



# Concordance Between Point-of-Care Urine Ethyl Glucuronide Alcohol Tests and Self-Reported Alcohol Use in Persons with HIV in Uganda

Karl C. Alcover<sup>1</sup> · Nneka I. Emenyonu<sup>2</sup> · Robin Fatch<sup>2</sup> · Allen Kekibiina<sup>3</sup> · Kara Marson<sup>4</sup> · Gabriel Chamie<sup>4</sup> · Winnie R. Muyindike<sup>5</sup> · Brian Beesiga<sup>6</sup> · Moses R. Kamyra<sup>7</sup> · Sara Lodi<sup>8</sup> · Jeremy C. Kane<sup>9</sup> · Judith A. Hahn<sup>10</sup> · Michael G. McDonell<sup>11</sup>

Accepted: 20 January 2022 / Published online: 1 February 2022

This is a U.S. government work and not under copyright protection in the U.S.; foreign copyright protection may apply 2022

## Abstract

Screening and assessing alcohol use accurately to maximize positive treatment outcomes remain problematic in regions with high rates of alcohol use and HIV and TB infections. In this study, we examined the concordance between self-reported measures of alcohol use and point-of-care (POC) urine ethyl glucuronide (uEtG) test results among persons with HIV (PWH) in Uganda who reported drinking in the prior 3 months. For analyses, we used the screening data of a trial designed to examine the use of incentives to reduce alcohol consumption and increase medication adherence to examine the concordance between POC uEtG (300 ng/mL cutoff) and six measures of self-reported alcohol use. Of the 2136 participants who completed the alcohol screening, 1080 (50.6%) tested positive in the POC uEtG test, and 1756 (82.2%) self-reported using alcohol during the prior 72 h. Seventy-two percent of those who reported drinking during the prior 24 h had a uEtG positive test, with lower proportions testing uEtG positive when drinking occurred 24–48 h (64.7%) or 48–72 h (28.6%) prior to sample collection. In multivariate models, recency of drinking, number of drinks at last alcohol use, and Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) score were associated with uEtG positivity. The highest area under the curve (AUC) for a uEtG positive test was for recency of drinking. Overall, we concluded that several measures of drinking were associated with POC uEtG positivity, with recency of drinking, particularly drinking within the past 24 h, being the strongest predictor of uEtG positivity.

**Keywords** Alcohol · HIV · Tuberculosis (TB) · Latent TB infection · Africa

**Disclaimer:** The opinions and assertions expressed herein are those of the author(s) and do not necessarily reflect the official policy or position of the Uniformed Services University of the Health Sciences or the Department of Defense.

✉ Karl C. Alcover  
karl.alcover@usuhs.edu

<sup>1</sup> Department of Medicine, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Rd, Bethesda, MD 20814, USA

<sup>2</sup> Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

<sup>3</sup> Mbarara University of Science and Technology, Mbarara, Uganda

<sup>4</sup> Division of HIV, Infectious Diseases and Global Medicine, University of California, San Francisco, San Francisco, CA, USA

<sup>5</sup> Department of Internal Medicine, Faculty of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda

<sup>6</sup> Infectious Diseases Research Collaboration, Kampala, Uganda

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

<sup>8</sup> Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA

<sup>9</sup> Department of Epidemiology, Columbia University Mailman School of Public Health, New York, NY, USA

<sup>10</sup> Departments of Medicine and Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA

<sup>11</sup> Behavioral Health Innovations, Elson S. Floyd College of Medicine, Washington State University, Spokane, WA, USA

## Short Summary

Recency of alcohol consumption was the best predictor of a positive uEtG test among persons with HIV in Uganda. Our findings are consistent with earlier research showing that a uEtG threshold of > 300 ng/mL for a positive test has optimum sensitivity and specificity when detecting self-reported use in the prior two days.

## Introduction

Alcohol use influences outcomes of HIV infection, potentially through poor anti-retroviral therapy (ART) adherence and immune dysregulation [10, 25]. In addition, alcohol use is associated with increased risks for tuberculosis (TB) disease and mortality among persons with HIV (PWH) [2] and those without HIV [19, 23, 24]. In regions with high rates of alcohol use as well as HIV and TB infections, it is important to accurately screen and assess alcohol use to maximize positive treatment outcomes. In this study, we examined the concordance between self-reported alcohol use and results from a commercial dipstick test for an alcohol biomarker among PWH and latent TB in sub-Saharan Africa, where the prevalence of heavy episodic drinking is among the highest in the world, occurring in almost 20% of the general population [26].

Integrating alcohol treatment into HIV care can improve outcomes among PWH (Scott-Sheldon et al., 2017), and accurate alcohol screening is an essential first step in linking PWH to appropriate alcohol services. In previous studies, people in HIV care, including PWH in Uganda, the location of the present study, under-reported alcohol use, likely due to social desirability [1, 3, 17]. Social desirability impacts the reporting of drinking, especially among women and younger persons [1].

Direct metabolites of alcohol use, such as phosphatidylethanol (PEth) from blood and ethyl glucuronide (EtG) from urine, are sensitive and specific measures of alcohol use and can be used to objectively assess alcohol consumption. These biomarkers are detectable for longer periods of time than breath or blood alcohol, allowing for a longer window of detection of alcohol use. However, the standard methods for conducting PEth and EtG tests require relatively expensive laboratory testing, limiting the use of these biomarkers in low resource settings.

EtG in urine (uEtG) can be detected for up to five days after drinking, with variability depending on the recency and amount of use, individual factors, and the threshold for detection used [4, 11, 15, 16]. EtG is only formed in the presence of alcohol, and our studies demonstrate that even

at a low threshold, such as 100 ng/mL uEtG, positive uEtG tests are associated with non-beverage alcohol exposure (e.g., use of alcohol-containing hand sanitizer [13]). Until recently, uEtG could only be assessed by using an immunoassay that required the purchase of a \$30,000–\$40,000 benchtop analyzer or by sending samples to a reference laboratory for uEtG testing, with a cost per test of \$10 to \$15. Recently point-of-care (POC) dipcard uEtG tests with thresholds of 300 and 500 ng/mL have become available. However, research evaluating the accuracy of these tests is relatively limited. In a small study, there was a high rate of agreement (98%) between POC dipcard uEtG and benchtop uEtG results [14]. The only evaluation of POC dipcard uEtG results and self-reported alcohol use also showed a high agreement rate. Furthermore, a study of 211 PWH with hepatitis B coinfection in Zambia found strong concordance (98.5%) between self-reported alcohol use in the prior three days and a positive POC dipcard test with a uEtG cutoff of 500 ng/mL [22]. In contrast, only 16% of people who drank more than three days prior to sample collection had a uEtG positive test result. Moreover, sixty percent of those who engaged in unhealthy drinking, as assessed by the Alcohol Use Disorders Identification Test – Consumption (AUDIT-C), had uEtG positive results.

Given the lack of research evaluating correlates of POC uEtG tests, we investigated the concordance between self-reported alcohol use and uEtG detected by a POC dipcard test (300 ng/mL cutoff) among 2,136 PWH in Uganda who reported any recent (prior 3 months) alcohol consumption. We identified six self-reported alcohol measures assessing recency and amount of recent drinking to determine which of the measures was most closely related to uEtG positive results. We hypothesized that self-reported recent alcohol use and higher amounts of drinking would be associated with alcohol-positive POC uEtG test results.

## Methods

### Participants and Procedures

Data were drawn from the screening step of the Drinkers' Intervention to Prevent TB (DIPT) study, an ongoing randomized controlled trial (RCT) in Uganda (NCT #03,492,216) to examine the efficacy of economic incentives to reduce drinking and increase medication adherence while taking TB preventative therapy. Persons were recruited from four Health Center IV HIV clinics in southwestern Uganda. Briefly, to be eligible for the DIPT study screening, participants had to (1) be HIV-infected adults ( $\geq 18$  years old) with prescribed antiretroviral therapy (ART) for at least 6 months; (2) report current alcohol use, which was defined as any use in the prior 3 months to reduce underreporting; (3) be fluent

in Runyankole or English; (4) be without a history of active TB, TB treatment, or TB preventive therapy; (5) be living within two-hour travel time or 60 km of the study site, with no plans to move; (6) not be currently taking or planning to take anti-convulsion medications; and (7) not be pregnant.

The study was approved by the University of California, San Francisco Institutional Review Board, the Mbarara University of Science and Technology Research Ethics Committee, the Makerere University School of Medicine Research Ethics Committee, and the Ugandan National Council for Science and Technology. Participants provided written consent prior to study participation.

## Measure of Alcohol Use

### Urine Ethyl Glucuronide (uEtG)

Urine was collected at the screening study visit, and appropriate urine temperature (32–38 degrees Celsius) was verified with a color-changing temperature strip to prevent tampering. The dipcard uEtG test, which is based on an immunoassay, was conducted by immersing the absorbent tip in the urine sample for 10–15 s and then laying the dipcard flat on a non-absorptive, clean surface for five minutes before the results were read by the laboratory technician. The dipcard display indicates two lines for a negative result, one line for a positive result. Blank dipcards were considered invalid. Digital photos of the dipcard results were taken for quality control purposes. The threshold for a uEtG positive test was set at 300 ng/mL. uEtG was measured in the screening study as a DIPT trial entry criterion – those with positive uEtG results were eligible for further study procedures. We also conducted post hoc re-reading of sample sets of dipcard photos, based on the three laboratory technicians who originally read the tests. We randomly sampled 50 cards from each original technician for re-reading, with each technician re-reading 100 total cards that were originally read by the other two technicians.

### Self-reported Alcohol Use

Self-reported alcohol consumption was measured during screening. The three-item AUDIT-C was used [5, 6], with modification, to measure drinking in the prior 3 months [8]. The AUDIT-C scale ranges from 0 to 12, with higher scores indicating greater consumption. Using the AUDIT-C, we determined the frequency of alcohol use in the past 3 months (0–3 days per week or 4–7 days per week), the number of drinks on a typical drinking day in the past 3 months (0 drinks, 1–2 drinks, 3–4 drinks, 5–6 drinks, 7–9 drinks, or 10 or more drinks), and the frequency of

six or more drinks on one occasion in the past 3 months (never, less than monthly, monthly, weekly, daily or mostly daily). The screening survey also assessed when alcohol was last consumed, from which we calculated the number of days since last alcohol use [0 days (<24 h), 1 day (24 to <48 h), 2 days (48 to <72 h), 3 days (72 to <96 h), 4–6 days (96 to <168 h), and 7 or more days (168 or more hours)] and the number of standard drinks consumed on the last drinking occasion (1–2, >2–4, >4–6, >6–9, and >9 drinks).

## Demographics

The sociodemographic characteristics collected were age (range: 18 to 78) and sex (male or female). These sociodemographic characteristics were included as covariates in the analysis.

## Statistical Analysis

We present descriptive statistics overall and by sex, since prior studies suggest that women are more likely to under-report use. We calculated proportions for categorical variables, and medians and interquartile ranges (IQRs) for continuous variables. To examine the distributions, we used  $X^2$  tests for categorical variables and Mann–Whitney tests for continuous variables. We then estimated the associations between demographic characteristics (i.e., age and sex) and uEtG positive test using bivariate logistic regression. To examine the associations between uEtG positive test and self-reported alcohol use measures, we used unadjusted logistic regression and then multivariable logistic regression to control for potential confounders (age, sex, and recruitment site). In our multivariable logistic regression analyses, we fitted six models, each with one self-reported alcohol use measure as the predictor: number of days since last alcohol use (model 1); number of drinks at last alcohol use (model 2); AUDIT-C score (model 3); frequency of alcohol use in the past 3 months (model 4); number of drinks on a typical drinking day in the past 3 months (model 5); and frequency of 6 or more drinks on one occasion in the past 3 months (model 6). Finally, we estimated the predictive performance of these logistic models using the receiver operator characteristics area under the curve (ROC-AUC) c-statistic. To account for potential clustering at the study site level, we estimated the model using (1) robust standard error rather than standard error from maximum likelihood estimation, and (2) generalized estimating equations (GEE) [7].

To assess the degree of agreement between the original uEtG reading and the re-reads, we computed the pairwise Cohen's Kappa measure of agreement. As an overall measure of agreement, we computed the Fleiss Kappa statistic.

## Results

From April 2018 through November 2019, a total of 2,136 individuals participated in uEtG screening at one of the four participating sites in southwest Uganda: Mbarara Municipal Clinic (MMC,  $n = 715$ ); Mbarara Regional Referral Hospital (MRRH) Immune Suppression Syndrome Clinic (ISS;  $n = 390$ ); Ruhoko Health Center IV ART Clinic ( $n = 527$ ); and Rugazi Health Center IV ART Clinic ( $n = 504$ ). Descriptive statistics for demographics and alcohol use by sex are presented in Table 1. Among the 2136 participants, 1,080 (50.6%) tested uEtG positive, with most being male (67.6%), and 1756 (82.2%) reported that they had consumed alcohol within the past 3 days. There were also significant differences in the male/female distribution by site, uEtG test result, days since last alcohol use, AUDIT-C score in the past 3 months, frequency of alcohol use in the past 3 months, number of drinks on a typical drinking day in the past 3 months, frequency of 6 or more drinks on one occasion in the past 3 months, and number of drinks at last alcohol use.

Table 2 presents comparisons of positive uEtG test results by demographic characteristics and levels of self-reported alcohol use. The proportion of participants with positive uEtG test results varied by sex ( $\text{Chi}^2 = 12.28$ ;  $p < 0.001$ ) and study site ( $\text{Chi}^2 = 41.62$ ;  $p < 0.001$ ). All measures of self-reported alcohol use were associated with positive uEtG results, with recency of drinking having the strongest association with uEtG result. Similar results were found in multivariable analyses (Table 3) that examined the associations of self-reported alcohol use and positive uEtG results, adjusting for age, sex, and study site. Nearly all measures of self-reported drinking were associated with uEtG results, with drinking within the last two days being the strongest predictor of uEtG positivity.

The ROC-AUC was highest for model 1 ( $\text{AUC} = 0.73$ ), with days since last alcohol use as the predictor of a POC uEtG positive test, indicating fair prediction, followed by AUDIT-C score as the predictor (model 3:  $\text{AUC} = 0.63$ ). The ROC-AUC for model 4, which used the frequency of alcohol use in the past 3 months as the predictor, was 0.62. Models 2, 5, and 6, which used the number of drinks at last alcohol use, the number of drinks on a typical drinking day in the past 3 months, and the frequency of 6 or more drinks on one occasion in the past 3 months, respectively, as predictors had the lowest ROC-AUC estimates ( $\text{AUC} = 0.61$ ). These results did not materially change in models accounting for clustering of individuals by recruitment site.

Pairwise comparisons of the uEtG readings showed ~85% agreement between the three different pairs. The kappa statistics ranged from 0.71 to 0.73 across sites, and the combined Fleiss kappa statistic for all three readings was 0.72.

## Discussion

In this study of current alcohol use in PWH recruited from four sites in Uganda, we found that recency of drinking, specifically drinking within the prior two days, was the best predictor of a positive uEtG test. Such detection of recent alcohol consumption will help identify the necessary steps to reduce alcohol use and potentially increase adherence to treatment in populations with rapidly progressing infectious diseases.

The findings reported here are consistent with earlier research results showing that the 300 ng/mL threshold for a positive uEtG test using a lab-based uEtG immunoassay [15] has optimum sensitivity ( $> 0.75$ ) and specificity ( $> 0.83$ ) when detecting self-reported alcohol use in the prior 2 days. The AUC analyses also supported these results with an AUC of 0.73, which suggests fair prediction. While measures of the quantity and frequency of alcohol consumed in the past 3 months were also associated with uEtG results, these associations were not as strong as the association between recency of drinking and uEtG, as measured by the AUC. Also, as expected, the proportion of positive uEtG tests decreased as the number of days since last use increased.

Similar to the only other large study of uEtG dipcards [22], we found an association between recent self-reported alcohol use and positive uEtG. Interestingly, despite using a more sensitive threshold for detecting alcohol use than this other study (300 ng/mL vs. 500 ng/mL), only ~56% of the participants in our study who reported drinking in the past three days had a positive uEtG test. In contrast, Vinikoor and colleagues found that ~99% of participants who self-reported alcohol use in the prior three days had a positive uEtG test [22]. A number of factors might account for this discrepancy. The previous study recruited its sample from an on-going cohort study in which participants might be more aware of their alcohol use or more likely to accurately disclose their alcohol use, resulting in better concordance between uEtG positive results and self-report. Our data were gathered during screening for a study that had financial rewards, and those who reported using alcohol in the prior 3 months were eligible to participate. Therefore, there was a perceived incentive for participants in our study to report recent alcohol use, even if it did not occur. Additionally, a large proportion (38.4%) of our sample reported light drinking (1 or 2 standard drinks) and we did not collect data on the types of alcohol consumed (some local brews have low alcohol concentrations). With a threshold of 300 ng/mL, it is likely that uEtG might not be able to detect this magnitude of drinking in the prior 3 days. Further studies should explore the association between self-reported alcohol use and POC uEtG results in diverse clinical samples with

**Table 1** Participant characteristics of those screened for the DIPT study through November 2019 ( $N=2136$ ), stratified by sex

	Overall	Sex		Chi2 ( $p$ -value)*
	$n$ (%) or median (IQR)	Male $n$ (%) or median (IQR)	Female $n$ (%) or median (IQR)	
Age, median (IQR)	38 (32, 47)	40 (33, 48)	35 (28, 43.5)	9.70 (<0.001)*
Sex				
Male	1444 (67.6)	–	–	–
Female	692 (32.4)	–	–	–
DIPT study site				10.27 (0.016)
MMC	715 (33.5)	495 (34.3)	220 (31.8)	
Ruhoko Clinic	527 (24.7)	347 (24.0)	180 (26.0)	
Rugazi Clinic	504 (23.6)	319 (22.1)	185 (26.7)	
MRRH	390 (18.3)	283 (19.6)	107 (15.5)	
uEtG test result				12.28 (<0.001)
Negative	1056 (49.4)	676 (46.8)	380 (54.9)	
Positive	1080 (50.6)	768 (53.2)	312 (45.1)	
Days since last alcohol use				25.76 (<0.001)
0 days	90 (4.2)	68 (4.7)	22 (3.2)	
1 day	1152 (54.0)	822 (57.0)	330 (47.8)	
2 days	315 (14.8)	200 (13.9)	115 (16.6)	
3 days	199 (9.3)	127 (8.8)	72 (10.4)	
4–6 days	220 (10.3)	137 (9.5)	83 (12.0)	
7 or more days	158 (7.4)	89 (6.2)	69 (10.0)	
Number of drinks at last alcohol use				24.95 (<0.001)
1–2	820 (38.4)	508 (35.2)	312 (45.1)	
> 2–4	757 (35.5)	520 (36.0)	237 (34.2)	
> 4–6	399 (18.7)	297 (20.6)	102 (14.7)	
> 6–9	90 (4.2)	64 (4.4)	26 (3.8)	
> 9	69 (3.2)	54 (3.7)	15 (2.2)	
AUDIT-C score, past 3 months	6 (4, 8)	6 (5, 8)	5 (4, 7)	12.98 (<0.001)*
Frequency of alcohol use, past 3 months				34.89 (<0.001)
0–3 days per week	1594 (74.6)	1022 (70.8)	572 (82.7)	
4–7 days per week	542 (25.4)	422 (29.2)	120 (17.3)	
Number of drinks on a typical drinking day, past 3 months				143.28 (<0.001)
None	12 (0.6)	5 (0.3)	7 (1.0)	
1 or 2	59 (2.8)	17 (1.2)	42 (6.1)	
3 or 4	825 (38.6)	468 (32.4)	357 (51.6)	
5 or 6	768 (36.0)	573 (39.7)	195 (28.2)	
7 to 9	237 (11.1)	189 (13.1)	48 (6.9)	
10 or more	235 (11.0)	192 (13.3)	43 (6.2)	
Frequency of 6 or more drinks on one occasion, past 3 months				131.78 (<0.001)
Never	576 (27.0)	281 (19.5)	295 (42.6)	
Less than monthly	656 (30.7)	473 (32.8)	183 (26.4)	
Monthly	518 (24.3)	388 (26.9)	130 (18.8)	
Weekly	275 (12.9)	216 (15.0)	59 (8.5)	
Daily or mostly daily	111 (5.2)	86 (6.0)	25 (3.6)	

\*Mann–Whitney  $Z$  statistic

**Table 2** Bivariate associations [Odds Ratios (OR) and 95% Confidence Intervals (CI)] between predictors and positive uEtG test results among those screened for the DIPT Study through November 2019 ( $N=2136$ , 1444 males and 692 females)

	uEtG negative $n$ (%)	uEtG positive $n$ (%)	OR (95% CI)	$Chi^2$ ( $p$ -value)*
Age, median (IQR)	38 (31, 46)	39 (32, 48)	1.01 (1.00, 1.02)	2.62 (0.009)*
Sex				12.24 (<0.001)
Male	676 (46.8)	768 (53.2)	1.00	
Female	380 (54.9)	312 (45.1)	0.72 (0.60, 0.87)	
Study site				41.08 (<0.001)
MMC	375 (52.5)	340 (47.6)	1.00	
Ruhoko Clinic	210 (39.9)	317 (60.2)	1.66 (1.33, 2.09)	
Rugazi Clinic	236 (46.8)	268 (53.2)	1.25 (1.00, 1.57)	
MRRH	235 (60.3)	155 (39.7)	0.73 (0.57, 0.93)	
Days since last alcohol use				249.25 (<0.001)
0 days	25 (27.8)	65 (72.2)	7.67 (4.28, 13.76)	
1 day	407 (35.3)	745 (64.7)	5.40 (3.70, 7.88)	
2 days	204 (64.8)	111 (35.2)	1.61 (1.05, 2.46)	
3 days	142 (71.4)	57 (28.6)	1.18 (0.74, 1.90)	
4–6 days	160 (72.7)	60 (27.3)	1.11 (0.69, 1.76)	
7 or more days	118 (74.7)	40 (25.3)	1.00	
Number of drinks at last alcohol use				15.46 (0.004)
1–2	445 (54.3)	375 (45.7)	1.00	
> 2–4	349 (46.1)	408 (53.9)	1.39 (1.14, 1.69)	
> 4–6	178 (44.6)	221 (55.4)	1.47 (1.16, 1.87)	
> 6–9	47 (52.2)	43 (47.8)	1.09 (0.70, 1.68)	
> 9	37 (53.6)	32 (46.4)	1.03 (0.63, 1.68)	
AUDIT-C score, past 3 months, median (IQR)	5 (4, 7)	6 (5, 8)	1.11 (1.07, 1.15)	5.65 (<0.001)*
Frequency of alcohol use, past 3 months				31.70 (<0.001)
0–3 days per week	845 (53.0)	749 (47.0)	1.00	
4–7 days per week	211 (38.9)	331 (61.1)	1.77 (1.45, 2.16)	
Number of drinks on a typical drinking day, past 3 months				17.67 (0.003)
None	9 (75.0)	3 (25.0)	1.00	
1 or 2	37 (62.7)	22 (37.3)	1.78 (0.44, 7.30)	
3 or 4	436 (52.9)	389 (47.2)	2.68 (0.72, 9.96)	
5 or 6	345 (44.9)	423 (55.1)	3.68 (0.99, 13.69)	
7 to 9	111 (46.8)	126 (53.2)	3.41 (0.90, 12.89)	
10 or more	118 (50.2)	117 (49.8)	2.97 (0.79, 11.26)	
Frequency of 6 or more drinks on one occasion, past 3 months				26.10 (<0.001)
Never	334 (58.0)	242 (42.0)	1.00	
Less than monthly	321 (48.9)	335 (51.1)	1.44 (1.15, 1.80)	
Monthly	231 (44.6)	287 (55.4)	1.71 (1.35, 2.18)	
Weekly	122 (44.4)	153 (55.6)	1.73 (1.30, 2.31)	
Daily or mostly daily	48 (43.2)	63 (56.8)	1.81 (1.20, 2.73)	

\*\*Mann–Whitney  $Z$  statistic

differing patterns of drinking to better characterize the performance of these tests.

The proportions of participants with uEtG positive results were significantly different between males and females in unadjusted analyses. This is consistent with the differences we found by gender in self-reported alcohol use. Gender

was not associated with uEtG results in models 1 and 3, suggesting that the differences between men and women in EtG positivity were likely due to different levels of alcohol consumption by gender.

The proportions of uEtG positive tests varied by study site. Therefore, laboratory staff from the different sites

**Table 3** Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI) for positive uEtG test results among those screened for the DIPT Study through November 2019 (N=2136)

	Model 1 AOR (95% CI)	Model 2 AOR (95% CI)	Model 3 AOR (95% CI)	Model 4 AOR (95% CI)	Model 5 AOR (95% CI)	Model 6 AOR (95% CI)
<b>Days since last alcohol use</b>						
0 days	8.57 (4.71, 15.61)					
1 day	6.89 (4.64, 10.23)					
2 days	1.92 (1.23, 2.97)					
3 days	1.33 (0.82, 2.15)					
4–6 days	1.13 (0.70, 1.81)					
7 or more days	1.00					
<b>Number of drinks at last alcohol use</b>						
1–2		1.00				
> 2–4		1.45 (1.18, 1.78)				
> 4–6		1.59 (1.24, 2.05)				
> 6–9		1.20 (0.77, 1.88)				
> 9		1.13 (0.68, 1.88)				
AUDIT-C score, past 3 months –			1.16 (1.11, 1.20)			
<b>Frequency of alcohol use, past 3 months</b>						
0–3 days per week –				1.00		
4–7 days per week –				2.06 (1.66, 2.54)		
<b>Number of drinks on a typical drinking day, past 3 months</b>						
None –					1.00	
1 or 2 –					1.94 (0.46, 8.16)	
3 or 4 –					2.40 (0.63, 9.16)	
5 or 6 –					3.59 (0.94, 13.72)	
7 to 9 –					3.84 (0.99, 14.92)	
10 or more –					3.33 (0.86, 12.95)	
<b>Frequency of 6 or more drinks on one occasion, past 3 months</b>						
Never –						1.00
Less than monthly –						1.29 (1.01, 1.63)
Monthly –						1.56 (1.22, 2.01)
Weekly –						1.71 (1.26, 2.32)
Daily or mostly daily –						1.92 (1.26, 2.94)
<b>Covariates</b>						
Age	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
<b>Sex</b>						
Male	1.00	1.00	1.00	1.00	1.00	1.00
Female	0.82 (0.67, 1.00)	0.75 (0.62, 0.91)	0.86 (0.70, 1.05)	0.77 (0.63, 0.93)	0.80 (0.66, 0.98)	0.80 (0.66, 0.97)
<b>Study site</b>						
MMC	1.00	1.00	1.00	1.00	1.00	1.00
Ruhoko	2.39 (1.85, 3.09)	1.82 (1.43, 2.30)	2.20 (1.72, 2.82)	1.84 (1.46, 2.33)	1.93 (1.51, 2.48)	1.81 (1.43, 2.29)
Rugazi	1.33 (1.03, 1.72)	1.16 (0.92, 1.48)	1.50 (1.17, 1.91)	1.42 (1.11, 1.80)	1.24 (0.97, 1.59)	1.26 (0.99, 1.61)
MRRH	0.66 (0.51, 0.87)	0.73 (0.56, 0.94)	0.80 (0.62, 1.04)	0.66 (0.51, 0.85)	0.73 (0.56, 0.94)	0.78 (0.60, 1.01)
Area under ROC curve:	0.73	0.61	0.63	0.62	0.61	0.61



re-read a random sample of digitally recorded test results. We found that the accuracy of uEtG result interpretation did not differ by site, with an overall agreement of 85% and a kappa of 0.72. While this was acceptable and similar to other POC drug tests, interpretation of results can be challenging. Indeed, our results suggest that manufacturers should continue to improve POC uEtG tests so that results are easier to interpret.

Other factors should also be considered when interpreting our study results. The reliance on self-report of alcohol use as a method for validating POC uEtG is imperfect. Self-reported alcohol use is affected by a number of factors including social desirability and other contingencies, such as needing to report use to gain study entry [1, 20]. In addition to social desirability, another source of bias is inaccurate recollection of alcohol use, which includes unintentionally incorrect reporting as well as variability arising from differences in the actual product, frequency, and quantity of alcohol consumed [12]. Alternative approaches to validating uEtG results include comparisons to results from tests for other biomarkers (such as PEth and transdermal alcohol monitors) or to results from alcohol-administration studies in which alcohol intake is controlled and uEtG is determined at regular intervals over time. However, it should be used with caution, and approaches to adjust for measurement errors of the biomarker itself may be needed (Parast et al., 2020). While some of these approaches have been used to validate uEtG, they have not been used to validate POC uEtG tests.

This study has several strengths. First, uEtG is a biomarker that was shown to measure alcohol consumption levels with high sensitivity and specificity for drinking in the two days prior to the test. Such early detection of problematic alcohol consumption will help clinicians plan appropriate treatments as well as identify steps to increase adherence to treatments, which are necessary in populations with rapidly progressing infectious diseases. Second, the use of POC uEtG provided objective measures as well as the ability to detect possible underreporting of alcohol use in Uganda, where disclosure of alcohol use to health care providers might be perceived to result in denial of treatment [3, 9]. Finally, in addition to objective measures, the large sample size ( $N=2,136$  participants) used in our study increased the precision of our estimates.

Overall, our results suggest that POC uEtG tests can be utilized in low resource settings to screen for recent alcohol use in clinical populations where accurate measurement of alcohol use is essential to effective health care. In epidemiological studies, POC uEtG use may help increase internal validity while maintaining low costs, as POC uEtG tests remain relatively inexpensive (e.g., \$5 per test; [14]. Further studies similar to the current study are needed to better characterize the performance of POC uEtG tests in various clinical settings, in populations with different drinking patterns,

and in settings where use of other biomarkers is feasible, as additional POC tests become increasingly available.

**Funding** This work was supported by the National Institute of Alcohol Abuse and Alcoholism (U01 AA026223, U01 AA026221, K24 AA022586, K01 AA026523).

## Declarations

**Conflict of interest** The authors have no conflicts of interest to disclose.

## References

1. Adong J, Fatch R, Emenyonu NI, Cheng DM, Muyindikie WR, Ngabirano C, Kekibiina A, Woolf-King SE, Samet JH, Hahn JA. Social desirability bias impacts self-reported alcohol use among persons with HIV in Uganda. *Alcohol Clin Exp Res*. 2019;43:2591–8.
2. Alemu YM, Awoke W, Wilder-Smith A. Determinants for tuberculosis in HIV-infected adults in Northwest Ethiopia: a multicentre case-control study. *BMJ Open*. 2016;6:e009058.
3. Bajunirwe F, Haberer JE, Boum Y, Hunt P, Mocello R, Martin JN, Bangsberg DR, Hahn JA. Comparison of self-reported alcohol consumption to phosphatidylethanol measurement among HIV-infected patients initiating antiretroviral treatment in Southwestern Uganda. *PLoS ONE*. 2014;9:e113152.
4. Beck O, Stephanson N, Bottcher M, Dahmen N, Fehr C, Helander A. Biomarkers to disclose recent intake of alcohol: potential of 5-hydroxytryptophol glucuronide testing using new direct UPLC-tandem MS and ELISA methods. *Alcohol Alcohol*. 2007;42:321–5.
5. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcoholism Clin Exp Res*. 2007;31:1208–17.
6. Bush K. The AUDIT Alcohol Consumption Questions (AUDIT-C): an effective brief screening test for problem drinking. *Arch Intern Med*. 1998;158:1789.
7. Freedman DA. *Statistical Models: Theory and Practice*. 2nd ed. Cambridge: Cambridge University Press; 2009.
8. Hahn JA, Emenyonu NI, Fatch R, Muyindikie WR, Kekibiina A, Carrico AW, Woolf-King S, Shiboski S. Declining and rebounding unhealthy alcohol consumption during the first year of HIV care in rural Uganda, using phosphatidylethanol to augment self-report: Alcohol use in HIV care in Uganda. *Addiction*. 2016;111:272–9.
9. Hahn JA, Fatch R, Kabami J, Mayanja B, Emenyonu NI, Martin J, Bangsberg DR. Self-report of alcohol use increases when specimens for alcohol biomarkers are collected in persons with HIV in Uganda: JAIDS. *J Acquir Immune Defic Syndr*. 2012;61:e63–4.
10. Hahn JA, Samet JH. Alcohol and HIV disease progression: weighing the evidence. *Curr HIV/AIDS Rep*. 2010;7:226–33.
11. Helander A, Bottcher M, Fehr C, Dahmen N, Beck O. Detection times for urinary ethyl glucuronide and ethyl sulfate in heavy drinkers during alcohol detoxification. *Alcohol Alcohol*. 2008;44:55–61.
12. Hill-McManus D, Angus C, Meng Y, Holmes J, Brennan A, Sylvia Meier P. Estimation of usual occasion-based individual drinking patterns using diary survey data. *Drug Alcohol Depend*. 2014;134:136–43.
13. Jatlow PI, Agro A, Wu R, Nadim H, Toll BA, Ralevski E, Nogueira C, Shi J, Dziura JD, Petrakis IL, O'Malley SS. Ethyl glucuronide



- and ethyl sulfate assays in clinical trials, interpretation, and limitations: results of a dose ranging alcohol challenge study and 2 clinical trials. *Alcohol Clin Exp Res*. 2014;38:2056–65.
14. Leickly E, Skalisky J, McPherson S, Orr MF, McDonnell MG. High agreement between benchtop and point-of-care dipcard tests for ethyl glucuronide. *Ther Drug Monit*. 2017;39:461–2.
  15. Lowe JM, McDonnell MG, Leickly E, Angelo FA, Vilardaga R, McPherson S, Srebnik D, Roll J, Ries RK. Determining ethyl glucuronide cutoffs when detecting self-reported alcohol use in addiction treatment patients. *Alcohol Clin Exp Res*. 2015;39:905–10.
  16. McDonnell MG, Skalisky J, Leickly E, McPherson S, Battalio S, Nepom JR, Srebnik D, Roll J, Ries RK. Using ethyl glucuronide in urine to detect light and heavy drinking in alcohol dependent outpatients. *Drug Alcohol Depend*. 2015;157:184–7.
  17. Muyindike WR, Lloyd-Travaglini C, Fatch R, Emenyonu NI, Adong J, Ngabirano C, Cheng DM, Winter MR, Samet JH, Hahn JA. Phosphatidylethanol confirmed alcohol use among ART-naïve HIV-infected persons who denied consumption in rural Uganda. *AIDS Care*. 2017;29:1442–7.
  18. Parast L, Garcia TP, Prentice RL, Carroll RJ. Robust methods to correct for measurement error when evaluating a surrogate marker. *Biometrics*. 2020. <https://doi.org/10.1111/Biom.13386>.
  19. Rehm J, Samokhvalov AV, Neuman MG, Room R, Parry C, Lönnroth K, Patra J, Poznyak V, Popova S. The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review *BMC Public Health*. 2009;9:450.
  20. Schell C, Godinho A, Cunningham JA (2020) To thine own self, be true: Examining change in self-reported alcohol measures over time as related to socially desirable responding bias among people with unhealthy alcohol use. null 1–7.
  21. Scott-Sheldon LAJ, Johnson BT, Carey MP, The MASH Research Team. Behavioral interventions targeting alcohol use among people living with HIV/AIDS: a systematic review and meta-analysis. *AIDS Behav*. 2017;21:126–43.
  22. Vinikoor MJ, Zyambo Z, Muyoyeta M, Chander G, Saag MS, Cropsey K. Point-of-care urine ethyl glucuronide testing to detect alcohol use among HIV-hepatitis B virus coinfecting adults in Zambia. *AIDS Behav*. 2018;22:2334–9.
  23. Volkmann T, Moonan PK, Miramontes R, Oeltmann JE. Excess alcohol use and death among tuberculosis patients in the United States, 1997–2012. *JTR*. 2016;04:18–22.
  24. Volkmann T, Moonan PK, Miramontes R, Oeltmann JE. Tuberculosis and excess alcohol use in the United States. 2016;1997–2012:16.
  25. Williams EC, Hahn JA, Saitz R, Bryant K, Lira MC, Samet JH. Alcohol use and Human Immunodeficiency Virus (HIV) Infection: Current knowledge, implications, and future directions. *Alcohol Clin Exp Res*. 2016;40:2056–72.
  26. World Health Organization (2018) Global Status Report on Alcohol Use and Health 2018. Geneva.

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