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# Patient-Reported Bothersome Symptoms Attributed to Alcohol Use Among People With and Without HIV

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## Abstract

Helping people with HIV (PWH) and without HIV (PWoH) understand the relationship between physical symptoms and alcohol use might help motivate them to decrease use. In surveys collected in the Veterans Aging Cohort Study from 2002 to 2018, PWH and PWoH were asked about 20

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common symptoms and whether they thought any were caused by alcohol use. Analyses were restricted to current alcohol users (AUDIT-C > 0). We applied generalized estimating equations. The outcome was having any Symptoms Attributed to Alcohol use (SxAA). Primary independent variables were each of the 20 symptoms and HIV status. Compared to PWoH, PWH had increased odds of SxAA (OR 1.54; 95% CI 1.27, 1.88). Increased AUDIT-C score was also associated with SxAA (OR 1.32; 95% CI 1.28, 1.36), as were trouble remembering, anxiety, and weight loss/wasting. Evidence that specific symptoms are attributed to alcohol use may help motive people with and without HIV decrease their alcohol use.

## Keywords

AUDIT-C; Symptoms; Alcohol; HIV

## Introduction

The spectrum of unhealthy alcohol use ranging from at-risk drinking to alcohol use disorder (AUD) [1] is common in people with and without HIV and has a major impact on morbidity and mortality. Unhealthy alcohol use is particularly harmful for people with HIV (PWH), and over 25% of PWH engaged in care screen positive for unhealthy alcohol use [2, 3]. Unhealthy alcohol use among PWH is associated with worse outcomes at each stage of the HIV care continuum [4]; increased risk of medical comorbidities (e.g., cardiovascular disease, malignancy, liver disease) [5]; mental health problems [6]; and sexual risk behaviors associated with HIV transmission [7]. Furthermore, observational data indicate that consumption of 30 or more drinks per month among PWH is associated with a 30% increase in mortality compared to drinking 1–2 drinks per month [8], a finding indicating that PWH may be more sensitive to adverse effects of alcohol, and at lower levels, than people without HIV (PWoH). However, we do not know whether PWH are more or less likely to attribute particular physical symptoms to their alcohol use. This is important because patients may be more motivated to change their drinking behavior if they believe that decreasing their alcohol consumption will alleviate a bothersome symptom or symptoms.

Further, despite harms associated with unhealthy alcohol use, particularly among PWH, patients often do not receive evidence-based treatments, including counseling and medication-based interventions [9]. While this treatment gap is partially due to provider- and clinic-level factors [10, 11], patients often do not prioritize alcohol use reduction and it may be challenging to engage in formal AUD treatment [12–14]. A critical aspect of counseling interventions include provision of personalized feedback regarding drinking norms [15] and helping patients understand the direct connections between their alcohol use, physical symptoms, medical conditions, and overall health status [16–18]. This awareness can help patients see potential discrepancies between drinking behaviors and goals they may have for maintaining good health [1]. Understanding this awareness may help clinical providers better engage patients regardless of HIV status, and tailor care and education to the symptoms patients are experiencing. If PWH are more likely to both experience specific

bothersome symptoms and more likely to attribute them to alcohol use, they may be more motivated to reduce unhealthy alcohol use and to initiate AUD treatment.

However, it would be of interest to know if symptoms attributed to alcohol differ by HIV status as this will help develop more effective interventions for both groups. The harm of unhealthy alcohol use is pervasive, yet patients are not consistently motivated to receive treatment to reduce their drinking and finding opportunities to engage and motive change in alcohol use are needed.

Bothersome symptoms remain common among PWH even in the current antiretroviral therapy (ART) era [19], and there is increasing attention focused on identifying modifiable factors such as alcohol use reduction that may help decrease symptoms [20]. These are symptoms that are also common among PWoH [21]. Both PWH and PWoH would benefit from interventions that aim to reduce or eliminate alcohol use, and these interventions would likely be more successful in the context of increased motivation to reduce patient-centered symptoms. We sought to identify bothersome symptoms attributed to alcohol use and to determine whether this attribution was more or less likely among PWH compared to PWoH.

## Methods

We used survey data from the Veterans Aging Cohort Study (VACS), an ongoing multi-site, cohort study of people with and without HIV receiving care from one of eight Veterans Health Administration (VA) facilities, including Manhattan/Brooklyn, New York; Bronx, New York; Pittsburgh, Pennsylvania; Atlanta, Georgia; Houston, Texas; Baltimore, Maryland; Washington, DC; and Los Angeles, California [22]. VACS collects self-administered survey data from patients enrolled at those sites approximately annually, and survey data are linked to VA electronic health record (EHR) data, which includes diagnoses, laboratory, and pharmacy data, as well as administrative data. This longitudinal study contains variables from seven waves of surveys from 2002 to 2018. We used surveys that included the HIV Symptom Index and the outcome of interest (described below). The Institutional Review Boards at Yale University, VA Connecticut Healthcare System and each participating site approved the study.

### Measures

**Primary Independent Variables—**Baseline HIV status, which was confirmed at the study site. Level of alcohol use, which was measured with the 3-item Alcohol Use Disorders Identification Test Consumption (AUDIT-C) questionnaire, which has been validated to identify unhealthy alcohol use [23, 24]. AUDIT-C scores range from 0 to 12 with higher scores indicating greater alcohol consumption and increased likelihood of AUD [25]. We generated two measures indicating level of alcohol use, which included continuous AUDIT-C scores (1–12) and a dichotomous measure of screening positive for unhealthy alcohol use defined as AUDIT-C score    4 based on validation studies [23, 24]. The HIV Symptom Index was self-administered and asks about 20 symptoms commonly reported by both people with and without HIV [21]. While the index was originally developed in PWH, its indices were based on symptoms common to people without HIV. The HIV Symptom Index specifically uses the following prompt: "The following questions ask about symptoms you

might have had during the past four weeks. Please fill in the circle of the one response that best describes how much you have been bothered by each symptom." Participants were prompted to indicate the degree of bother, based on a five-point Likert scale: 0 = I do not have this symptom, 1 = I have this symptom and it doesn't bother me, 2 = I have this symptom and it bothers me a little, 3 = I have this symptom and it bothers me, and 4 = I have this symptom and it bothers me a lot. A symptom was considered to be bothersome (a binary yes/no indicator) when participant selected 2 or higher, similar to prior work [26].

**Outcome**—The main outcome was bothersome **S**ymptoms **A**ttributed to **A**lcohol use (SxAA) based on a yes response to, "Do you think your symptoms are caused by drinking alcohol?" Persons who reported no bothersome symptoms were coded as 'no'.

**Covariates**—Covariates included demographics (age, race/ethnicity, and sex) and prior diagnosis for lifetime AUD to simultaneously adjust for them and assess their independent association with SxAA. Race/ethnicity was derived from survey data and EHR when survey was missing and categorized as Black/non-Hispanic (reference group), White/non-Hispanic, Hispanic, and other (which included Native America, Asian, mixed race, Pacific Island/ Hawaiian and unknown). Age at each survey wave was calculated using date of birth from the EHR and categorized as age < 50, 50–64, and 65 years and older (common cut points for aging adults). Prior diagnosis of lifetime AUD was based on EHR documentation of International Classification of Disease, Ninth Revision, Clinical Modification codes.

**Analysis**—Because we sought to identify symptoms patients attributed to their ongoing alcohol use, the sample was restricted to participants reporting current alcohol use (i.e., AUDIT-C > 0). Descriptive analysis of the study sample was conducted, both overall and by HIV status, using the first survey completed. We used t-test for continuous variables, or a nonparametric counterpart, Wilcoxon test, for non-normally distributed continuous variables, and chi-square ($\chi^2$) for categorical variables. Using generalized estimating equations (GEE) to account for within-subject correlation and a logistic regression model specification since the outcome was dichotomous, we assessed factors associated with any SxAA across five waves of data. We ran models overall and stratified by HIV status to see if there were differing contributing factors (i.e., potential interaction that we would then formally test). Analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina). Statistical significance was determined by a two-sided p-value of < 0.05.

## Results

### Participant Sociodemographic and Clinical Characteristics

Among an analytic sample of 5464 who reported current alcohol use, 2810 (51%) were PWH (75% of whom were on ART) and 2654 (49%) were PWoH. The median and interquartile range for the number of surveys completed was 2 (1, 3). Among these patients, 5% were female, 63% were 50 years old and older (14% of whom were  65), 64% were Black, 38% had an AUDIT-C score of 4 or greater, 23% had AUD, and 7% endorsed any SxAA (Table 1). PWH compared to PWoH were less likely to have AUD (18% vs. 28%; $\chi^2$ = 80, p < 0.001) and marginally more likely to have SxAA (8% vs. 6%; $\chi^2$ = 4, p = 0.05).

PWH were also more likely to report symptoms as bothersome overall and were more likely to report loss of appetite (27% vs. 21%; $\chi^2 = 30$, p < 0.001), diarrhea (32% vs. 19%; $\chi^2 = 130$, p < 0.001), fever/chills (25% vs. 20%; $\chi^2 = 25$, p < 0.001), fatigue (51% vs. 47%; $\chi^2 = 8$, p = 0.004), nausea/vomiting (16 vs. 12%; $\chi^2 = 25$, p < 0.001), problems with sex (39% vs. 36%; $\chi^2 = 7$, p = 0.009), skin problems (37% vs. 33%; $\chi^2 = 10$, p = 0.002), and problems with weight loss or wasting (27% vs. 20%; $\chi^2 = 34$, p < 0.001), specifically (Fig. 1).

### Factors Associated with SxAA

In a multivariable GEE model, women compared to men [OR (95% CI) = 0.45 (0.25, 0.81)], and White participants compared to Black participants [OR (95% CI) = 0.45 (0.34, 0.61)] were less likely to endorse SxAA, while age 50–64 compared to age < 50 years old [OR (95% CI) = 1.37 (1.12, 1.67)], PWH compared to PWoH [OR (95% CI) = 1.54 (1.27, 1.88)], higher AUDIT-C scores [OR (95% CI) = 1.32 (1.28, 1.36)], and having AUD versus not [OR (95% CI) = 2.95 (2.42, 3.58)] were associated with a greater likelihood of SxAA (Table 2). Trouble remembering [OR (95% CI) = 1.39 (1.11, 1.74)], nervous/anxious [OR (95% CI) = 1.35 (1.05, 1.74)], and weight loss or wasting [OR (95% CI) = 1.28 (1.03, 1.59)] were bothersome symptoms associated with SxAA.

### Factors Associated with SxAA by HIV Status

In models stratified by HIV status, controlling for demographic factors and levels of alcohol, there were only modest differences in factors associated with SxAA. Among PWH, hair loss or change, trouble remembering, and problems with weight loss or wasting were significantly associated with SxAA (Fig. 2). Changes in the way the body looks, such as fat deposits, was of borderline statistical significance. Among PWoH, fatigue and nausea or vomiting were bothersome symptoms associated with SxAA (Fig. 2). Among the modest differences by HIV status (i.e., the stratified models), only the formal test of the interaction term between HIV status and nausea or vomiting was significant [OR (95% CI) = 0.51 (0.33, 0.76); p = 0.001].

## Discussion

In a national diverse sample of matched PWH and PWoH with current alcohol use, PWH were more likely to attribute bothersome symptoms to alcohol than PWoH, with greater levels of alcohol use increasing likelihood of symptom attribution for both groups. The presence of bothersome symptoms related to alcohol use presents an opportunity to engage and encourage patients, especially PWH, to reduce drinking. Reducing alcohol use may be a preferred alternative to medication-based treatment of many common health symptoms in light of medication side effects as well as the harm of polypharmacy (conventionally defined as taking five or more medications) [27]. Studies have demonstrated that PWH are at elevated risk of polypharmacy because they are more likely to have chronic conditions treated by medications (e.g., high blood pressure, pain) in addition to life-preserving ART, which puts them at or closer to the threshold for polypharmacy at an earlier age [28]. Nonpharmacological approaches (such as alcohol reduction/cessation) would avoid this

risk while addressing desired patient-centered health outcomes (i.e., reducing bothersome symptoms).

We found that level of alcohol use and presence of AUD had the strongest association with SxAA. For each unit increase in AUDIT-C, the odds of SxAA (i.e., attributing symptoms to alcohol) increased by 32%. Participants were almost three times as likely to endorse SxAA if they had a diagnosed AUD compared to those who did not, indicating that participants had some awareness of the role of unhealthy alcohol use in causing their symptoms.

Interestingly, while our sample had a small proportion of women, we found that compared to their male counterparts, women were less likely to endorse SxAA both in unadjusted and adjusted models. This is in the context of women being more likely to report symptoms as bothersome than men (data not shown). However, women did report lower alcohol use on average and were less likely to have AUD; therefore, it is reasonable that they would not suspect that alcohol contributed to their symptoms.

Additionally, there were symptom differences by HIV status, notably nausea. For PWoH, targeting bothersome nausea or vomiting may be an effective means of reducing unhealthy alcohol use. While for PWH, targeting trouble memory and weight loss may motive them to reduce their alcohol use.

To our knowledge, this is the first study to examine bothersome symptoms attributed to alcohol among PWH and matched PWoH. However, some prior research has explored other contributing factors. Using national survey data in France, Boyer and colleagues investigated factors associated with moderate or high number of bothersome symptoms reported by PWH. They found that a higher likelihood of reporting moderate or high number of symptoms was associated with feeling alone, experiencing discrimination, and being female (and among women, the likelihood increased in the presence of injection drug use) [29]. The authors did consider excessive alcohol consumption (more than 4 alcohol unit/day for men and 3 alcohol unit/day for women), but found no significant difference by bothersome symptoms grouping and it was not included in the regression model.

Our findings should be interpreted with some limitations in mind. The sample was predominantly male, receiving care in the VA Healthcare System, and may not be generalizable to women living with HIV, or to those receiving care elsewhere. Also, owing to the nature of data obtained through self-reported questionnaires, there is a potential for under- and over-reporting. Nonetheless, there is no reason to suspect that this effect would result in biased comparisons. In addition, the mean age of participants was 52 years old, and results may not be consistent across the lifespan for PWH.

Our study has important strengths. It is a diverse nationwide sample that included HIV status, AUDIT-C, AUD, and a validated symptom index, and found, after controlling for these measures and demographics, there were modifiable bothersome symptoms that were independently associated with SxAA. Evidence that specific bothersome symptoms are associated with alcohol use may help motive people with and without HIV to decrease their alcohol use.

## Conclusion

In this sample of Veterans receiving care in the VA Healthcare System, specific bothersome symptoms were attributed to alcohol use. Future work evaluating alcohol reduction and cessation effects on trouble remembering, anxiety, and weight loss or wasting, especially in an aging HIV population, are warranted. These findings represent important opportunities to engage and encourage patients to reduce or abstain from alcohol use. Alcohol reduction may be an important alternative to treating symptoms with medications.

## Funding

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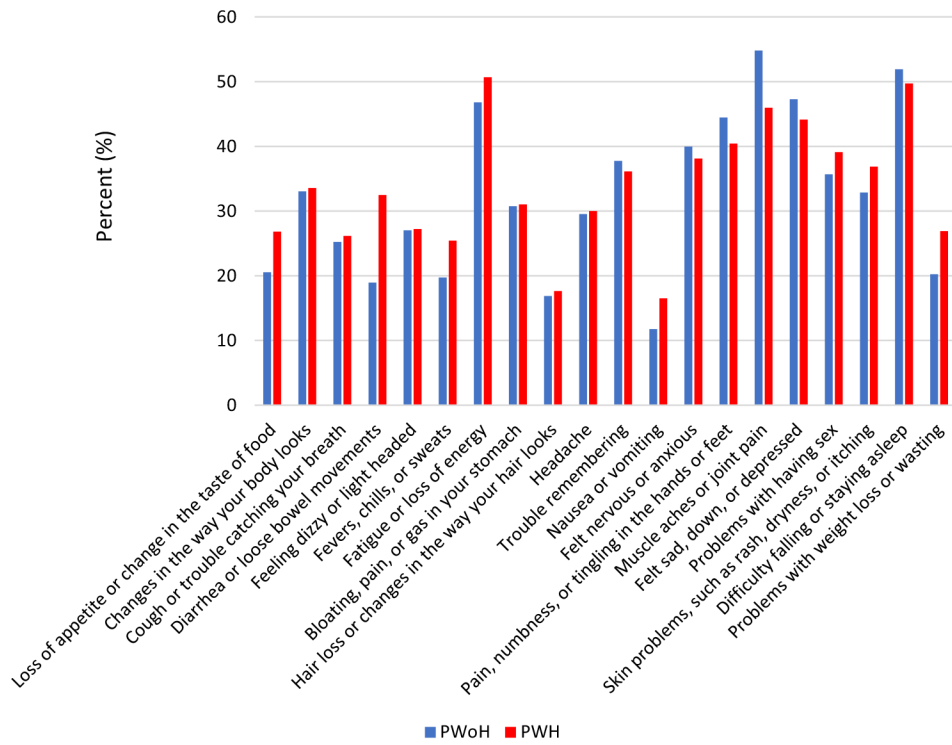
PWoH = people without HIV; PWH = people with HIV

**Fig. 1.**
Proportion reporting bothersome symptoms by HIV status. *PWoH* people without HIV, *PWH* people with HIV
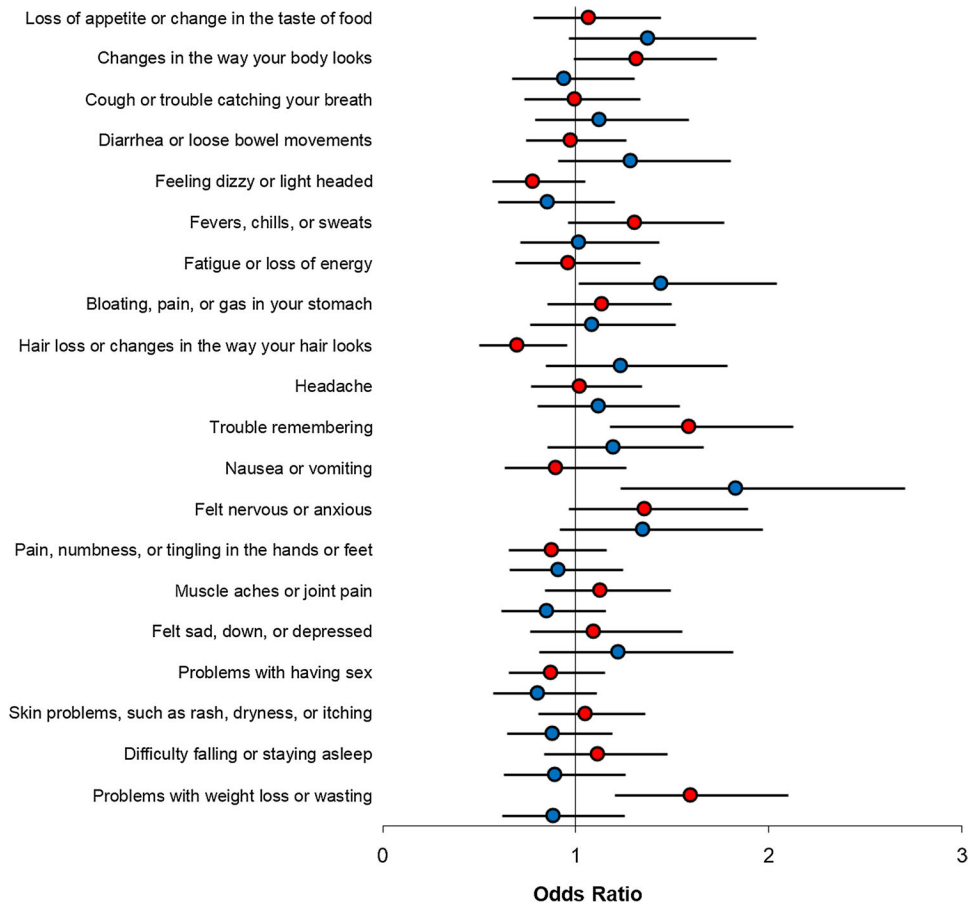
**Fig. 2.**
Forest plot of adjusted OR (95% CI) of the association between patient-reported bothersome symptoms and SxAA by HIV status from stratified models using GEE logistic regression. Blue circles represent PWoH and red circles PWH. Model was adjusted for age, race, sex, AUDIT-C and AUD. The only significant interaction by HIV status was nauseas or vomiting [OR (95% CI) = 0.51 (0.33, 0.76); p = 0.001]. *SxAA* symptoms attributed to alcohol use, *PWoH* people without HIV, *PWH* people with HIV

## Table 1

Characteristics of VACS participants reporting current alcohol use, overall and stratified by HIV status at first survey

| | Overall, n = 5464 | PWoH, n = 2654 (49%) | PWH, n = 2810(51%) | $\chi^2$ | p value |
|---|---|---|---|---|---|
| Sex, n (%) | | | | 76 | < 0.001 |
| Female | 260 (4.8) | 195 (7.4) | 65 (2.3) | | |
| Male | 5204 (95.2) | 2459 (92.6) | 2745 (97.7) | | |
| Age group, n (%) | | | | 46 | < 0.001 |
| < 50 | 2022 (37.0) | 865 (32.6) | 1157 (41.2) | | |
| 50–64 | 2941 (53.8) | 1510 (56.9) | 1431 (50.9) | | |
| 65 | 501 (9.2) | 279 (10.5) | 222 (7.9) | | |
| Race/ethnicity, n (%) | | | | 10 | 0.02 |
| White non-Hispanic | 1155 (21.1) | 586 (22.1) | 569 (20.2) | | |
| Black non-Hispanic | 3485 (63.8) | 1648 (62.1) | 1837 (65.4) | | |
| Hispanic | 531 (9.7) | 283 (10.7) | 248 (8.8) | | |
| Other | 293 (5.4) | 137 (5.2) | 156 (5.6) | | |
| AUDIT-C, median (IQR) | 3 (1, 5) | 3 (1, 5) | 2 (1, 4) | 26 | < 0.001 |
| 4, n (%) | 2073 (37.9) | 1098 (41.4) | 975 (34.7) | 26 | < 0.001 |
| AUD, n (%) | 1268 (23.2) | 755 (28.4) | 513 (18.3) | 80 | < 0.001 |
| SxAA, n (%) | 382 (7.0) | 167 (6.3) | 215 (7.6) | 4 | 0.05 |
| CD4 cell count (cells/mm$^3$), median IQR | n/a | n/a | 425 (263, 612) | n/a | n/a |
| HIV viral load, median IQR | n/a | n/a | 109 (50, 3953) | n/a | n/a |

*VACS* Veterans Aging Cohort Study, *PWoH* people without HIV, *PWH* people with HIV, *AUD* alcohol use disorder, *SxAA* symptoms attributed to alcohol use, *IQR* interquartile range, $\chi^2$ Chi-square

**Table 2**

GEE model with a logistic regression model specification assessing factors associated with SxAA

| Variables | OR (95% CI) | p value |
|---|---|---|
| Age 50–64 (ref age < 50) | 1.37 (1.12, 1.67) | **0.002** |
| Age 65 (ref age < 50) | 1.30 (0.91, 1.86) | 0.15 |
| Female | 0.45 (0.25, 0.81) | **0.01** |
| White non-Hispanic (ref Black non-Hispanic) | 0.45 (0.34, 0.61) | **< 0.001** |
| Hispanic (ref Black non-Hispanic) | 0.96 (0.70, 1.30) | 0.77 |
| Other (ref Black non-Hispanic) | 1.01 (0.69, 1.47) | 0.97 |
| HIV | 1.54 (1.27, 1.88) | **< 0.001** |
| AUDIT-C | 1.32 (1.28, 1.36) | **< 0.001** |
| AUD | 2.95 (2.42, 3.58) | **< 0.001** |
| Loss of appetite or change in the taste of food | 1.17 (0.93, 1.48) | 0.17 |
| Changes in the way your body looks, such as fat deposits or weight gain | 1.12 (0.91, 1.39) | 0.28 |
| Cough or trouble catching your breath | 1.04 (0.83, 1.30) | 0.74 |
| Diarrhea or loose bowel movements | 1.10 (0.89, 1.35) | 0.38 |
| Feeling dizzy or lightheaded | 0.82 (0.65, 1.03) | 0.09 |
| Fevers, chills, or sweats | 1.19 (0.95, 1.50) | 0.13 |
| Fatigue or loss of energy | 1.13 (0.89, 1.44) | 0.33 |
| Bloating, pain, or gas in your stomach | 1.11 (0.90, 1.38) | 0.34 |
| Hair loss or changes in the way your hair looks | 0.86 (0.67, 1.10) | 0.22 |
| Headache | 1.04 (0.85, 1.29) | 0.70 |
| Trouble remembering | 1.39 (1.11, 1.74) | **0.004** |
| Nausea or vomiting | 1.18 (0.91, 1.52) | 0.22 |
| Felt nervous or anxious | 1.35 (1.05, 1.74) | **0.02** |
| Pain, numbness, or tingling in the hands or feet | 0.88 (0.71, 1.09) | 0.25 |
| Muscle aches or joint pain | 0.98 (0.79, 1.21) | 0.85 |
| Felt sad, down, or depressed | 1.15 (0.88, 1.50) | 0.32 |
| Problems with having sex, such as loss of interest or lack of satisfaction | 0.84 (0.68, 1.04) | 0.11 |
| Skin problems, such as rash, dryness, or itching | 0.97 (0.79, 1.18) | 0.73 |
| Difficulty falling or staying asleep | 1.02 (0.82, 1.28) | 0.83 |

| Variables | OR (95% CI) | p value |
|---|---|---|
| Problems with weight loss or wasting | 1.28 (1.03, 1.59) | **0.02** |

*GEE* generalized estimating equations, *SxAA* symptoms attributed to alcohol use, *AUD* alcohol use disorder, *ref* reference

The bold values indicate variables that were statistically significant at $p < 0.05$