a car or being pushed) were not included.

Main independent variables and covariates

The AUDIT-C score was used to examine alcohol exposure as the primary independent variable (Bush et al., 1998). The score is calculated from the 3 questions in the AUDIT-C survey about alcohol consumption. 1) How often do you drink alcohol? 2) How many drinks do you drink on a typical day when you drink alcohol? And 3) How often do you have 6 or more drinks on one occasion? The response options for the latter question are daily/almost daily, weekly, monthly, less than monthly, and never. The scores range from 0 to 4 for each item, and the most severe score is 12. In addition to the overall AUDIT-C score, we also used the third question of the AUDIT-C, which asks about drinking 6 or more drinks in an occasion to define heavy use (secondary independent variable) given that a fall may occur after one episode (or occasion) of heavy alcohol use.

DSM-5 criteria for AUD were used to define two symptom-based measures of alcohol exposure 1) total number of criteria (primary independent variable) and 2) AUD severity category as defined by DSM-5 (moderate-severe, mild, and none) (secondary).

Potential confounders were selected based upon research and clinical knowledge about alcohol and falls: age; gender; race/ethnicity (only in Boston cohort given Russia participants were uniformly white); CD4 <200 (yes vs no); HIV viral load suppression; homeless (yes vs no); depressive symptoms (CES-D) (≥16 vs below) (Radloff and Sawyer, 1977); body mass index (BMI) (underweight, obese, vs normal/overweight); social support score (Modified MOS-SS [Boston] (Moser et al., 2012), Duke/UNC Functional Social Support Questionnaire [Russia) (Broadhead et al., 1988) (above vs below median); physical functioning score (VR-12) (continuous) (Selim et al., 2009); and three separate measures of substance use in the past 30 days derived from the Addiction Severity Index (i.e., cocaine use, illicit opioid use, and illicit sedative use) (McLellan et al., 1992).

Descriptive characteristics not included in the analyses included symptoms associated with falls, specifically, dizziness/lightheadedness, pain/numbness/tingling in hands or feet, trouble remembering (HIV symptom index) (Justice et al., 2001); fear of falling ("Have you been concerned with losing your balance and falling while doing your usual activities?" responding "quite a bit" or "very much"); cognitive functioning (Medical Outcomes Study HIV Health Survey) (Wu et al., 1991); and pain interference (Brief Pain Inventory) (Tan et al., 2004).

Statistical analyses

We present baseline descriptive statistics summarizing the study participant characteristics for each cohort stratified by fall vs no fall. We checked a Spearman correlation matrix for all independent variables to assess potential multi-collinearity and identified any pairs of variables with Spearman correlation > 0.40.

We used all available data for the logistic regression analyses on cross-sectional associations of alcohol use and falls. For the AUDIT-C analyses, these were data collected at baseline and for AUD analyses, baseline and follow-up. We modeled the association of total AUDIT-C score and fall (yes/no) using logistic regression after assessing the Hosmer-Lemeshow goodness of fit test to assess the appropriateness of assuming a linear association of AUDIT-C score with the odds of falls. Given the myriad of factors that predispose to a fall (and a limited number of falls occurred in the current study), we used an empirical approach to identify the covariates to include in adjusted models. We performed a series of analyses adding each covariate individually to the logistic regression model to compare the adjusted odds ratio (AOR) for a one-point higher AUDIT-C score with the unadjusted OR. After identifying the covariate that changed the parameter estimate of the AUDIT-C score the most, the covariate stayed in the final model if the AOR changed by ≥10% in either direction. We then performed another series of logistic regression analyses adding each remaining covariate individually, identifying the covariate that changed the AUDIT-C score the most, and keeping the covariate in the model if the AOR for AUDIT-C changed by ≥10%. Once the final set of potential confounders were determined through this iterative process, we ran a logistic model that forced in AUDIT-C and the chosen covariates. If no covariate changed the AOR by more than 10%, the unadjusted OR was the final model. We also performed a sensitivity analysis excluding participants who had not had a drink in the past 12 months given that some individuals stop drinking because of a worsening health situation such as a fall (i.e., "sick quitter" hypothesis) (Liang and Chikritzhs, 2013). Therefore, some individuals abstaining from alcohol are not an accurate comparator to assess the risk of a fall associated with alcohol use. Because we could not differentiate "sick quitters" from the overall pool of participants without alcohol use, we used the first question of the Alcohol Use Disorder section, "Have you had any alcoholic drinks (such as beer, wine, or liquor), even once, in the past 12 months?" to identify abstainers. This analysis was performed only in the Boston cohort because heavy alcohol use was one of the study eligibility criteria in the Russia cohort.

To examine whether heavy alcohol consumption (drinking 6 or more drinks in an occasion) was associated with a fall, we first examined the effect of any heavy consumption (yes/no) in

the Boston cohort. Because heavy alcohol consumption was an eligibility criterion for study entry in the Russia cohort, we performed an analysis using a dichotomous measure of the frequency of heavy use based upon the distribution of responses (“weekly” or “daily/almost daily” vs “monthly” or “less than monthly”) to parallel the analysis in the Boston cohort of a dichotomous measure of (any) heavy alcohol use. Finally, we examined the frequency of heavy use as a 4-level categorical variable based again upon the distribution of responses in each cohort i.e., daily/almost daily, weekly, monthly, and less than monthly in the Russia cohort, and weekly or more frequent, monthly, less than monthly, and never in the Boston cohort. The strategy for selecting covariates for inclusion in the adjusted model was the same as the one used in the analyses of the AUDIT-C score.

We used a similar analytic strategy to examine whether the number of DSM-5 AUD criteria was associated with a fall. Subjects contributed up to two observations to these analyses because AUD data was assessed at baseline and follow-up in both cohorts. We used GEE models to account for the correlation arising from using multiple observations for the same participant. Like the AUDIT-C analyses, we performed a series of adjusted logistic regression models to identify which covariates to include in the final model.

We also performed secondary analyses using DSM-5 diagnostic criteria to define AUD severity as a 3-level categorical variable, namely, no use disorder (0–1 criteria), mild use disorder (2–3 criteria), and moderate-severe (4–11 criteria) as defined by the DSM-5. In the Boston cohort analyses, the referent group was no AUD. In the Russia cohort, mild AUD severity was the referent group because there were very few in the no AUD group by design (34/400 or 9%).

RESULTS

Study participant characteristics for each cohort overall and stratified by a reported fall are presented in Table 1. Notable characteristics include mean age, 52 years (standard deviation [SD] 10) in the Boston cohort (n=251), more than a decade older than the Russia (n=400) cohort (mean age of 39 years [SD 6]). Few of the Boston cohort were employed (25%), in contrast to most participants in the Russia cohort (65%). Homelessness was primarily a feature only of the Boston cohort (15%) with very few in the Russia cohort (1%) reporting any night in a shelter or on the street.

Most of the Boston cohort reported depressive symptoms (54%), in contrast to 39% of the Russia cohort. A substantial proportion of the Boston cohort also experienced symptoms associated with falls including pain or numbness in hands or feet (32%, 81/251), dizziness (18%, 45/251), and trouble remembering (32%, 80/251). These symptoms were reported by relatively few (<10%) in the Russia cohort.

Viral suppression was almost universal in the Boston (87%) but only in a majority (57%) of the Russia cohort. Accordingly, nearly a quarter (24%) of the Russia cohort had a CD4 <200, in contrast to very few in the Boston cohort (although not negligible, 8.6%).

Median AUDIT-C score was high in the Russia cohort (10, interquartile range [IQR] 8, 10) but only 3 (IQR 0, 5) for the Boston cohort. Similarly, heavy alcohol use was universal in the

Russia cohort (by study design), whereas almost half of the Boston cohort (45%) reported heavy use.

Alcohol use disorder followed a similar pattern. Most of the participants in the Russia cohort met criteria for a moderate or severe alcohol use disorder (64%, 256/400), while only a minority did in the Boston (27%, 66/251) cohort.

The most common illicit drug in the Boston cohort was cocaine (24% 61/251) and in the Russia cohort, opioids (24% 97/400).

A fall was reported in the past 6 months by 35% (87/251) of the Boston cohort and 12% (46/400) of the Russia cohort

Bivariate associations between study sample characteristics and fall

All characteristics significantly associated with a fall in the Russia cohort were also significantly associated with a fall in the Boston cohort and included the following: worse physical functioning; higher HIV symptom count; depressive symptoms; illicit sedative use; feeling numbness/tingling in hands or feet; dizziness; and fear of falling (Table 1).

The characteristics unique to the Boston cohort that were significantly associated with a fall were female gender, race/ethnicity, homelessness, greater pain interference (with daily functioning), lower cognitive functioning, trouble remembering, and illicit opioid use. The latter was reported by 26% of participants who had a fall vs 10% by those who did not.

CD4 count and HIV viral suppression were not associated with a fall in either cohort.

Results of logistic regression analyses

AUDIT-C score was not significantly associated with odds of having had a fall (OR 1.06; 95%CI 0.97, 1.16 and OR 1.16; 95%CI 0.97, 1.39 per one-point higher AUDIT-C score in the Boston and Russia cohorts, respectively) (Tables 2 and 3). No covariate changed the parameter estimate of the OR for a higher AUDIT-C score by more than 10%. Results of analyses removing abstainers were not substantially different (OR 1.05; 95%CI 0.94, 1.17) (data not shown).

Heavy alcohol use (any vs none) was associated with more than twice the odds of a fall (AOR 2.24; 95%CI 1.21, 4.13) in the Boston cohort. The frequency of heavy alcohol use was not associated with a fall in either cohort.

Each additional DSM-5 criterion for AUD was associated with a greater risk of fall in both the Boston and Russia cohorts with similar parameter estimates (OR 1.10; 95% CI 1.02, 1.18 for Boston and OR 1.10; 95%CI 1.02, 1.18 for Russia (Tables 4 and 5). This was the final model because no covariate changed the parameter estimate by more than 10%.

Those with a moderate-severe AUD were more likely to fall than those without a use disorder in both the Boston cohort (OR 1.74; 95%CI 1.07, 2.83) and Russia cohort (OR 1.93; 95%CI 1.01, 3.70) in unadjusted models. After adjustment for potential confounders,

this remained significant in the Boston cohort (AOR 1.85; 95%CI 1.10, 3.10) but not in the Russia cohort (AOR 1.74; 95%CI 0.85, 3.58).

Notably, the covariate homelessness (any night in a street or shelter) was significantly associated with more than twice the odds of a fall in the Boston cohort in the analyses of frequency of heavy alcohol use (AOR 2.93; 95%CI 1.22, 7.06) and AUD severity (AOR 2.57; 95%CI 1.42, 4.65).

DISCUSSION

The study objective was to examine whether a consumption and/or a symptom-based measure of alcohol severity is associated with a higher risk of a fall in two global cohorts of PWH. In terms of the primary measures of alcohol severity, the results were consistent in the Boston and Russia cohorts. Specifically, the risk of a fall was higher with each additional DSM-5 AUD criteria but not with a higher AUDIT-C score, a consumption/frequency measure of alcohol exposure. These results were consistent in two very different PWH cohorts – one comprised of heavy drinkers (Russia) and another with a range of drinking patterns from abstinence to severe use disorder (Boston).

The results of the secondary analyses varied between cohort. Heavy alcohol use (any vs none) was associated with more than twice the odds of a fall in the Boston cohort. Given that about a third of the Boston cohort had reported a fall, this increase in risk is clinically significant. This analysis could not be performed with the Russia cohort because heavy alcohol use was a study entry criterion. We found the frequency of heavy drinking was not associated with a fall in either cohort. Regarding the secondary measure of AUD symptoms, the risk of fall was significantly greater for those with a moderate to severe AUD in unadjusted analyses in both the Boston and Russia cohorts. After adjustment for potential confounders, the association was still significant in the Boston cohort but not in the Russia cohort.

This study builds upon others that have examined the association of alcohol and falls with a consumption-based measure of alcohol exposure. Prior studies have examined an NIAAA-based measure of risky drinking (more than 7 or 14 drinks in a week for women and men, respectively) (Erlandson et al., 2019, 2016; Sharma et al., 2018; Tassiopoulos et al., 2017), although the method used to assess alcohol consumption was unclear. One exception is a study by Womack et al that used AUDIT-C score, obtained in clinical care, to define unhealthy alcohol use (AUDIT-C score of 3 or greater for women and 4 or greater for men) and found that unhealthy alcohol use was associated with serious falls in HIV-infected and uninfected patients in the VA (Womack et al., 2019). Interestingly, unhealthy alcohol consumption was significant in the combined sample but not in the HIV-infected sample. The current study extends these findings by demonstrating a link between a different AUDIT-C derived measure, heavy episodic alcohol use (>6 drinks in an occasion) assessed by standardized research assessment, and a broader spectrum of falls. Even falls that do not result in injury may have clinical significance if a fear of falling or reduction in physical activity follows. While any heavy use was significant, the frequency of heavy use was not in either cohort. It is plausible that differences in risk may be more difficult to detect with

somewhat imprecise categories of frequency as assessed in the AUDIT-C (monthly, weekly, less than weekly, etc.) rather than a binary measure of any versus none. Compared to clinical criteria for an AUD, heavy consumption amounts may vary across global settings.

Our study findings also extend the literature on alcohol and falls by demonstrating that a measure of functional symptoms, number of AUD criteria, appears to be useful for identifying those with a greater risk of fall. *C*hange in criteria count has been shown to be meaningful in terms of addiction treatment effectiveness (Kiluk et al., 2018). This study suggests that even an incremental decrease in number of DSM-5 criteria may be associated with fewer falls.

Interestingly, all characteristics associated with a fall in the Russia cohort were significant in the Boston cohort. There were no characteristics unique to the Russia cohort. Lower physical functioning was consistently associated with a greater risk of fall in Boston and Russia. Prior studies have also noted the association of falls with depressive symptoms and symptoms suggestive of autonomic or peripheral neuropathy such as numbness/tingling in hands or feet, dizziness, or off-balance (Robinson-Papp and Sharma, 2013). This suggests that risk factors may vary in frequency in different populations but when present, contribute to excess fall risk.

We found that homelessness was one of the strongest risk factors for falls independent of alcohol use in the Boston cohort. It is possible that fall risk is attributable in people who are homeless due to the accumulation of comorbidities associated with fall such as chronic pain, environmental hazards, or accelerated aging (Suh et al., 2020). Fall prevention has been cited as a pressing need for formerly homeless persons entering supportive housing programs in the United States (Henwood et al., 2020). It is notable that homelessness was primarily a characteristic of the Boston cohort. This raises the question of whether universal recommendations are ideal in all cases but rather should be tailored to the local population.

We found that about a third of the Boston study sample had experienced a fall in the past 6 months, notably higher than the Russia cohort despite on average, higher alcohol consumption in the Russia cohort. The Boston cohort was comprised of participants who were older, largely unemployed, with lower cognitive and physical functioning. A sizable proportion reported symptoms associated with falls including dizziness, pain or numbness in hands/feet, trouble remembering, and depressive symptoms (Erlandson et al., 2016; Sharma et al., 2020, 2018). These symptoms are associated with HIV infection as well as heavy alcohol use.

Limitations of the study include the cross-sectional analyses which limit causal inferences. It is possible, though unlikely, that people who fell subsequently increased their consumption of alcohol or developed a use disorder. Next, we were only able to use baseline data for the AUDIT-C analyses limiting the power to find a difference in fall risk whereas the longitudinal analyses of AUD criteria had more observations. Additionally, we did not have data on the number or type of prescribed medications or other factors associated with a fall such as low muscle mass/strength (sarcopenia) or frailty. Different study eligibility for the study cohorts limited our ability to conduct the same analyses in each cohort such as the

association of any heavy use in the Russia cohort. Another limitation is that we did not have information about whether alcohol was consumed prior to a fall. Our interests though were not limited to falls that may have occurred as a direct result of alcohol intoxication but also falls that occurred due to the impact of chronic exposure of alcohol on conditions that predispose to falls such as peripheral neuropathy or sarcopenia. This study's approach was to examine each AUD criterion with equal weight. Other studies have found that differential weighting of some criteria such as tolerance or withdrawal are important risk factors for other conditions (Lane and Sher, 2015). Future work to identify whether select criteria are predictive of falls may be useful for busy clinicians. Finally, these findings may not apply to PWH not enrolled in studies with entry criterion related to substance use.

Strengths of the study include the use of the same established fall questionnaire by both cohorts, which has also been used in other studies (Berner et al., 2019; Erlandson et al., 2019; Sharma et al., 2018). We had data on alcohol and other drug use assessed with well-established research protocols rather than clinically obtained data which can under detect alcohol use (Bradley et al., 2011a; McGinnis et al., 2016). The current study also considered the use of other substances in analyses. This is important given that the impact of opioids, cocaine, and sedatives on fall risk is not likely uniform across substance types.

The study has pragmatic implications. For populations with high levels of heavy alcohol consumption, assessment of AUD severity rather than frequency of heavy alcohol use or total consumption may be more useful for identifying those at higher risk of falls in PWH. For populations with a broader spectrum of alcohol consumption, risk assessment should also consider identification of heavy alcohol use. The study findings can also be used for individualized patient feedback about fall prevention. Patient education should include caution about exceeding daily limits even among those with no AUD or low overall consumption. PWH with AUDs should be counseled about their heightened need for fall prevention, stressing the importance of modifying environmental risk factors (e.g., removal of home hazards). Even a reduction in AUD severity may be beneficial for fall prevention. Fall prevention interventions effective in high risk and older general populations (Li et al., 2005) should be tested among PWH with AUD.

Despite different eligibility criteria and study sample characteristics in cohorts in two different countries, we found that the risk of a fall was higher with each additional AUD criteria but not with a higher AUDIT-C score in both cohorts. Any heavy use was significant in a cohort comprised of PWH with a range of drinking patterns from abstinence to severe use disorder. Given the potential impact of falls for PWH on fracture, ambulation, and frailty, this study highlights the need to determine whether reductions in AUD severity and heavy alcohol use result in lower risk of falls in global settings.

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Table 1:

Baseline characteristics of people with HIV in St. Petersburg, Russia, and Boston, United States stratified by fall status[a]

	Boston			Russia		
Characteristic	**Total n=251**	**Fall n=87**	**No fall n=164**	**Total n=400**	**Fall n=46**	**No fall n=354**
Age, mean (std)	52 (10)	53 (10)	52 (11)	39 (6)	40 (6)	39 (6)
Female	**82 (33%)**	**36 (41%)**	**46 (28%)**	137 (34%)	14 (30%)	123 (35%)
Race/ethnicity						
Hispanic	**53 (21%)**	**17 (20%)**	**36 (22%)**	---	---	---
Black, non-Hispanic	**131 (52%)**	**35 (40%)**	**96 (59%)**	---	---	---
White, non-Hispanic	**47 (19%)**	**25 (29%)**	**22 (13%)**	---	---	---
Employed	62 (25%)	23 (26%)	39 (24%)	260 (65%)	28 (61%)	232 (66%)
Lives alone	123 (49%)	40 (46%)	83 (51%)	---	---	---
Homeless	**38 (15%)**	**20 (23%)**	**18 (11%)**	3 (1%)	0	3 (1%)
Social support scale, mean (std)[b]	63 (28)	61 (30)	64 (27)	35 (6)	35 (7)	36 (6)
Body mass index (BMI)						
Underweight (BMI <18.5)	6 (3%)	2 (2%)	4 (3%)	34 (9%)	4 (9%)	30 (9%)
Obese (BMI ≥30)	79 (33%)	35 (43%)	44 (28%)	12 (3%)	0 (0%)	12 (3%)
CD4 count < 200	21 (9%)	8 (9%)	13 (8%)	94 (24%)	9 (20%)	85 (24%)
HIV viral suppression[c]	208 (87%)	71 (85%)	137 (88%)	228 (57%)	27 (59%)	201 (57%)
Depressive symptoms[d]	**136 (54%)**	**56 (64%)**	**80 (49%)**	**156 (39%)**	**25 (54%)**	**131 (37%)**
Physical functioning (VR-12), mean (std)	**43 (11)**	**37 (11)**	**46 (10)**	**50 (7)**	**47 (7)**	**50 (7)**
Brief Pain Inventory, Pain Interference, median (IQR)	**1 (0, 6)**	**5 (0,7)**	**0 (0,4)**	0 (0,0)	0 (0,0)	0 (0,0)
Cognitive functioning, mean (std)[e]	**72 (20)**	**63 (22)**	**77 (16)**	82 (15)	80 (13)	82 (15)
HIV symptom index						
Dizzy, lightheaded[f]	**45 (18%)**	**24 (28%)**	**21 (13%)**	**7 (2%)**	**3 (7%)**	**4 (1%)**
Pain, numbness, tingling of hands/feet[f]	**81 (32%)**	**41 (48%)**	**40 (24%)**	**21 (5%)**	**7 (15%)**	**14 (4%)**
Trouble remembering[f]	**80 (32%)**	**41 (48%)**	**39 (24%)**	32 (8%)	6 (13%)	26 (7%)
Fear of falling[g]	**44 (18%)**	**31 (36%)**	**13 (8%)**	**8 (2%)**	**5 (11%)**	**3 (1%)**
AUDIT-C, median (IQR)[h]	3 (0,5)	3 (0,5)	2 (0,5)	10 (8,10)	10 (9,10)	10 (8,10)

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	Boston			Russia		
Characteristic	**Total n=251**	**Fall n=87**	**No fall n=164**	**Total n=400**	**Fall n=46**	**No fall n=354**
Heavy alcohol use, any[h]	113 (45%)	44 (51%)	69 (42%)	400 (100%)	46 (100%)	354 (100%)
Frequency of heavy use[h]						
Daily or almost daily	6 (2%)	2 (2%)	4 (2%)	66 (16%)	7 (15%)	59 (17%)
Weekly	19 (8%)	10 (11%)	9 (5%)	250 (63%)	33 (72%)	217 (61%)
Monthly	43 (17%)	13 (15%)	30 (18%)	43 (11%)	3 (6%)	40 (11%)
Less than monthly	45 (18%)	19 (22%)	26 (16%)	26 (6%)	2 (4%)	24 (7%)
Never	138 (55%)	43 (49%)	95 (58%)	15 (4%)	1(2%)	14 (4%)
Alcohol use disorder severity (DSM-5 criteria)						
Moderate or severe	66 (27%)	27 (32%)	39 (24%)	256 (64%)	35 (76%)	221 (62%)
Mild	39 (16%)	14 (17)	25 (15)	110 (28%)	8 (17%)	102 (29%)
None	144 (58%)	44 (52%)	100 (61%)	34 (9%)	3 (7%)	31 (9%)
Past month drug use, any[i]						
Illicit opioid use	**40 (16%)**	**23 (26%)**	**17 (10%)**	97 (24%)	11 (24%)	86 (24%)
Illicit non-opioid sedative use	**20 (8%)**	**11 (13%)**	**9 (6%)**	**3 (1%)**	**2 (4%)**	**1 (0%)**
Cocaine use	61 (24%)	26 (30%)	35 (21%)	3 (1%)	0	3 (1%)

[a]Experienced a fall in past 6 months, all numbers are n (%) unless otherwise, specified. Bold indicates significant difference ($p<0.05$) between participants who fell and did not fall. "---" indicates a characteristic that was not collected.

[b]Modified MOS-SS transformed score 0–100 (Boston), Duke/UNC Functional Social Support Questionnaire (Russia)

[c]HIV viral load < 200 copies in Boston, <300 copies in Russia

[d]CES-D ≥10 (Boston) and CES-D ≥16 (Russia)

[e]Medical Outcomes Study HIV Health Survey, cognitive functioning questions (attention, concentration, planning), mean (std)

[f]"Bothers me" or "Bothers me a lot"

[g]"Have you been concerned with losing your balance and falling while doing your usual activities? "Quite a bit" or "Very much"

[h]AUDIT-C score (first 3 quantity frequency questions of AUDIT) Range 0–12. "Heavy alcohol use" based upon third question of the AUDIT-C, which asks about drinking 6 or more drinks in an occasion

[i]Addiction Severity Index (Boston); Drug Use Survey (Section 10) (Russia)

Table 2:

Results of separate logistic regression models assessing the association of 3 AUDIT-C derived measures of alcohol consumption and fall among PWH in Boston, Massachusetts[a]

	OR (95%CI)	AOR (95%CI)
AUDIT-C score (per 1-point higher score)	1.06 (0.97, 1.16)[b]	--
Any heavy alcohol use vs none[c,d]	1.41 (0.84, 2.38)	**2.24 (1.21,4.13)**
Better physical functioning	**0.93 (0.90, 0.95)**	**0.92 (0.90, 0.95)**
Race/ethnicity		
Hispanic	0.40 (0.18, 0.94)	0.40 (0.17, 0.99)
Black, non-Hispanic	0.32 (0.16, 0.64)	0.26 (0.12, 0.57)
White	Ref	Ref
Frequency of heavy alcohol use[c,e,f]		
Weekly or more frequent	1.26 (0.47, 3.37)	2.12 (0.56,8.05)[e]
Monthly	0.59 (0.25,1.43)	0.59 (0.20,1.72)[e]
Less than monthly	Ref	Ref
Never	0.62 (0.31, 1.24)	0.47 (0.20,1.12)[e]
Race/ethnicity		
Hispanic	**0.42 (0.18, 0.94)**	**0.30 (0.11, 0.84)**
Black, non-Hispanic	**0.32 (0.16, 0.64)**	**0.24 (0.10, 0.59)**
White	Ref	Ref
Homeless	**2.42 (1.20, 4.87)**	**2.93 (1.22,7.06)**
Better physical functioning	**0.93 (0.90, 0.95)**	**0.92 (0.89,0.95)**
CD4 count<200	1.16 (0.46, 2.92)	0.35 (0.10,1.28)
HIV viral load suppression	0.76 (0.35, 1.62)	0.79 (0.30,2.08)
Body mass index		
Underweight	1.22 (0.22, 6.91)	1.53 (0.23,10.09)
Obese	**1.94 (1.11, 3.42)**	1.92 (0.96,3.82)

[a]Separate regression models for each AUDIT-C derived measure of alcohol consumption using baseline data. Study sample n=251 in all analyses except as indicated below.

[b]Unadjusted model is final model because no covariate changed the parameter estimate by more than 10% in either direction

[c]3rd item of the AUDIT-C: "*How often do you have six or more drinks on one occasion?*"

[d]Model adjusted for physical functioning (VR-12, PCS score) and race/ethnicity.

[e]"Never" was not the referent group to avoid using a referent group with few participants

[f]Model adjusted for race/ethnicity, physical functioning (VR-12, PCS score), CD4 count<200, HIV viral load suppression, homelessness, and body mass index (referent is ideal/overweight).

Table 3:

Results of separate logistic regression models assessing the association of 3 AUDIT-C derived measures of alcohol consumption and fall among PWH in St. Petersburg, Russia[a]

	OR (95%CI)	AOR (95%CI)
AUDIT-C score (per 1-point higher score)	1.16 (0.97, 1.39)[b]	--
Heavy alcohol use[c, d]		
More frequent (weekly, almost daily/daily)	1.88 (0.77, 4.61)[b]	---
Less frequent (monthly or less than monthly)	Ref	
Frequency of heavy alcohol use[c,e, f]		
Daily or almost daily	1.58 (0.39, 6.49)	1.30 (0.31, 5.42)
Weekly	2.03 (0.59, 6.93)	2.01 (0.59, 6.92)
Monthly	Ref	Ref
Less than monthly	1.05 (0.20, 5.54)	0.97 (0.18, 5.14)
Better physical functioning	**0.96 (0.92, 0.99)**	**0.95 (0.91, 0.99)**

[a]Separate regression model for each AUDIT-C derived measure of alcohol consumption using baseline data. Study sample n=400

[b]Unadjusted model is final model because no covariate changed the parameter estimate by more than 10% in either direction

[c]3rd item of the AUDIT-C: “How often do you have six or more drinks on one occasion?”

[d]Comparison groups informed by study sample distribution.

[e]Less than monthly was not the referent group to avoid using a referent group with few participants

[f]Model adjusted for physical functioning using VR-12 (PCS) (AOR reported per each 1-unit higher score indicating better physical functioning

Table 4:

Association of two measures of alcohol use disorder (AUD) severity using number of DSM-5 criteria and fall among PWH in Boston, Massachusetts[a]

	OR (95%CI)	AOR (95%CI)
AUD criteria (per 1 additional criteria)	**1.10 (1.02, 1.18)** [b]	--
AUD severity[c]		
Moderate to severe use disorder	**1.74 (1.07, 2.83)**	**1.85 (1.10, 3.10)** [d]
Mild use disorder	1.02 (0.63, 1.64)	1.00 (0.60, 1.66)
No use disorder	Ref	Ref
Race/ethnicity		
Hispanic	**0.42 (0.21, 0.84)**	**0.38 (0.18, 0.80)**
Black, non-Hispanic	**0.32 (0.18, 0.56)**	**0.31 (0.17, 0.57**
White	Ref	Ref
Homeless	**3.10 (1.74, 5.51)**	**2.57 (1.42, 4.65)**

[a]Results of separate GEE regression models for a) number of AUD criteria and b) AUD severity. Number of observations n= 587

[b]No covariate changed parameter estimate >10% therefore unadjusted model is the final model.

[c]Number of DSM-5 criteria for moderate to severe, mild, and no use disorder are 4–11, 2–3, and 0–1, respectively

[d]Model adjusted for race/ethnicity and homelessness

Table 5:

Association of two measures of alcohol use disorder (AUD) severity using number of DSM-5 criteria and fall among PWH in St. Petersburg, Russia[a]

	OR (95%CI)	AOR (95%CI)
AUD criteria (per 1 additional criteria)	**1.10 (1.02, 1.18)** [b]	--
AUD severity[c]		
Moderate to severe use disorder	**1.93 (1.01, 3.70)**	1.74 (0.85, 3.58)[d]
Mild use disorder	Ref	Ref
No use disorder	0.77 (0.34, 1.74)	0.88 (0.34, 2.32)[d]
Better physical functioning	**0.93 (0.91, 0.96)**	**0.94 (0.91, 0.97)**
HIV viral suppression	0.99 (0.57, 1.73)	1.02 (0.57, 1.84)

[a]Results of separate GEE regression models for a) total number of AUD criteria and b) AUD severity. Number of observations n= 670

[b]No covariate changed parameter estimate >10% therefore unadjusted model is the final model.

[c]Number of DSM-5 criteria for moderate to severe, mild, and no use disorder are 4–11, 2–3, and 0–1, respectively. Mild use disorder was the referent group because of low number of participants with no use disorder

[d]Model adjusted for physical functioning (VR-12 PCS score) and HIV viral suppression