Differentiating Types of Self-Reported Alcohol Abstinence

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Abstract

We contrast three types of abstinence: quit after alcohol associated problems (Q-AP), quit for other reasons (Q-OR), and lifetime abstainer (LTA). We summarized the characteristics of people living with HIV (PLWH), and matched uninfected individuals, by levels of alcohol use and types of abstinence. We then identified factors that differentiate abstinence and determined whether the association with an alcohol biomarker or a genetic polymorphism is improved by differentiating abstinence. Among abstainers, 34% of PLWH and 38% of uninfected were Q-AP; 53% and 53% were Q-OR; and 12% and 10% were LTA. Logistic regression models found smoking, alcohol, cocaine, and hepatitis C increased odds of Q-AP, whereas smoking and marijuana decreased odds of LTA. Differentiating types of abstinence improved association. Q-APs and LTAs can be readily differentiated by an alcohol biomarker and genetic polymorphism. Differentiating type of abstinence may enhance understanding of alcohol health effects.

Key Words: Alcohol Use Disorder, HIV, veterans, *ADH1B*, Phosphatidylethanol

Introduction:

Harmful alcohol use, typically identified via diagnostic interview, is a world-wide problem which often goes unrecognized. Even when harmful use is recognized, treatments may be ineffective. New mechanistic insights from large-scale epidemiological, clinical, and genetic studies are needed to enable more effective recognition and treatment of this condition. However, due to the time and resources required, a diagnostic interview is impractical for use in large-scale studies. Further, while past patterns of alcohol consumption are well recognized among substance use researchers as an important independent predictor for many health outcomes(1, 2), alcohol exposure measures used in large scale epidemiologic and genetic studies often use state rather than lifetime (trait) measures, and therefore fail to consider patterns of past use that deviated from present use.

Many large genetic studies of harmful alcohol use have employed International Classification of Disease diagnostic codes for Alcohol Use Disorder (AUD) codes(3-6) or the full or abbreviated Alcohol Use Disorders Identification Test (AUDIT)(7, 8), both of which have limitations. AUD codes are widely used to document diagnoses during clinical encounters. They are meant to reflect active conditions justifying treatment. However, codes are only recorded if present, making it impossible to differentiate patients who were screened and found not to have the diagnosis from those who were not screened. Further, AUD codes are insensitive and biased; for example, controlling for quantity-frequency data, African American ancestry is associated with a twofold increased risk of having an AUD code compared with European ancestry(9). The AUDIT is a 10-item, self-reported, screening tool that measures alcohol consumption and

alcohol-related problems over the past year(10). AUDIT-Consumption (AUDIT-C) consists of the first 3 questions, which measure the quantity and frequency of alcohol consumption and the frequency of heavy drinking over the past year(11, 12). In some healthcare systems, such as the Veterans Administration Healthcare System (VA), the AUDIT-C score is measured annually. However, as a self-reported metric, AUDIT-C is subject to social desirability bias(13), which may be more pronounced among individuals who have experienced alcohol-associated problems such as liver disease(14).

Further, AUDIT-C measures only past-year consumption, a changeable state which may not encompass all those experiencing harm from alcohol. Most adults who report current abstinence drank in the past(15, 16), and some of these stopped due to problems associated with drinking. Few are lifelong abstainers. Many prior studies have demonstrated that failure to differentiate types of current abstinence based on prior drinking history likely diminishes statistical power and may contribute to biased results(17-23). Specifically, the often-reported u- or j-shaped association between level of alcohol consumption and cardiovascular disease may be confounded if the comparison group is comprised of abstinent individuals without regard to past drinking(2, 24-26). Similarly, recently reported genetic correlations may be misleading(7, 8). However, to our knowledge, no study has directly considered the implications of this misclassification for genetic discovery.

Some limitations of self-reported current state consumption measures such as AUDIT-C can be partially addressed using repeated measures. Using an average of seven AUDIT-C measures per participant, we demonstrated that long-term trajectories of AUDIT-C, compared to a single measurement, reduce the proportion designated as

abstinent and improved the association with a direct, shorter term (21 days), biomarker (phosphatidylethanol or PEth)(27). We also demonstrated stronger associations for AUDIT-C trajectories and age-adjusted mean AUDIT-C (AAM AUDIT-C) with polymorphisms of *ADH1B* among African Americans (AAs, rs2066702 or Arg369Cys)(9, 27) and European Americans (EAs, rs1229984 or Arg48His). This suggests that, while time frames of PEth and AUDIT-C are different, drinking patterns in middle age are comparatively stable and repeated longitudinal measures of self-report improve agreement with even a relatively short term (e.g. 21 days) biomarker.

Accurate assessment of alcohol use among those living with HIV is particularly important since their greater physiologic frailty(28) and polypharmacy(29) likely makes them more susceptible to adverse effects of ongoing alcohol consumption, even at levels that may not be considered harmful among uninfected individuals(28). In many ways, a direct biomarker such as PEth, repeated over many years of observation might be an ideal metric. PEth is: only formed in the presence of alcohol; associated with alcohol exposure in a dose-response manner; and substantially more sensitive and specific than indirect measures of alcohol exposure such as carbohydrate deficient transferrin (CDT), gamma-glutamyltransferase (GGT), mean corpuscular volume (MCV), or aminotransferases (AST or ALT)(30). PEth can differentiate abstainers from moderate drinkers as well as identify severe alcohol misuse(31). Compared with using self-reported AUDIT-C (>4), using a cutpoint of 250 ng/mL or more, PEth demonstrated a sensitivity of 87%, a specificity of 88%, a positive predictive value of 89% and a negative predictive value of 87%(31). Further, PEth is not subject to the issues of bias surrounding AUD codes or self-reported AUDIT-C. However, PEth can be insensitive

because it does not reflect past drinking beyond a 21-day interval. It would need to be repeated regularly to detect more widely spaced intervals of binge drinking. Further, PEth remains a “send out” test that can only be run by a few US laboratories with limited capacity, making large-scale longitudinal use of PEth impractical at present.

Thus, using data from the Veterans Aging Cohort Study (VACS), a well-characterized sample of people living with or without HIV that provides detailed self-reported alcohol data and both PEth and genetic assays in the same subset, we identified three types of abstinence: former drinkers who quit after alcohol associated problems (Q-AP); former drinkers who quit for other reasons (Q-OR); and lifetime abstainer (LTA). Because people living with HIV infection (PLWH) are particularly susceptible to alcohol-associated health problems(28), we hypothesized that a greater proportion of PLWH would be Q-AP, compared to uninfected individuals. We first compared characteristics of individuals reporting different types of abstinence with individuals reporting recent use. We then considered factors that distinguish Q-APs and LTAs. Finally, we determined whether differentiating types of abstinence improves associations with PEth and, among African Americans in the cohort, with the *ADH1B* polymorphism rs2066702, the minor allele of which is protective against harmful alcohol use(8, 32-35).

Methods:

Data

The *Veterans Aging Cohort Study (VACS)* survey sample is a cohort of PLWH and matched uninfected veterans consented for prospective, recurrent surveys on alcohol, drug use, and other health-related behaviors. These data are also linked to the

longitudinal VA electronic health record (EHR). The biomarker cohort is nested within the VACS survey sample and includes 1525 (69% AAs) PLWH and 843 (67% AAs) uninfected individuals who provided a blood sample in the period 2005-2007.

Our analytic sample was restricted to VACS participants who completed a survey between October 2012 and February 2018. Data included demographics (age, sex, race/ethnicity [white, yes/no]), self-reported alcohol use and problems with alcohol, smoking status (never, current, and past) and drug use. Other conditions were based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes and laboratory results extracted from the EHR. Our primary variable of interest was level of alcohol use according to AUDIT-C score and type of abstinence among those reporting abstinence (AUDIT-C=0). Alcohol use was categorized as lifetime abstainer (defined as never having had a drink of alcohol), quit drinking (AUDIT-C=0, but reported past alcohol use), current non-hazardous (AUDIT-C 1-3), and current hazardous (AUDIT-C≥4)(12, 36). Problems with alcohol were based on the questions "Have you EVER had problems with alcohol?" (yes/no), and "Did you stop drinking because of these problems?" (yes/no).

Other variables of interest included: Self-reported smoking based on 1) "Have you smoked at least 100 cigarettes (5 packs) in your entire life?", 2) "How many cigarettes do you smoke per day NOW?", 3) "How long has it been since you last smoked cigarettes?", and if participant selected 4) "Have already quit". Never smoker was based on answering no to smoking a least 100 cigarettes and having no indication of smoking, current smoker was based on questions 1, 2, and 3 – indication of smoking in the past 30 days, and past smoker was based on 3 and 4 – quitting and having smoked > 30

days ago. We were also interested in use of both current (in the past 12 months) and ever marijuana, cocaine, and heroin use based on “For each of the following drugs, please indicate how often in the 12 months you used each drug.”, 0=have never tried, 1=no use in the last year, 2=less than once a month, 3=one to three times a month, 4=one to three times a week, 5=four to six times a week, and 6=every day, where > 1 was current use and >0 was ever. Alcohol use disorder and drug use disorder were based on ICD-9 codes; depression was based on the Primary Care Evaluation of Mental Disorders (PRIME-MD) survey items, where a score ≥ 10 is indicative of depression; and Hepatitis C (HCV) infection was based on ICD-9 code, a positive antibody titer, and/or detectable HCV RNA. The VACS index score 2.0, a validated measure of mortality risk and an indicator of severity of illness(37, 38), is composed of age, CD4 cell count, HIV-1 RNA, hemoglobin, composite markers of liver and renal injury [Fibrosis-4 (FIB4) and estimated glomerular filtration rate (eGFR)], HCV infection status, albumin, white blood cell count, and body mass index.

Analyses

Characteristics were summarized across alcohol level and type of abstinence, by HIV status. Among individuals reporting abstinence, we evaluated factors associated with 1) Q-AP versus Q-OR and LTA and 2) LTA versus Q-AP and Q-OR using logistic regression. Model discrimination was assessed using the C-statistic, a measure comparable to area under the curve. Values range from 0.5 to 1.0, whereby C-statistic =1.0 denotes perfect discrimination.

In the biomarker cohort, which is predominantly African American, we compared the association of two criterion standards, PEth and the *ADH1B* polymorphism, with

AUDIT-C scores, with and without stratification by type of abstinence (Q-AP, Q-OR, or LTA). We created AAM AUDIT-C using all AUDIT-C measures collected in the VA EHR from 2007-2016. Using age 50 years as the reference point, we created weights to down-weight scores for individuals younger than 50 and up-weight scores for individuals older than 50 years. This procedure has been described in detail(9). We calculated proportions with PEth>20 ng/ml (cutoff used for forensic work(27)), by AAM AUDIT-C score among the 1791 for whom a PEth assay was completed. Because the *ADH1B* polymorphism is common among individuals of African American ancestry (rs2066702 or Arg369Cys) we calculated the percentage of African Americans with the minor 369Cys allele by AAM AUDIT-C score among the 1380 individuals with genotype data. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA) and Stata 14.2.

Results:

Study Sample, Levels of Self-Reported Alcohol, and Type of Abstinence

Among 4171 participants (2192 PLWH) the median age was 58 years (Table 1 a and b): 38% of PLWH versus 40% of uninfected reported abstinence (AUDIT-C=0, p= 0.14); 41% of PLWH versus 34% of uninfected reported non-harmful use (AUDIT-C:1-3, p<0.001); and 21% of PLWH versus 25% of uninfected reported harmful use (AUDIT-C: 4+, p=0.001). Of those reporting abstinence, 34% PLWH versus 38% uninfected were Q-AP; 53% versus 53% were Q-OR; and 12% versus 10% were LTA (p=0.19, 0.75, and 0.14 respectively).

After stratifying by age (Figure 1), the proportion of hazardous drinkers decreased with age from 44% of uninfected aged <45 years to 15% of PLWH aged 65+ years.

While the overall proportion of LTAs remained relatively constant by age, the overall proportion of Q-APs increased with age from 6% among uninfected individuals <45 years to 15% among PLWH who were 65+ years (p trend<0.001). The overall proportion of Q-ORs increased with age from 13% among uninfected individuals <45 years to 24% among PLWH who were 65+ years (p trend<0.001).

When LTAs, Q-ORs, and Q-APs were compared using a trend test (Table 1 a and b), LTAs were least likely, and Q-APs were most likely, to have HCV infection (p<0.001), alcohol use disorder (p<0.001), drug use disorder (p<0.001), and depression (p=0.10 for PLWH and 0.001 for uninfected). Q-APs were also most likely to currently smoke or smoked tobacco in the past (p<0.001) and used marijuana, cocaine, or heroin in the past (p<0.001).

Multivariable Models

Among all patients reporting abstinence (810 PLWH, 716 uninfected), models accurately predicted Q-APs overall (Table 2, C-statistic: 0.71; 95% CI 0.68, 0.73) and stratified by HIV status (C-statistic: for PLWH 0.71; 95% CI 0.67, 0.74; for uninfected 0.72; 95% CI 0.68, 0.76). In all models, current (overall OR 2.53; 95% CI 1.83, 3.48, PLWH OR 2.56; 95% CI 1.62, 4.02, and uninfected OR 2.54; 95% CI 1.60, 4.04; p<0.001 for all) and past (overall OR 2.85; 95% CI 2.07, 3.94, PLWH OR 2.82; 95% CI 1.81, 4.40, and uninfected OR 3.04; 95% CI 1.89, 4.91; p<0.001 for all) smoking were the strongest predictors indicating a nearly 3-fold increased risk of being a Q-AP, compared to never smokers. Having an AUD code doubled the risk of Q-AP in all models. Among PLWH, HCV infection (OR 1.53; 95% CI 1.06, 2.19) and past cocaine use (OR 1.74; 95% CI 1.13, 2.66) were important indicators. Also, having a higher CD4

cell count increased the odds of being a Q-AP (sqrt of CD4 OR 1.04; 95% CI 1.01, 1.07). Among uninfected individuals, past cocaine use (OR 1.79; 95% CI 1.06, 3.03) and AUD (OR 3.12; 95% CI 1.95, 4.97) were strong indicators of Q-AP.

Models also accurately predicted LTAs overall (Table 3, C-statistic: 0.80; 95% CI 0.77, 0.84) and by HIV status using the same variables as in models predicting Q-AP (Table 2). Models predicting LTAs showed largely opposite associations to those predicting Q-APs. For example, past (OR 0.14; 95% CI 0.09, 0.23) or current (OR 0.26; 95% CI 0.16, 0.40) smokers were much less likely to be LTAs. LTAs were also unlikely to have used marijuana in the past (OR 0.39; 95% CI 0.23, 0.66).

Except for white race being less common among LTAs (OR 0.45; 95% CI 0.26, 0.78), demographic factors (age, sex, race/ethnicity) were not important indicators. Neither HIV status, VACS Index, nor depression were discriminating indicators for Q-AP or LTA membership.

Association of PEth and ADH1B Polymorphism

Among 1719 participants with AAM AUDIT-C scores and PEth assays, of which 12% had PEth>20ng/ml, 750 (43.6%) cumulatively reported abstinence (AAM AUDIT-C=0). Abstinent individuals sorted into the follow types: 58% Q-APs (n=435); 29% Q-ORs (n=216); and 13% LTAs (n=99). Compared with using one overall abstinent group, differentiating types of abstinence (Figure 2) did not improve the strength of the statistical association of AAM AUDIT-C with PEth (p trend 2.79 $X10^{-86}$ vs 3.20 x 10^{-79}). Among the 1380 African American individuals with genotype data, 44% (n=610) reported cumulative abstinence (AAM AUDIT-C=0) and stratified into 58% (n=356) Q-APs, 28% (n=168) Q-ORs, and 14% (n=86) LTAs. Compared with grouping abstinent individuals,

differentiating type of abstinence (Figure 3) improved association of AAM AUDIT-C with rs 2066702 (p trend 0.03 vs 0.007).

Discussion:

Approximately 40% of adults in VACS, with or without HIV infection, report alcohol abstinence (AUDIT C=0) and, of these, 10% are Lifetime Abstainers (LTAs), a third are people who quit drinking after alcohol associated problems (Q-AP), and more than half are people who quit drinking for other reasons (Q-OR). LTAs were very distinct from Q-APs. Among abstainers, multivariable logistic models demonstrated good discrimination (C-statistics ≥0.70) of Q-APs and LTAs. While differentiation of abstinence type did not statistically improve association with a short-term biomarker for alcohol exposure (PEth), it substantially increased the genetic trait association with the *ADH1B* polymorphism, which is protective against harmful alcohol use and is common among African Americans (rs2066702). Contrary to our hypothesis, PLWH were not more likely to report abstinence or to be Q-APs than uninfected comparators.

Our work extends prior studies. Studies in the general population have long recognized the likelihood that some adults who quit drinking do so because of health problems(21, 22, 26, 39, 40) and this recognition led to including past alcohol use history(39), excluding individuals who endorse past alcohol use(22), or including in the comparison group only those who drink occasionally(23). None of these studies identified Q-APs or considered how they differed from Q-ORs. This is important because Q-APs and Q-ORs demonstrated different associations with PEth and with the genetic trait criterion standard.

Among PLWH, Crane et al., using data from the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS), found that 36% of those reporting current abstinence (AUDIT=0) had a prior AUD code(1). Among those reporting abstinence, indicators of a prior AUD code included HCV coinfection and substance use. Unlike our analyses, these investigators had no means of identifying Q-APs. While AUD codes were an important indicator of Q-APs in our study, only a minority of Q-APs (24% PLWH, 43% of uninfected) had an AUD code. Further, we previously reported that controlling for AUDIT-C, African Americans are twice as likely to be given an AUD code(41), suggesting that AUD codes are assigned in a racially biased manner. A limitation which Q-AP, Q-OR, and LTA would not have.

Importantly, we are not aware of any prior study demonstrating that differentiating Q-APs among abstainers increases the magnitude of the association with a genetic trait criterion standard. Given the need for innovative approaches to prevent and treat hazardous alcohol use and the difficulty in obtaining diagnostic interview data in large samples, our approach offers a way forward for enhanced genetic discovery. We are currently applying this approach in the Million Veteran Program(42).

There were a few distinct patterns observed among PLWH. While PLWH were not more likely to report abstinence or to be Q-APs, PLWH were more likely to be infected with HCV, which was especially prevalent among Q-APs. Further, PLWH who were Q-APs demonstrated higher CD4 cell counts and undetectable HIV-1 RNA, suggesting better access and adherence to antiretroviral therapy. Note, CD4 was an important indicator for Q-AP and HIV-1 RNA for LTA. PLWH who were Q-APs may have recognized that HIV infection is a serious illness in which close adherence to treatment is critical. In fact, both PLWH and uninfected Q-ORs had higher VACS Index scores than

Q-APs suggesting that those who endorsed having quit alcohol due to associated problems may be more invested in their health care. It would be interesting to see whether Q-APs are also more likely to adhere to treatments for diabetes or hypertension, but this is beyond the scope of the current study.

It is particularly important that genetic studies conducted among middle-aged and older adults differentiate among abstainers to avoid misclassification. As expected, the proportion of LTAs remained relatively stable across ages. However, the proportion of Q-ORs doubled and the proportion of Q-APs tripled from under 45 years of age to 65+ years. This was true among PLWH and uninfected. Further compounding potential misclassification, as witnessed by some PEth values greater than 20 ng/ml, some individuals who report abstinence continue to drink. Individuals with a medical reason not to drink (e.g., HCV infection) are more likely to report abstinence despite a positive PEth(14). Of note, Q-APs were three times as likely to have a PEth>20 ng/ml than LTAs and more than twice as likely as Q-ORs.

Despite representing a largely middle-aged and older sample, large-scale genetic studies of hazardous alcohol use including UK Biobank(43), 23andMe(8), and the Million Veteran Program(42) have not differentiated among abstainers and have included them as controls. Dropping all individuals who report current abstinence from a genome-wide association study is certainly problematic as it entails the loss of one-quarter to one-half of the sample. Dropping these individuals omits LTAs and Q-ORs as well, both of whom may represent useful comparators; LTAs because they have chosen not to drink and Q-ORs because they drank in the past without experiencing alcohol associated problems. As we demonstrate, it may be possible to identify likely Q-APs based upon available indicators such as past or current smoking, past cocaine use, and AUD diagnosis codes.

Assigning a probability of being a Q-AP among those reporting abstinence would allow them to be removed, statistically down weighted, or adjusted for as a confounder, preserving the use of those unlikely to be Q-APs as controls.

Our failure to demonstrate an increased association with PEth likely reflects trait vs. state differences in the criterion standards employed. *ADH1B* genotype is a trait, while PEth reflects alcohol use in the past 21 days and is a changeable state. In fact, the calendar period over which AAM AUDIT-C was estimated preceded the 21-day window for the PEth assay. We included these results because they suggest that self-reported alcohol use may be differentially inaccurate by abstainer group. Specifically, people who report abstinence, particularly Q-APs, may be more likely to currently drink. It is noteworthy that the VACS Index was not associated with type of abstinence. This suggests that being a Q-AP has more to do with psychosocial problems from alcohol and related substance use or specific health problems such as liver disease than with the overall physiologic frailty measured by the VACS Index(28, 29, 44).

Our analyses have important strengths. Data on alcohol and other substance use were collected in several ways, allowing us to compare AUDIT-C survey responses with alcohol use disorder and other indicators of substance use both from self-reported surveys and the electronic health record. We consider comorbid physical and mental health conditions and look at associations with two criterion standards for alcohol (PEth and the *ADH1B* minor allele frequency). We were also able to consider genetic associations among African American ancestry, a substantially under studied group.

Our study also has limitations. We were not able to differentiate current abstainers according to when they last drank regularly. Further, self-reported alcohol consumption is subject to social desirability bias.

Conclusion:

In conclusion, despite being grouped together in most genetic studies of alcohol, not all those reporting current abstinence are alike and what determines membership in these groups is largely consistent by HIV status. Q-APs are distinct from LTAs in predictable ways. Treating individuals who report abstinence as a single group likely causes misclassification and confounding, weakening associations, especially among middle-aged and older adults. Omitting all abstinent individuals would be associated with a dramatic reduction in sample size and loss of important comparator groups. As an alternative, it may be possible to probabilistically identify likely Q-APs among those reporting abstinence. Investigators might then censor, down weight, or control for these observations, minimizing misclassification and confounding, maintaining sample size and power, and including useful comparator groups.

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Conflicts of interest

There are no conflicts of interest.

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Table 1a. Characteristics by Current Alcohol Use among People Living with HIV

	People Living with HIV					
	Current Abstinence (AUDIT C = 0)				Non-Hazardous AUDIT C 1-3	Hazardous AUDIT C 4+
%	LTA	Q-OR	Q-AP	p trend		
n	102	445	288	--	894	463
Age, mean (SD)	57 (10)	59 (8)	59 (7)	0.11	56 (10)	56 (10)
Black	75	64	68	0.67	67	71
Hispanic	13	10	9	0.40	8	10
White	8	19	15	0.57	20	14
Male	99	97	97	0.42	97	98
Hepatitis C	22	36	50	<0.001	26	31
Alcohol use disorder	6	11	24	<0.001	10	22
Drug use disorder	9	20	31	<0.001	19	24
Depression	19	17	24	0.10	16	20
Past marijuana	25	47	57	<0.001	41	38
Current marijuana	10	14	13	0.55	31	43
Past cocaine	21	37	54	<0.001	34	35
Current cocaine	6	7	7	0.63	12	30
Past heroin	16	20	39	<0.001	16	23
Current heroin	3	3	3	0.71	4	5
Current smoker	22	33	40	<0.001	38	57
Past smoker	15	38	46	<0.001	27	20
VACS index 2.0, IQR	46 (36, 58)	49 (39, 62)	48 (41, 62)	0.21	46 (35, 58)	48 (38, 61)
CD4, IQR	516 (330, 728)	532 (344, 741)	554 (399, 789)	0.10	532 (353, 707)	478 (315, 694)
Viral Load ≤75 copies/mL	76	84	84	0.18	79	71

Column % are reported unless otherwise specified. IQR – interquartile range, FIB4 – Fibrosis-4 score, Q-AP – Quit after alcohol associated problems, Q-OR – Quit for other reasons, LTA – Lifetime Abstainer

Table 1b. Characteristics by Current Alcohol Use among Uninfected

	Uninfected					
	Current Abstinence (AUDIT C = 0)				Non-Hazardous AUDIT C 1-3	Hazardous AUDIT C 4+
%	**LTA**	**Q-OR**	**Q-AP**	**p trend**		
n	79	419	300	--	679	502
Age, mean (SD)	60 (9)	60 (10)	59 (8)	0.21	57 (10)	55 (11)
Black	76	68	67	0.25	66	65
Hispanic	9	11	10	0.81	10	13
White	13	16	18	0.24	18	16
Male	89	90	96	0.002	92	97
Hepatitis C	18	25	35	0.0004	17	20
Alcohol use disorder	14	22	43	<0.001	29	52
Drug use disorder	27	37	49	<0.001	38	49
Depression	10	19	26	0.001	20	27
Past marijuana	19	42	55	<0.001	42	44
Current marijuana	9	13	12	0.63	24	33
Past cocaine	15	35	51	<0.001	30	35
Current cocaine	5	9	12	0.06	20	28
Past heroin	9	25	37	<0.001	16	21
Current heroin	4	5	4	0.95	6	5
Current smoker	18	40	47	<0.001	48	66
Past smoker	11	32	38	<0.001	22	17
VACS index 2.0, IQR	36 (30, 45)	38 (30, 47)	37 (30, 45)	0.75	34 (27, 42)	34 (27, 43)

Column % are reported unless otherwise specified. IQR – interquartile range, FIB4 – Fibrosis-4 score, Q-AP – Quit drinking after alcohol associated problems, Q-OR – Quit drinking for other reasons, LTA – Lifetime Abstainer

Table 2. Among 1526 Reporting Abstinence (AUDIT-C=0) Indicators of Quit Drinking After Alcohol Associated Problems (Q-AP) from Multivariable Logistic Regression.

	Overall, n=1526		PLWH, n=810		Uninfected, n=716	
Variables	**OR (95 %CI)**	**p value**	**OR (95 %CI)**	**p value**	**OR (95 %CI)**	**p value**
Age per 10yrs increment	0.94 (0.80, 1.11)	0.48	0.92 (0.72, 1.18)	0.51	0.90 (0.69, 1.17)	0.42
Female vs. male	0.69 (0.39, 1.25)	0.22	1.38 (0.51, 3.73)	0.53	0.48 (0.23, 1.02)	0.06
White non-Hispanic	1.20 (0.89, 1.63)	0.24	1.07 (0.69, 1.66)	0.76	1.39 (0.90, 2.15)	0.13
Hepatitis C	1.51 (1.16, 1.96)	0.002	1.53 (1.06, 2.19)	0.02	1.42 (0.93, 2.16)	0.10
Current smoker vs. never	2.53 (1.83, 3.48)	<0.001	2.56 (1.62, 4.02)	<0.001	2.54 (1.60, 4.04)	<0.001
Past smoker vs. never	2.85 (2.07, 3.94)	<0.001	2.82 (1.81, 4.40)	<0.001	3.04 (1.89, 4.91)	<0.001
Depression	1.25 (0.94, 1.65)	0.12	1.24 (0.84, 1.83)	0.28	1.24 (0.83, 1.87)	0.30
Current cocaine use	1.39 (0.87, 2.22)	0.17	1.28 (0.64, 2.55)	0.49	1.58 (0.82, 3.05)	0.17
Past cocaine use	1.76 (1.27, 2.44)	0.001	1.74 (1.13, 2.66)	0.01	1.79 (1.06, 3.03)	0.03
Current marijuana use	0.87 (0.58, 1.30)	0.49	0.97 (0.56, 1.69)	0.93	0.78 (0.42, 1.44)	0.42
Past marijuana use	1.06 (0.77, 1.48)	0.71	1.11 (0.72, 1.74)	0.63	1.07 (0.64, 1.77)	0.81
Alcohol use disorder	2.73 (1.93, 3.84)	<0.001	2.30 (1.36, 3.89)	0.002	3.12 (1.95, 4.97)	<0.001
Drug use disorder	0.76 (0.55, 1.05)	0.10	0.98 (0.62, 1.55)	0.92	0.59 (0.37, 0.96)	0.03
VACS index 2.0 by 5	0.98 (0.93, 1.03)	0.37	1.03 (0.96, 1.11)	0.35	0.94 (0.86, 1.04)	0.22
HIV	0.95 (0.73, 1.24)	0.72				
CD4*			1.04 (1.01, 1.07)	0.01		
Viral Load ≤75 copies/mL			1.11 (0.68, 1.81)	0.68		
C Statistics (95% CI)	0.71 (0.68, 0.73)		0.71(0.67, 0.74)		0.72 (0.68, 0.76)	

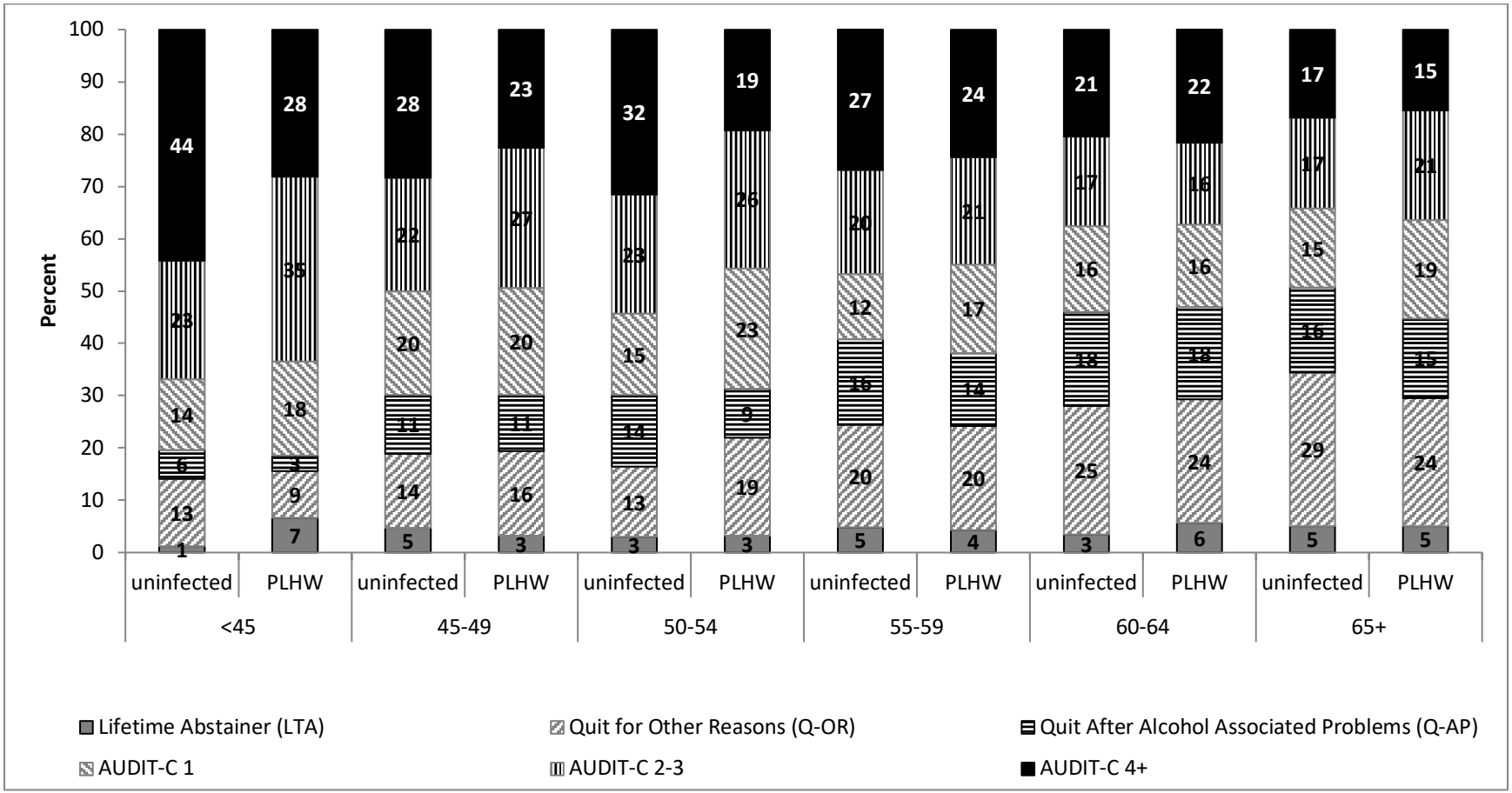
*To normalize square root of CD4 was used

Table 3. Among 1526 Reporting Current Abstinence (AUDIT-C=0) Indicators of Being a Lifetime Abstainer (LTA)

	Overall, n=1526		PLWH, n=810		Uninfected, n=716	
Variables	**OR (95 %CI)**	**p value**	**OR (95 %CI)**	**p value**	**OR (95 %CI)**	**p value**
Age per 10yrs increment	0.97 (0.78, 1.20)	0.76	1.12 (0.81, 1.53)	0.50	0.98 (0.69, 1.40)	0.92
Female vs. male	0.69 (0.33, 1.47)	0.33	0.24 (0.03, 1.88)	0.17	1.00 (0.42, 2.38)	1.00
White non-Hispanic	0.45 (0.26, 0.78)	0.005	0.35 (0.16, 0.77)	0.01	0.61 (0.27, 1.34)	0.22
Hepatitis C	0.66 (0.41, 1.05)	0.08	0.65 (0.35, 1.21)	0.18	0.92 (0.41, 2.05)	0.83
Current smoker vs. never	0.26 (0.16, 0.40)	<0.001	0.32 (0.18, 0.57)	0.0001	0.18 (0.09, 0.36)	<0.001
Past smoker vs. never	0.14 (0.09, 0.23)	<0.001	0.17 (0.09, 0.32)	<0.001	0.11 (0.05, 0.24)	<0.001
Depression	0.96 (0.60, 1.55)	0.87	1.12 (0.62, 2.04)	0.71	0.73 (0.32, 1.66)	0.45
Current cocaine use	0.86 (0.38, 1.97)	0.72	1.17 (0.37, 3.66)	0.79	0.53 (0.15, 1.87)	0.33
Past cocaine use	0.82 (0.46, 1.47)	0.50	0.92 (0.45, 1.87)	0.82	0.62 (0.22, 1.72)	0.36
Current marijuana use	0.62 (0.33, 1.18)	0.15	0.47 (0.20, 1.11)	0.08	0.93 (0.35, 2.48)	0.88
Past marijuana use	0.39 (0.23, 0.66)	0.0004	0.37 (0.19, 0.71)	0.003	0.38 (0.16, 0.91)	0.03
Alcohol use disorder	0.52 (0.26, 1.06)	0.07	0.70 (0.23, 2.12)	0.53	0.45 (0.18, 1.12)	0.09
Drug use disorder	0.86 (0.47, 1.55)	0.61	0.52 (0.20, 1.34)	0.18	1.39 (0.61, 3.18)	0.43
VACS index 2.0 by 5	1.02 (0.95, 1.10)	0.56	0.93 (0.83, 1.05)	0.24	1.07 (0.92, 1.25)	0.40
HIV	1.07 (0.71, 1.62)	0.75				
CD4*			0.97 (0.93, 1.02)	0.22		
Viral Load ≤75 copies/mL			0.52 (0.26, 1.03)	0.06		
C Statistics (95% CI)	0.80 (0.77, 0.84)		0.81(0.76, 0.85)		0.82 (0.77, 0.87)	

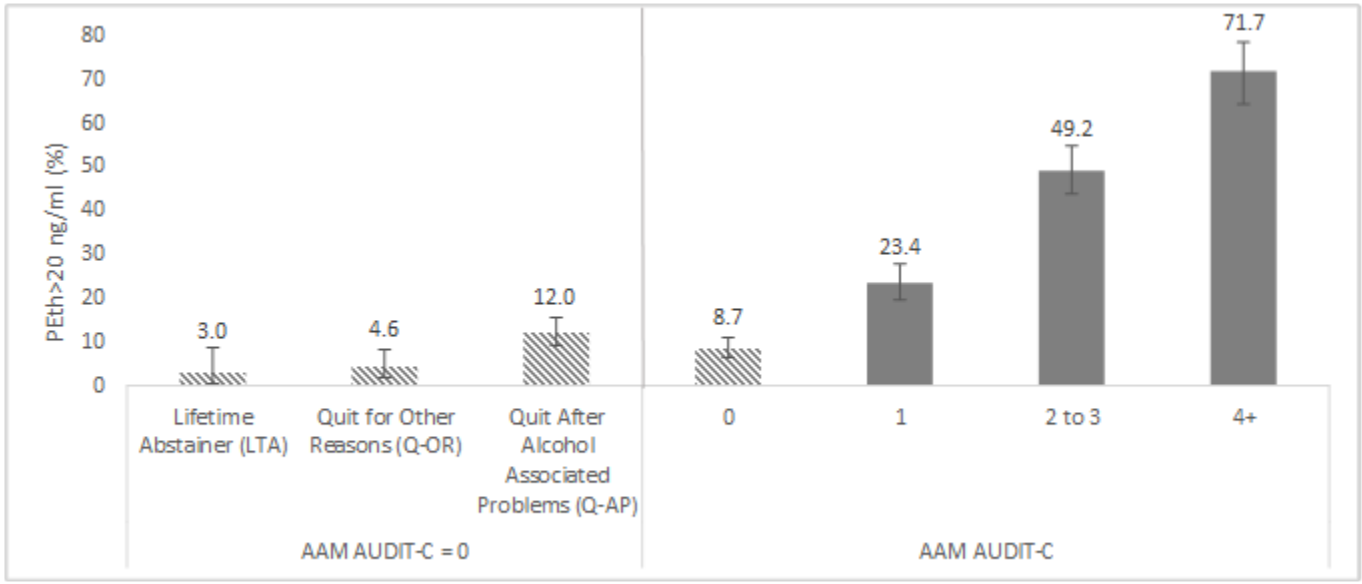
*To normalize the square root of CD4 was used

Figure 1. Current Alcohol Use by Age and HIV Status



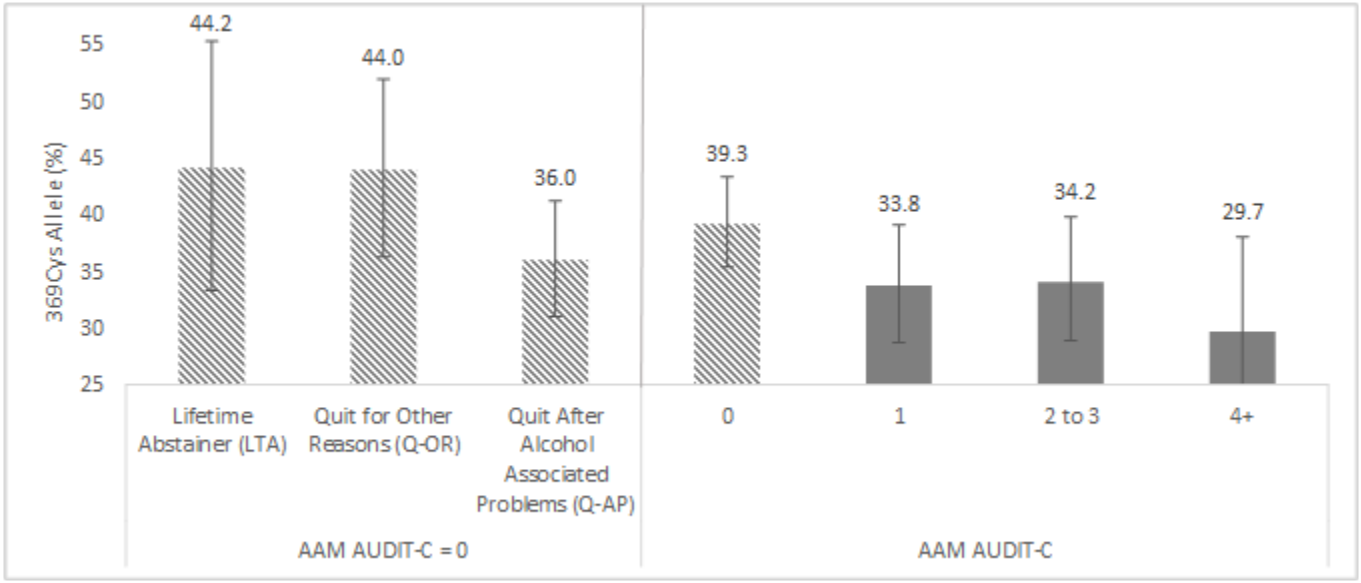
PLHW – people living with HIV

Figure 2. Percent with PEth>20 ng/ml by AAM AUDIT-C and Abstainer Type



P for trend across all 6-levels, $p = 3.20 \times 10^{-79}$; across the 4-levels of AUDIT-C=0, $p = 2.780 \times 10^{-86}$

Figure 3. Percent with ADH1B rs2066702 Minor Allele by AAM AUDIT-C and Abstainer Type



P for trend across all 6-levels, p = 0.0034; across the 4-levels of AUDIT-C=0, p = 0.018