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Self-reported alcohol use versus phosphatidylethanol in behavioral trials: A study of people living with HIV in Tshwane, South Africa

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Abstract

Background: Accurately quantifying alcohol use among persons with HIV (PWH) is important for validly assessing the efficacy of alcohol reduction interventions.

Methods: We used data from a randomized controlled trial of an intervention to reduce alcohol use among PWH who were receiving antiretroviral therapy in Tshwane, South Africa. We calculated agreement between self-reported hazardous alcohol use measured by the Alcohol Use Disorders Identification Test (AUDIT; score ≥8) and AUDIT-Consumption (AUDIT-C; score ≥3 for females and ≥4 for males), heavy episodic drinking (HED) in the past 30 days, and heavy drinking in the past 7 days with a gold standard biomarker--phosphatidylethanol (PEth) level (≥50 ng/mL)--among 309 participants. We used multiple logistic regression to assess whether underreporting of hazardous drinking (AUDIT-C vs. PEth) differed by sex, study arm, and assessment time point.

Results: Participants' mean age was 40.6 years, 43% were males, and 48% were in the intervention arm. At 6 months, 51% had PEth ≥50 ng/mL, 38% and 76% had scores indicative of hazardous drinking on the AUDIT and AUDIT-C, respectively, 11%

reported past 30-day HED, and 13% reported past 7-day heavy drinking. At 6 months, there was low agreement between AUDIT-C scores and past 7-day heavy drinking relative to PEth ≥50 (sensitivities of 83% and 20% and negative predictive values of 62% and 51%, respectively). Underreporting of hazardous drinking at 6 months was associated with sex (OR = 3.504. 95% CI: 1.080 to 11.364), with odds of underreporting being greater for females.

Conclusions: Steps should be taken to decrease underreporting of alcohol use in clinical trials.

KEYWORDS
alcohol consumption, HIV, intervention, phosphatidylethanol, self-report

INTRODUCTION

Per capita consumption of alcohol in South Africa is 9.3 L of pure alcohol (the equivalent of 186 L of 5% alcohol), and 59% of adults who drink alcohol report engaging in heavy episodic drinking (HED) at least once in the past 30 days (World Health Organization, 2018). South Africa is also challenged by HIV, with an estimated 8.2 million persons living with HIV (PWH) of whom about three-quarters receive antiretroviral therapy (ART; Statistics South Africa, 2021). There is a strong nexus between alcohol consumption and HIV, with studies showing that hazardous drinking (including HED) directly contributes to ART nonadherence (Velloza et al., 2019), declines in CD4 counts, nonsuppression of HIV viral load (Myers et al., 2021), and HIV disease severity (Marshall et al., 2017). As a result, interventions to reduce the quantity of alcohol consumed among PWH are crucial to optimizing ART adherence and HIV treatment outcomes (Shuper, 2021). An important step in facilitating this involves accurately detecting hazardous or harmful drinking among PWH as a prelude to offering alcohol reduction interventions.

Self-report measures are commonly used to assess for hazardous and harmful alcohol use. The Alcohol Use Disorders Identification Test (AUDIT) is one of the most widely used, reliable, and valid self-report alcohol screeners (Babor et al., 2001). The total score on the 10-item AUDIT is used to classify patterns of alcohol use into low-risk, hazardous, harmful, or probable dependence. The reliability and validity of the full AUDIT and briefer versions, including the three-item AUDIT-C (Bush et al., 1998), has been supported by numerous studies in sub-Saharan Africa (Morojele et al., 2017). Alternatively, single-item questions about frequency and quantity of alcohol consumption are used to assess volume of alcohol consumption, including frequency of heavy drinking (defined as consumption of 60 g of absolute alcohol) in the past 7 days (Schaus & Schaus, 2020). Frequency of heavy drinking and presence of HED is also assessed through the TimeLine Follow-Back method, which collects daily drinking data over a specified period (Sobell & Sobell, 1992). However, a potential challenge with self-report measures of alcohol consumption is the accuracy of recall. In addition, people may underreport their drinking if they anticipate stigmatizing responses

from their health providers or if they are in settings where there is societal stigma toward drinking (Magidson et al., 2022; Regenauer et al., 2022). Over-report, on the contrary, is possible in settings in which there is stigma toward abstinence (Lancaster et al., 2020), and by persons wishing to engage in research for which they are not eligible (Devine et al., 2013).

More recently, focus has shifted to using the biomarker phosphatidylethanol (PEth) to objectively assess recent hazardous drinking. Blood spots for PEth testing are relatively easy to collect (via finger prick), and PEth allows for a longer detection period (approximately 21 days) and offers better sensitivity and specificity compared with other biomarkers (Hahn, Fatch, et al., 2012; Viel et al., 2012). This biomarker has been used in research in several African countries including Kenya (Papas et al., 2016), South Africa (Magidson et al., 2019, 2021; Raggio et al., 2019), Tanzania (Francis et al., 2015), and Uganda (Bajunirwe et al., 2014; Hahn, Emenyonu, et al., 2016; Muyindike et al., 2017; Raggio et al., 2019), among patients in HIV clinics on ART (Bajunirwe et al., 2014; Magidson et al., 2019, 2021; Papas et al., 2016) or not on ART (Hahn, Emenyonu, et al., 2016; Muyindike et al., 2017; Raggio et al., 2019), and community samples (Francis et al., 2015).

Researchers have articulated the need for improving the validity of self-reported alcohol use among patients in HIV care settings (Hahn, Fatch, et al., 2012); however, the logistics and cost of PEth testing limits its applicability. Thus, examining discordance between self-report and biomarkers can be useful in identifying where problems with self-report data on drinking are most likely to occur. This information is needed to guide efforts to increase the validity of self-report measures. Discordance is most likely to be affected by sex (Siegfried et al., 2001), age (Meier & Seitz, 2008), the biomarker used (Kader et al., 2012), and the setting in which the question is asked as stigma varies from context to context (Hahn, Fatch, et al., 2012; Kader et al., 2012). For example, in the case of sex, due to stigma against women drinking, self-report measures of alcohol use are likely to reflect an underreporting of such use in certain African contexts (Siegfried et al., 2001). Other studies conducted in southern and eastern Africa (Francis et al., 2015; Hahn, Dobkin, et al., 2012; Magidson et al., 2019, 2021; Papas et al., 2016) have identified

discrepancies between self-report measures of alcohol use and PEth from 0% (Magidson et al., 2019) to 52% (Francis et al., 2015). In randomized controlled trials (RCTs), it is also possible that social desirability might be greater among participants who receive alcohol reduction interventions than in a control group. However, with only one exception (Papas et al., 2016), none of the prior studies were conducted in the setting of an RCT. Therefore, there is a need to compare self-report to objective biomarkers in alcohol intervention trials to determine the extent and predictors of misreport, to guide future intervention research.

This substudy, conducted as part of a RCT of an alcohol reduction intervention (Parry et al., 2014), aimed to assess the agreement between total AUDIT scores (≥8), AUDIT-C (≥3 for women and ≥4 for men), HED (≥60 g absolute alcohol in a single occasion), and heavy drinking in the past 7 days with the biomarker PEth (≥50 ng/mL) and to identify factors associated with underreporting of self-reported hazardous drinking (AUDIT ≥8 or AUDIT-C ≥3 for females/≥4 for males) among PWH on ART attending HIV clinics in Tshwane, South Africa.

METHODS

Study design

The substudy assessed data coming from a two-arm RCT with outcomes measured at baseline (BL) and three- and 6-month postrandomization (3MFU and 6MFU), respectively. Trial methods are fully described in Parry et al. (2014).

Population and sample

Trial participants comprised 626 patients attending HIV clinics at six hospitals in Tshwane, South Africa, recruited between May 2016 and October 2017. Patients who (a) were on ART for HIV for at least 3 months; not being treated for tuberculosis; ≥18 years old; (b) met criteria for current (past year) harmful/hazardous drinking (AUDIT-C score ≥4 for men and ≥3 for women), but not for alcohol dependence (total AUDIT score <23 of possible 40; Babor et al., 2001; Bush et al., 1998); (c) were resident in/around Tshwane Metro; not enrolled in another trial; and (d) did not have an extremely poor general health/functional status (Karnofsky clinical score >50; Karnofsky & Burchenal, 1949) were eligible for inclusion.

Instruments and procedure

At BL, registered nurses conducted finger pricks on 50% of the participants ($N = 313$) randomly chosen (via a computer-generated list) at each time period for dried blood spots (DBS) to assess PEth levels (Jones et al., 2011). The analysis of the DBS was undertaken by the United States Drug Testing Laboratories Inc. using previously published methods (Jones et al., 2011). PEth was considered positive if the value was ≥50 ng/mL. This cutoff was chosen based on prior validation studies in persons with liver disease (https://pubmed.ncbi.nlm.nih.gov/24848614/), where a cutoff of 50 ng/mL was 93% sensitive and 89% specific for drinking at least two or more drinks per day on average over 2 weeks (S. Stewart, personal communication). Demographic and outcome data were collected after the blood samples were taken through interviewer-administered questionnaires available in English and seTswana, at BL and each follow-up. The questionnaires assessed a range of demographic variables, including patients' age, gender, education, employment status, and relationship status. The primary outcome for the trial was the number of standard drinks (15 mL pure alcohol) consumed over the past 30 days assessed by questions asked at BL, 3MFU, and 6MFU. The secondary outcomes included alcohol consumption, self-reported ART adherence, and viral load. Secondary alcohol outcomes included total AUDIT score (Babor et al., 2001), the AUDIT-C score (Bush et al., 1998), and PEth ng/mL. The reporting period of the AUDIT and AUDIT-C was changed from 12 to 3 months at BL and at each of the follow-up periods to avoid overlap of reporting periods.

Participants randomized to the alcohol reduction arm were asked to return within 2 weeks to receive their first intervention session. All participants, irrespective of condition assignment, were asked to return for repeated data collection at 3MFU and 6MFU points. Participants received grocery vouchers to reimburse them for their time and participation (ZAR 80 for initial visit and ZAR 100 for follow-up assessments). Transport expenses were also reimbursed (ZAR 50 per visit).

Statistical analyses

Characteristics of participants at BL and study end points were summarized by means and standard deviations for continuous variables and by frequencies and percentages for categorical variables. Given the skewed distribution for PEth, median and interquartile ranges are presented for this variable. Initially, bivariate statistics were presented to indicate the concordance between the self-reported alcohol variables and PEth level (<50, ≥50 ng/mL), comparing scores at BL with 3MFU and BL and 6MFU using chi-square tests of association and independent samples t-tests. We chose this cutoff as commensurate with hazardous alcohol use as reported in other studies (Hahn, Emenyonu, et al., 2016). Concordance was also assessed via calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Kappa statistics for the proportion of participants with total AUDIT scores ≥8 AUDIT-C scores ≥3 for females, ≥4 for males, HED in the past 30 days (≥6 drinks per occasion at least once), and heavy drinking in the past 7 days (>7 for women and >14 for men—the US National Institute on Alcohol Abuse and Alcoholism's criteria for heavy drinking[1] at BL, 3MFU, and 6MFU as compared to PEth ≥50 ng/mL). We then identified the self-report measure with the highest sensitivity and NPV compared with PEth ≥50, for further analysis of self-report versus PEth. For this

analysis, we defined underreporting as being when self-reported AUDIT-C scores indicated no hazardous alcohol use, but where PEth levels were indicative of hazardous alcohol use. We conducted multiple logistic regression to assess whether this discordance between the AUDIT-C scores and PEth differed by sex, age, and study arm at BL, 3MFU, and 6MFU. Certain analyses focus on the 6MFU as this is the time period giving study participants the longest possible exposure to the intervention. A sensitivity analysis was conducted with PEth<20/≥20 ng/mL as a cutoff and the proportion of persons having hazardous alcohol use as measured by the number of drinks consumed on a typical drinking day in the past 3 months, the percentage of at least weekly drinking of six or more drinks per occasion, and having AUDIT-C scores above the three for females/four for males cutoff levels, but having nonelevated PEth scores.

Ethical considerations

Ethics approval for the study was granted by the Research Ethics Committee of the South African Medical Research Council (EC003-2/2014). Permission for the study was obtained from the hospitals, the health districts, and Gauteng Province. The trial was registered in the Pan African Clinical Trials Register (PACTR201405000815100).

RESULTS

Demographic, BL self-reported alcohol use and PEth data

Self-report and PEth data were collected on 309 PWH receiving ART at BL, 255 at 3MFU, and 278 at 6MFU. The mean age of study participants at BL was 40.6 years (SD=9.06), with 57% being female (Table 1). Just over 40% had a high school education, and 55.7% were employed (or self-employed) in the informal or formal sectors. In keeping with study inclusion criteria, at BL, over 80% consumed five or more drinks on a typical drinking day during the past 3 months, with 9.6% drinking six or more drinks per occasion weekly. At 3MFU, this changed to 67.8% and 9.7%, respectively, and at 6MFU to 68.9% and 12.3%, respectively. Mean AUDIT scores at BL, 3MFU, and 6MFU were 8.7 (SD=4.7), 7.4 (SD=4.4), and 7.2 (SD=4.7), respectively. At BL, 3MFU, and 6MFU 93.8%, 74.9%, and 75.8% scored above the cutoffs on the AUDIT-C, respectively. At BL, 3MFU, and 6MFU 54.7%, 48.6%, and 51.4%, respectively, had PEth ≥50 ng/mL.

Concordance between self-reported drinking and PEth data

The bivariate analyses (Table 2) show the degree of concordance between self-reported drinking measures and PEth scores above and below the threshold of 50 ng/mL at each time point. While mean total AUDIT scores were substantially higher in persons with PEth ≥50 at both 3MFU and 6MFU compared to those with PEth <50 (mean of 8.75 vs. 5.98 at 3MFU and 8.62 vs. 5.50 at 6MFU), there was a high proportion of persons with PEth <50 with AUDIT-C scores above the cutoff for hazardous drinking at both 3MFU and 6MFU (42.1% and 41.0%). Furthermore, between 27.1% and 44.4% of participants with low scores on the AUDIT-C had PEth ≥50.

Table 3 shows self-reported alcohol measures compared with PEth ≥50 at BL, 3MFU, and 6MFU. Overall, the AUDIT-C was identified as the self-report measure with the highest sensitivity and NPV when compared to PEth ≥50. Kappa coefficients, used to assess agreement between the various measures and PEth, were generally low, but slightly higher for the full AUDIT: for example, 0.37 at BL, 0.23 at 3MFU (same as for the AUDIT-C), and 0.30 at 6MFU.

Factors associated with discordance between self-reported hazardous alcohol use and PEth ≥50 at BL, 3MFU, and 6MFU

At baseline, the 3MFU, and the 6MFU, eight of 166 (4.8%), 16 of 118 (13.6%), and 24 of 139 (17.3%) of participants with PEth ≥50 ng/mL were below the AUDIT-C cutoff for hazardous drinking (Table 4). This discordance appears to have increased over time. The odds of such discordance at BL and 3MFU were not associated with sex, age, or intervention arm. Sex (OR=3.504, 95% CI: 1.080 to 11.364), but neither age (OR=0.953, 95% CI: 0.906 to 1.003) nor study arm (OR=0.405, 95% CI: 0.159 to 1.032) were associated with discordance at 6MFU, with the risk of discordance in the direction of self-report measures not indicating hazardous drinking with Peth ≥50 being greater for females than males (Table 5).

Sensitivity analysis

A sensitivity analysis was conducted with PEth <20/≥20 ng/mL as a cutoff, and the proportion of persons not having hazardous alcohol use as measured by the number of drinks consumed on a typical drinking day in the past 3 months, the percentage of persons weekly drinking less than six drinks per occasion, and having AUDIT-C scores below the three for females/four for males cutoff levels, but having elevated PEth scores. With the lower cutoff for PEth of 20 ng/mL this proportion was found to be much greater, for example, at BL, with 61.1% of persons scoring low on the AUDIT-C but with PEth ≥20 ng/mL versus 44.4% with PEth ≥50 (Table 6). Similarly, 44.3% versus 27.1% at 3MFU and 50.9% versus 38.1 at 6MFU when comparing persons with low AUDIT-C scores but with PEth ≥20 ng/mL and PEth ≥50 ng/mL. The discordance was equally greater for the lower cut point (20 ng/mL) when looking at the proportion of persons not at least weekly drinking six or more drinks per occasion but scoring above the cutoff for PEth (71.2% vs. 53.8 at BL, 66.2% vs. 47.2% at 3MFU, and 66.5% vs. 50.7% at 6MFU). When comparing

TABLE 1 Sample demographic characteristics and outcome variables (unadjusted).

Variable	Baseline Total (n = 309)	3MFU Total (n = 255)	6MFU Total (n = 278)
Age: mean (SD)	40.56 (9.06)	40.93 (9.07)	41.26 (9.12)
Gender: n (%)			
Male	133 (43.0%)	115 (45.1%)	126 (45.3%)
Female	176 (57.0%)	140 (54.9%)	152 (54.7%)
Education: n (%)			
≤Primary school	36 (11.7%)	30 (11.8%)	33 (11.9%)
Some high school	146 (47.3%)	123 (48.2%)	131 (47.1%)
High school or equivalent	87 (28.2%)	71 (27.8%)	80 (28.8%)
Some post-high school education	40 (12.9%)	31 (12.2%)	34 (12.2%)
Marital status: n (%)			
Married/living with someone	121 (39.2%)	99 (38.8%)	106 (38.1%)
Single, divorced, separated, widowed	188 (60.8%)	156 (61.2%)	172 (61.9%)
Employment status: n (%)			
Unemployed	137 (44.3%)	121 (47.5%)	126 (45.3%)
Employed part-time (formal sector)	50 (16.2%)	43 (16.9%)	44 (15.8%)
Employed full-time (formal sector)	91 (29.5%)	67 (26.3%)	82 (29.5%)
Self-employed	31 (10.0%)	31 (9.4%)	26 (9.4%)
Group: n (%)			
Control	162 (52.4%)	145 (56.9%)	150 (54.0%)
Intervention	147 (47.6%)	110 (43.1%)	128 (46.0%)
Number of drinks consumed on a typical drinking day in the past 3 months: n (%)			
1 or 2	17 (5.5%)	11 (4.7%)	20 (7.7%)
3 or 4	41 (13.3%)	65 (27.5%)	61 (23.5%)
5 or 6	130 (42.1%)	70 (29.7%)	85 (32.7%)
7 to 9	76 (24.6%)	60 (25.4%)	55 (21.2%)
10 or more	45 (14.6%)	30 (12.7%)	39 (15.0%)
At least weekly drinking of 6 or more drinks per occasion: n (%)	28 (9.6%)	23 (9.7%)	28 (12.3%)
AUDIT total score: M (SD)	8.70 (4.69)	7.38 (4.42)	7.17 (4.68)
AUDIT ≥8	142 (48.6%)	102 (41.5%)	98 (37.7%)
AUDIT-C: n (%)			
<3 (females) or <4 (males)	18 (6.2%)	59 (25.1%)	55 (24.2%)
≥3 (females or ≥4 (males)	274 (93.8%)	176 (74.9%)	172 (75.8%)
PEth scores			
PEth: median (IQR)	60 (14; 203.50)	46 (11; 228)	53.5 (11; 193)
PEth <50 ng/mL: n (%)	140 (45.3%)	131 (51.4%)	135 (48.6%)
PEth ≥50 ng/mL: n (%)	169 (54.7%)	124 (48.6%)	143 (51.4%)

Abbreviations: ART, antiretroviral therapy; AUDIT, Alcohol Use Disorders Identification Test; MI, motivational interviewing; PT, problem-solving therapy; TAU, treatment as usual.

the kappas in Table 3 with those when compared to PEth ≥20, they were lower at all time points for AUDIT, HED in the past 30 days, and the number of drinks in the past 7 days, but higher with the 20 ng/mL cutoff for AUDIT-C at BL (0.05 vs. 0.03), 3MFU (0.31 vs. 0.23), and 6MFU (0.22 vs. 0.16). In comparison with the data for PEth ≥50 in Table 4, discordance was also higher with the lower (20 ng/mL) cutoff on PEth at BL (5.1% vs. 4.8%), 3MFU (15.7% vs. 13.6%), and 6MFU (18.1% vs. 17.3%). With the lower cutoff for PEth, the odds of such discordance were not associated with sex, age, or intervention arm at any of the time points.

TABLE 2 Bivariate analyses PEth (50 ng/mL cutoff) vs other variables (n (%) unless otherwise specified) at baseline, 3MFU, and 6MFU.

Variable	Baseline			3MFU			6MFU		
	PEth <50[a] n=140	PEth ≥50[a] n=169	p-value	PEth <50[a] n=131	PEth ≥50[a] n=124	p-value	PEth <50[a] n=135	PEth ≥50[a] n=143	p-value
Number of drinks consumed on a typical drinking day past 3 months: n (%)									
1 or 2	14 (82.4)	3 (17.7)	<0.001	10 (90.9)	1 (9.1)	0.001	15 (75.0)	5 (25.0)	0.001
3 or 4	24 (58.5)	17 (41.5)		39 (60.0)	26 (40.0)		33 (54.1)	28 (45.9)	
5 or 6	62 (47.7)	68 (52.3)		37 (52.9)	33 (47.1)		45 (52.9)	40 (47.1)	
7 to 9	24 (31.6)	52 (68.4)		19 (31.7)	41 (68.3)		17 (30.9)	38 (69.1)	
10 or more	16 (35.6)	29 (64.4)		13 (43.3)	17 (56.7)		11 (28.2)	28 (71.8)	
At least weekly drinking of six or more drinks per occasion: n (%)									
No	122 (46.2)	142 (53.8)	0.001	113 (52.8)	101 (47.2)	0.001	113 (49.3)	116 (50.7)	0.004
Yes	4 (14.3)	24 (85.7)		4 (17.4)	19 (82.6)		6 (20.7)	23 (79.3)	
AUDIT total score: M (SD)	6.76 (3.83)	10.16 (4.77)	<0.001	5.98 (4.00)	8.75 (4.39)	<0.001	5.50 (3.99)	8.62 (4.76)	<0.001
AUDIT-C: n (%)									
<3 (females) or <4 (males)	10 (55.6)	8 (44.4)	0.273	43 (72.9)	16 (27.1)	<0.001	39 (61.9)	24 (38.1)	0.004
≥3 (females or ≥4 (males)	116 (42.3)	158 (57.7)		74 (42.1)	102 (58.0)		80 (41.0)	115 (59.0)	

[a]ng/mL.

TABLE 3 Self-reported alcohol measures compared with PEth ≥50 at baseline, 3MFU, and 6MFU.

		Percent					
		Prevalence	Sensitivity	Specificity	PPV	NPV	Kappa
Baseline							
PEth	≥50 ng/mL	55					
AUDIT	≥8	49	76	61	65	73	0.37
AUDIT-C	≥3 females, ≥4 males	94	95	8	58	56	0.03
Heavy episodic drinking in past 30 days[a]	Yes	10	15	97	86	46	0.10
# of drinks in past 7 days	>7 women, >14 men	18	24	91	77	48	0.13
3MFU							
PEth	≥50 ng/mL	49					
AUDIT	≥8	42	53	70	63	60	0.23
AUDIT-C	≥3 females, ≥4 males	75	86	37	58	73	0.23
Heavy episodic drinking in past 30 days[a]	Yes	10	16	97	83	53	0.12
# of drinks in past 7 days	>7 women, >14 men	15	22	92	74	54	0.14
6MFU							
PEth	≥50 ng/mL	51					
AUDIT	≥8	38	52	79	74	59	0.30
AUDIT-C	≥3 females, ≥4 males	76	83	33	59	62	0.16
Heavy episodic drinking in past 30 days[a]	Yes	11	17	95	79	49	0.11
# of drinks in past 7 days	>7 women, >14 men	13	20	95	82	51	0.14

[a]≥6 drinks per occasion.

DISCUSSION

When compared to PEth ≥50 at BL and 3MFU, there is better concordance between the AUDIT measures than self-report measures of the past 30-day HED and heavy drinking in the past 7 days, offering better sensitivity and NPV. Even so, agreement between the AUDIT and AUDIT-C and PEth was not strong, with kappa coefficients only in the "fair" range. While over five indicators of concordance (sensitivity, specificity, PPV, NPV, and Kappas), the AUDIT is the self-report measure that is best aligned with PEth ≥50, and the AUDIT-C generally had the highest sensitivity and NPV at follow-up. Given that the full AUDIT assesses not only alcohol consumption

TABLE 4 Discordance between AUDIT-C scores and PEth: baseline, 3MFU, 6MFU (n (column %)).

	PEth <50	PEth ≥50	Total
Baseline			
AUDIT-C			
<3 females, <4 males	10 (7.9)	8 (4.8)	18 (6.2)
≥3 females, ≥4 males	116 (92.1)	158 (95.2)	274 (93.8)
3MFU			
AUDIT-C			
<3 females, <4 males	43 (36.8)	16 (13.6)	59 (25.1)
≥3 females, ≥4 males	74 (63.2)	102 (86.4)	176 (749)
6MFU			
AUDIT-C			
<3 females, <4 males	39 (32.8)	24 (17.3)	63 (24.4)
≥3 females, ≥4 males	80 (67.2)	115 (82.7)	195 (75.6)

(items 1 to 3) but also alcohol dependence (items 4 to 6) and alcohol-related problems (items 7 to 10), it is not surprising that the AUDIT-C (Bush et al., 1998) which just measures alcohol consumption has better sensitivity. The finding of high sensitivity for the AUDIT-C and AUDIT against PEth with reasonable specificity concurs with the finding of Francis et al.'s (2015) study in northern Tanzania. A study of male veterans attending infectious disease clinics in the USA (McGinnis et al., 2021) found similar sensitivity for the AUDIT-C (84%) when validated against PEth scores (in this case PEth ≥20) to that found in our study (83% at 6MFU).

Discordance between the AUDIT-C and PEth ranged between 4.8% and 17.3% depending on the assessment time point. It is difficult to compare this with other studies as they tended to compare participants' self-reported alcohol use (yes/no) among those who were PEth positive (Francis et al., 2015; Papas et al., 2016; Raggio et al., 2019) or PEth ≥8 (Bajunirwe et al., 2014). From a clinical point of view, the biggest risk associated with discordance is self-report measures not identifying people with hazardous alcohol use who would be identified through the use of a biomarker (underreporting). Biomarkers are more likely to be objective markers of the amount people drink while not assessing the consequences of unhealthy drinking. It is such patients who would fail to be identified for an intervention and who are likely to be at risk for ongoing alcohol-related negative consequences, such as poor adherence to ART, treatment failure and HIV disease progression and possibly increased mortality (Marshall et al., 2017; Myers et al., 2021). Additionally, we noted an increase in underreporting of alcohol use over time. This could be attributed to social desirability bias and underreporting of drinking to please study personnel. Furthermore, the high percentage of study

TABLE 5 Multiple logistic regression analysis of discordance (underreporting) of PEth positivity (PEth ≥50) when using AUDIT-C (≥3 for females/≥4 for males) at baseline, 3MFU, and 6MFU.

Model	OR	Std. Err.	z	p > |z|	95% Conf. Int. Lower limit	95% Conf. Int. Upper limit
Baseline (n = 166)						
Sex-female	2.691	2.322	1.15	0.251	0.496	14.607
Calculated age	1.030	0.045	0.69	0.493	0.946	1.121
Intervention arm	0.615	0.454	−0.66	0.510	0.145	2.616
Constant	5.111	9.757	0.85	0.393	0.121	215.566
3MFU (n = 118)						
Sex-female	1.423	0.839	0.60	0.550	0.448	4.519
Calculated age	1.040	0.035	1.17	0.243	0.974	1.111
Intervention arm	0.414	0.229	−1.60	0.110	0.140	1.222
Constant	1.492	2.244	0.270	0.790	0.078	28.463
6MFU (n = 139)						
Sex-female	3.504	2.103	2.09	0.037	1.080	11.364
Calculated age	0.953	0.025	−1.84	0.066	0.906	1.003
Intervention arm	0.405	0.193	−1.89	0.058	0.159	1.032
Constant	41.017	50.961	2.99	0.003	3.592	468.303

TABLE 6 Bivariate analyses PEth (20 ng/mL cutoff) versus other variables (n (%) unless otherwise specified) at baseline, 3MFU, and 6MFU.

Variable	Baseline			3MFU			6MFU		
	PEth <20[a] n = 90	PEth ≥20[a] n = 219	p-value	PEth <20[a] n = 99	PEth ≥20[a] n = 192	p-value	PEth <20[a] n = 82	PEth ≥20[a] n = 160	p-value
Number of drinks consumed on a typical drinking day past 3months: n (%)									
1 or 2	12 (70.6)	5 (29.4)	0.001	8 (72.7)	3 (27.3)	<0.001	14 (77.8)	4 (22.2)	<0.001
3 or 4	13 (31.7)	28 (68.3)		31 (46.3)	36 (53.7)		16 (31.4)	35 (68.6)	
5 or 6	40 (30.8)	90 (69.2)		16 (21.6)	58 (77.4)		26 (34.7)	49 (65.3)	
7 to 9	17 (22.4)	59 (77.6)		7 (11.7)	53 (88.3)		11 (22.9)	37 (77.1)	
10 or more	8 (17.8)	37 (82.2)		13 (43.3)	17 (56.7)		5 (14.3)	30 (85.7)	
At least weekly drinking of 6 or more drinks per occasion: n (%)									
No	76 (28.8)	188 (71.2)	0.014	74 (33.8)	145 (66.2)	0.003	66 (33.5)	131 (66.5)	0.040
Yes	2 (7.1)	26 (92.9)		1 (4.2)	23 (95.8)		4 (14.3)	24 (85.7)	
AUDIT total score: M (SD)	6.45 (3.66)	9.51 (4.77)	<0.001	5.61 (3.95)	8.08 (4.38)	<0.001	5.33 (4.38)	8.26 (4.59)	<0.001
AUDIT-C: n (%)									
<3 (females) or <4 (males)	7 (38.9)	11 (61.1)	0.228	34 (56.7)	26 (43.3)	<0.001	27 (49.1)	28 (50.9)	0.001
≥3 (females or ≥4 (males)	71 (25.9)	203 (74.1)		41 (22.7)	140 (77.4)		43 (25.3)	127 (74.7)	

[a] ng/mL.

participants who had PEth <50 at BL suggests that some may have exaggerated their drinking to get into the study.

In this study, being female was the best predictor of underreporting alcohol use at 6MFU, as indicated by discordance between the AUDIT-C and PEth results. Age and being in the intervention arm, however, were not found to be significantly related to underreporting. Sex differences could possibly occur because drinking among women is subject to more societal and health worker stigma (Anvari et al., 2022; Sorsdahl et al., 2012), and therefore, women might be more likely to underreport their drinking and associated negative consequences as compared to males, or they may have more desire to please the study staff by reporting low alcohol use.

We could not identify any intervention trials that investigated concordance between self-report and alcohol biomarkers and that examined differences between participants in the intervention versus control group. One might expect more discordance between self-reported use and biomarker assessment of alcohol use in the intervention group as they may have been subject to greater levels of social desirability bias after receipt of an alcohol reduction intervention. However, at each time point in the present trial, blood was drawn for PEth before the self-report alcohol questions were asked, and this could have encouraged participants to be more forthcoming about their alcohol use.

The results of studies looking at discordance between self-reported alcohol use and PEth scores broadly (and not in terms of our narrow definition) have been mixed. A study of patients in HIV care on ART in Uganda found that men were more likely than women to underreport their drinking (Bajunirwe et al., 2014). However, a study of young women with HIV receiving medical care in Russia (Littlefield et al., 2017) could not identify any consistent predictors of underreporting. With regard to age, a community study conducted in the USA (Cherrier et al., 2020) has found that middle-aged adults (35 to 59 years old) evidenced higher PEth levels than older adults at comparable drinking rates. In contrast, a meta-analysis study found no associations of sex, age, race/ethnicity, or method of blood collection with PEth sensitivity. In models that additionally included biologic variables, persons with higher BMI and PWH had lower odds of PEth sensitivity (Hahn et al., 2021). Therefore, it is possible that HIV status, BMI, and other unmeasured variables could have accounted for some of the discordance between self-report and biomarker levels in this study. Other possible reasons for discordance between self-report measures and PEth that have been posited include the sustained PEth levels after the cessation of previously heavy drinking due to elimination dynamics (Hahn, Anton, & Javors, 2016).

Strengths and limitations

While adding to the growing literature on the association between self-reported alcohol use and the biomarker PEth, this study is subject to several limitations. First, the study was limited to participants on ART attending public HIV clinics in the Tshwane Metropole in South Africa and the findings may not be generalizable beyond that geographic area. Another limitation is that we only included people who self-reported hazardous alcohol use at baseline. If we conducted this with a broader, nonlimited spectrum of PWH on ART, many would not be drinking. By including this latter group of individuals, who would likely have been negative on both AUDIT and PEth measures, concordance would have increased. Furthermore, the questions were interviewer administered which could have increased response bias compared with a confidential self-administered survey. In addition, PEth cutoffs for hazardous alcohol use have not been widely validated, and as mentioned above, biologic factors may decrease PEth sensitivity (Hahn et al., 2021). Furthermore, the sensitivity analysis found that the proportion of persons with elevated self-report alcohol measures was much lower than for a 50 ng/mL cutoff on PEth, suggesting that for some people a 50 ng/mL cutoff on PEth was possibly too high a threshold rather than over-(self) reporting of hazardous alcohol use.

CONCLUSIONS

Given the likely continued reliance on self-reported alcohol use measures in clinical settings to identify PWH at greater risk of alcohol-related negative outcomes, our findings suggest steps are needed to increase the validity of these self-reported screening tools. In particular, effort is needed to create a nonstigmatizing environment to put female patients at ease when enquiring about their alcohol use. Additional qualitative research to explore how PWH experience questions about their drinking and their preferences for alcohol screening may further identify strategies for improving the detection of hazardous alcohol use in this vulnerable population.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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ENDNOTE

¹ https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking.

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