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A UTILITARIAN COMPARISON OF TWO ALCOHOL USE BIOMARKERS WITH SELF-REPORTED DRINKING HISTORY COLLECTED IN ANTENATAL CLINICS

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Abstract

Background—Alcohol use is reported accurately among pregnant women in some populations.

Methods—Self-reported alcohol use via the AUDIT and 90-day recall for 193 women from antenatal clinics was compared to biomarker results: phosphatidylethanol (PEth) from bloodspots and ethyl glucuronide (EtG) in fingernails.

Results—AUDIT was positive for 67.9% of respondents, and 65.3% directly reported drinking. Individual biomarkers detected less drinking (PEth = 57.0%, EtG = 38.9%) than self-report. But 64.8% had drinking-positive values (>8ng) on one or both biomarkers, which was not significantly different from self-report. Biomarkers indicated that 3.1% – 6.8% of drinkers denied drinking. Combined biomarker sensitivity was 95% – 80% and specificity 49% –76% for drinking in the previous 7 to 90 days. Combined biomarker results have their best yield (89.6%) and accuracy (78.8%) when measuring 90 day drinking.

Conclusions—Women reported their alcohol use accurately, and the combined use of PEth and EtG is supported.

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1. Introduction

In parts of the Western Cape Province (WCP) of South Africa (SA) there is a subculture of regular binge drinking. It is common for 35 to 50% of women of childbearing age to drink 2 to 9 alcoholic beverages each night on most Fridays and Saturdays [1,2]. This is the major factor creating a high prevalence of fetalalcohol spectrum disorders (FASD) in the general population of some communities of the WCP. These communities have the highest documented prevalence of FASD anywhere in the world; 17 to 28% of children in first grade classes have been found to have FASD [3–6].

Over the past twenty years, members of our SA research team have judged the local reporting of alcohol use to be extremely candid and forthright among women and men in the WCP [1,2,7,8]. Furthermore, we have found that reports of alcohol use, childbearing, and other personal information across various datasets collected in these populations were reliable. Associations between self-reported alcohol use data and specific alcohol-related outcomes, specifically diagnoses within the continuum of FASD, correlated significantly with seemingly credible levels of alcohol exposure in multiple samples and studies [3–6,8,9], yet the accuracy of the basic alcohol reporting had not been tested against biomarkers of alcohol use. Therefore, we embarked on this study to assess the accuracy of alcohol-use reporting in these SA communities.

In studies of alcohol use reporting carried out in some populations, women are believed to be less than honest and accurate when providing alcohol-use information, [10–12] especially in prenatal clinic settings in Western Europe. This finding has been reported when sensitive alcohol-specific biomarkers were employed using appropriate biological specimens [13–16]. However, there is also ample evidence that many populations report quite accurately if proper interviewing techniques are used, rapport is built, and multiple measures of alcohol use over time are used [16–23].

1.1 Study Objectives: Cross Validation for a Utilitarian Understanding

There were two objectives in this study. The first objective was to assess whether the maternal population of the WCP of SA is accurate in the overall reporting of alcohol use during pregnancy by utilizing objective biomarkers of drinking. Second, we sought to estimate how accurate, sensitive, and specific each of the two biomarkers was for detecting any level of alcohol use in this population through comparison of the biomarker results with self-report. It is a comparative validity study of the two methods to determine their utility for use in both antenatal clinic applications and for research purposes.

This manuscript compares positive and negative results from two self-reported alcohol-use measurements with results from two alcohol-use biomarkers. The self-report measures are the World Health Organization Alcohol Use Disorders Identity Test (AUDIT) [21], and standard measures of alcohol use by quantity and frequency (Q-F) [7]. The two biomarkers are ethyl glucuronide (EtG) and phosphatidylethanol (PEth), two metabolites of alcohol consumption that can be measured in various biological specimens (e.g. urine, blood, or cutaneous substances). They both have been found to be specific to alcohol use and are sensitive to moderate to heavy intake of alcohol over specific windows in time [25,26].

2. Methods

2.1 Measures and Sampling

The two biomarkers were measured from different biological materials. Phosphatidylethanol (PEth) was measured in bloodspots from finger pricks and ethyl glucuronide (EtG) was measured in fingernail clippings totalling 50 to 100*mg* or more. Both specimens were collected from 193 pregnant women attending community health care antenatal clinics that serve the vast majority of the local community population. The average gestation of the respondents at the time of bloodspot collection and simultaneous interview was 19.7 (±SD of 7.5) weeks. These participant interviews contained an array of maternal risk factors encountered during the index pregnancy, with an emphasis on dietary intake and alcohol consumption. The questionnaire contained two techniques for collecting and summarizing self-reported alcohol use. The AUDIT [21] was used with a cut off score of 4 for a high degree of sensitivity for measuring current alcohol use at the light to moderate range and above.Also well-established quantity/frequency (Q-F) questions were used that covered alcohol use at time of interview and specific time periods up to three months prior to the interview. All participants lived in one of two small towns and surrounding rural areas of the WCP.

2.2 Key Time Periods for Measuring Prior Alcohol Use

The three categories and time periods of particular interest for the biomarker analyses were: a) those using alcohol seven days prior to the interview, b) those consuming alcohol 30 to 90 days prior to the interview, and c) those who were self-reported abstainers throughout the previous 90 days. Both PEth and EtG are reported to be sensitive, direct, alcohol-specific biomarkers for most individuals [24–26]. PEth as a biomarker in blood samples has a half-life of five to seven days, and is accurate for measuring moderate consumption in the past seven days, and sustained, heavy consumption up to three weeks [27]. EtG collected from fingernails is purported to be accurate for detecting moderate to heavy drinking up to three months prior to sample collection [28,29]. Because most drinking occurs over the weekends for over 90% of alcohol users in this particular SA population [2,7], bloodspots and interviews for the PEth biomarker analyses were collected only on Monday or Tuesday clinics to provide accurate measures of drinking. Furthermore, since the fingernail samples record longer-term alcohol use, they were collected at either first contact, at the same time as the blood samples and interviews were collected, or at a scheduled return visit to the participant’s home 1 to 2 weeks later, once the nails had grown to an appropriate length (3 mm).

2.3 Maternal Questionnaire

The self-report questionnaire was developed specifically for epidemiology studies of the prevalence and characteristics of FASD via active case ascertainment and the clinical diagnosis of FASD in the WCP. To establish rapport, nonthreatening questions about general maternal health and diet were asked first, and the interview moves to information on health, diet, and childbearing. Alcohol consumption responses are more accurate in such a format, especially embedded within the context of dietary questions [30]. Multiple measures of alcohol use in the previous 90 days were asked, paying special attention to alcohol brands

and containers commonly used in this population (vessels measurement), as respondents were shown pictures of standard containers of local brands. This sequencing and vessels technique assists in accurate reporting and calibration of the amounts consumed [31,32]. Alcohol was measured in standard US units where one drink equals: a 340 ml can/bottle of beer (5 to 5.5% ethanol), 120 ml of wine (11% ethanol), 95 ml of wine (13.5% ethanol), or 44 ml of distilled spirits (43% ethanol). Experienced research staff employed by the grant, mainly nurses and social workers, conducted the maternal interviews.

2.4 Biomarker Analysis and Utilitarian Purposes

The biological specimens were shipped to the United States where the United States Drug Testing Laboratories of Des Plaines, Illinois prepared the samples for processing and performed the analyses for both of the biomarkers. Neither of these specimen types (blood spots and fingernails clippings) required special processing on site or refrigeration when shipping. The blood spots were squeezed from finger pricks onto paper blood collection cards and allowed to dry. Fingernails were clipped with a common fingernail clipper and placed in a small envelope for shipping. For both EtG and PEth, a liquid chromatography-tandem mass spectrometry method was used to analyse the specimens [26,33]. For the analyses presented in this paper, the cut-off level for positive or negative alcohol use was ≥8ng/mL for either EtG or PEth as past analyses have indicated both accuracy and sensitivity at this level. [24,26]

The results of the biomarker tests and the self-report measures, as analyzed and presented here, provide binary measures of positive or negative alcohol use. We call this analytic approach utilitarian because we focused the analysis on the validity or utility of one or both markers to detect any alcohol use that is meaningful for research and/or clinical purposes. For the clinic: does this person use alcohol (yes/no)? If yes, preventive measures might be instituted for this individual. For research purposes: can a positive result on one or both of the biomarkers be compared with self-reported use to determine accuracy of reporting and the case classified as an alcohol-exposed pregnancy?

2.5 Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) [34] was used for statistical analyses. Chi-square tests of significance were used for comparisons of the binary (positive/negative) data. *Z*-tests of proportions were used to compare positive results by various binary criteria. Analyses of strength of association were performed with squared phi coefficients. To compensate for inflation of Type I error rate due to the exploratory nature of the analyses and redundancies among them, criterion α has been set to .01 for all tests of statistical significance, as per Tabachnick and Fidell [35].

3. Results

3.1 Prevalence of Alcohol Use Measured Independently by Self-Report and Individual Biomarkers

One hundred ninety-five paired biomarker samples were collected (one of each biomarker for each woman) in the antenatal clinics, stored, and shipped across the Atlantic. And 193

pairs were processed successfully to yield results within a meaningful range of values. Each of these respondents completed the interview containing the self-reported alcohol use measures. Sixty-eight percent (67.9%) of the participants scored positive on the AUDIT when set at a level for high sensitivity (>4). The average AUDIT score for the entire sample was 11.1 (SD = 9.1), and 16.1 (SD = 6.6) for the drinkers only, and a value ≥8 is considered problem or heavy drinking [18]. On the Q-F measures, 65.3% of the participants reported drinking. The average overall standard drinks per drinking day (DDD) over the past 30 days was 2.7 (SD=3.8). Calculated for the drinkers only, the average DDD was 5.2 (SD = 3.8) drinks per drinking day.

Table 1 indicates that PEth detected alcohol use in 57.0% of the respondents. EtG detected drinking in 38.9% of the respondents. A positive detection on either one or both biomarkers was found in 125 women or 64.8% of the sample, and alcohol use was detected by both biomarkers in 62 women or 32.1%.

3.2 Comparison of Biomarker Results Utilizing Self-Reported Alcohol Use as the Standard

Table 2 compares self-reported drinking on the AUDIT measure with the percentage of drinkers detected by the two biomarkers. One hundred-thirty-one (131) cases were AUDIT positive (score >4). Only 83.9% as many drinking-positive cases were identified by PEth from bloodspots, for 75 drinkers or 57.3% of the sample were identified by EtG alone as measured in fingernails. Both of these individual biomarker detection rates were significantly lower than self-reported information on the AUDIT when measured by either a conventional chi-square test or a Z-test of proportions (p<.001), in which the proportion of positive results detected by the biomarker(s) is divided by the proportion of positive results reported by the AUDIT score. But when the results of the two biomarkers are combined, 125 were positive on one or both of the biomarkers. This represents 95.4% as many cases as were detected by AUDIT. Self-reported alcohol use via the AUDIT was not significantly different (z= 2.37, p=.018) from that detected by the two biomarkers used individually.

In Table 3, self-reported drinking prevalence of any drinking on the Q-F questions in the past 90 days was compared to the positive results from the two biomarkers used individually and in combination. Measured by both chi-square and Z-test of proportions (as described above), the detection rate of the individual biomarkers is significantly less than self-reported drinking (Q-F). PEth detected drinking in 87.3% as many of the participants as those who reported drinking in the past 90 days. EtG produced a positive result in 59.5% of the participants. And the two biomarkers combined indicated that 125 of the respondents drank, which is 99.2% as many as reported drinking by quantity and frequency. The combined difference of proportions is not statistically significantly different (z = 0.825, p=.409) from that reported in interviews.

In Table 4, final, aggregate reports of drinking are compared by cases and percentages positive on one or both biomarkers. The AUDIT identified six more drinkers (4.8%), and the Q-F measures indicated one more case (0.8%) than the two biomarkers combined. A Z-test of proportions tested whether the proportion of cases identified as positive differed between detection by one or both biomarkers and self-report (separately tested for AUDIT and Q-F). Neither of these differences, was statistically significant (z =.664, p = .507 for AUDIT, and

z=.103, p = .918 for Q-F). Therefore, self-report and combined biomarker results produce similar overall prevalence findings in these aggregate comparisons of proportion of drinkers. Figure 1 summarizes the various detection rates.

3.3 Comparison of Self-Reported Alcohol Use with Biomarker Results as the Standard

Table 5 was constructed because the biomarkers identified some participants as drinkers who had not self-identified, and some participants who identified themselves as drinkers were not detected by a positive result on one or both of the biomarkers. Part A of Table 5 indicates that a positive value on one or both of the biomarkers identifies 112 (true positive) drinkers or 58.0% and 40 (20.7%) were identified as abstainers (true negatives). The remaining participants are possible deniers, for 13 cases (6.8%) may not have responded truthfully, by denying drinking when they were positive on one or both biomarkers. Finally, 28 or 14.5% were false negatives who were positive via self-report yet negative on both biomarkers. The test of proportions comparing participants who were positive on one or both biomarkers (n = 125, 64.8%), with those positive on one or more self-report measures (n= 140, 72.5%) is not statistically significant (z = 1.630, p=.103)

Shown in part B of Table 5, there are 55 cases categorized as true positives (28.4%) on both biomarkers (true positives). Seventy were classified as true negatives (36.3%) on both biomarkers, for they reported that they abstained, and the biomarker results are negative. Furthermore, 62 (32.1%) were categorized as false negatives, for they reported drinking yet they were negative on the biomarkers. Finally, six cases (3.1%) reported no drinking on either self-report measure, but were positive for drinking on one or both biomarkers.

These two comparisons indicate that six to 13 biomarker positive/self-report negative respondents may have falsely denied drinking. It is therefore likely that at least 3.1% to 6.8% of the women participants have concealed their drinking. The other 28 (14.5%) from Table 5A, to 62 (32.1%) from Table 5B, were cases who reported drinking but were classified as positive by one or both of the biomarkers. They are false negatives for they reported drinking, yet the biomarkers did not classify them as drinkers. Were they light and/or occasional drinkers and therefore not detected by these two biomarkers? Table 5, therefore, raises the question of the sensitivity and specificity of these biomarkers.

3.4 Sensitivity/Specificity Analysis Using Self-Report as the Standard

Given that lying, or denial of drinking when it actually occurred, seems to have been minimal, one can conclude that drinking is reported quite accurately in this population. Therefore, sensitivity analysis is appropriate using self-report as the standard. In Table 6, PEth measured in bloodspots is 91.7% (0.9167) sensitive and 58.7% (0.5865) specific when drinking occurred in the past seven days, and 72.1% sensitive and 83% specific when drinking occurred sometime in the past 90 days. EtG measured in fingernails is less sensitive but more specific overall, for it is 65% sensitive and 72.9% specific for drinking in the past seven days, and 50.1% sensitive and 92.5% over the 90-day period.

When the positive results of the two biomarkers are combined, the best sensitivity is obtained while maintaining reasonably high specificity. Positive on one or both biomarkers, seven-day sensitivity is 95% and specificity is 48.9%. Over the 90-day period, sensitivity for

the combined biomarkers is 80% and specificity is 75.5%. The positive predictive value (yield) is best for all measures when used over the longer time frame, 90 days. Accuracy in this population is good for PEth when measuring drinking in either the past 7 or 90 days and for EtG at 7 days up to 90 days. Finally, using the biomarkers together is most sensitive for measuring use in the past seven days (95%), most specific at 90 days (75.5%), and combined results have the best yield at 90 days (89.6%) and most accurate at 90 days (78.8%).

3.5 Association Analysis

Table 7 summarizes analyses of association to assess the individual, case-by-case variation in the accuracy of measures of alcohol use employed here. The strongest association for an individual biomarker is between PEth and reported quantity and frequency of alcohol use in the past 90 days ($\varphi^2 = .301$;, $p<.001$). The association between PEth and AUDIT was weaker although still statistically significant, $\varphi^2 = .187$, $p<.001$. The association between EtG and AUDIT was similar, $\varphi^2 = .170$, $p<.001$.

The association between the two biomarkers (PEth vs. EtG) is statistically significant, $\varphi^2 = .154$, $p<.001$. Finally the association between a positive value on one or both biomarkers and one or both self-report measures is second only to that between PEth and Q-F, $\varphi^2 = .268$, $p<.001$.

4. Discussion

The two questions posed in this study have been answered to a substantial degree by this utilitarian analysis. Are these respondents in the WCP of SA accurate reporters of alcohol use? And, are PEth and EtG, used individually or in combination, valid and useful binary (use/no use) measures of alcohol consumption, particularly in a population where a common drinking pattern is to engage in moderate to heavy consumption in a binge pattern on a weekly basis?

4.1 Accurate Reporting in This Population

The respondents in this sample of women recruited from antenatal clinics have been found to be accurate reporters of their alcohol use. A slightly higher percentage of the respondents reported alcohol use on both the AUDIT and by quantity and frequency than was detected by the biomarkers individually. And when positive results were combined for the two biomarkers, they were virtually the same (not statistically significant). This is particularly striking given the venue, for self-report studies from prenatal clinics in the United States and Europe have found that underreporting is frequently the norm when self-reported prevalence has been compared to a variety of biomarkers taken in the clinics (via urine and blood) and at birth via meconium, (e.g. fatty acid ethyl esters (FAEE), EtG, PEth, and others) [13,15,36–42]. One meta-analytic review found that biomarker testing of meconium for several different biomarkers produced 4.26 times more positive results than did matched self-reports [14].

Underreporting of the actual amounts of alcohol consumed in prenatal clinics has also been found to be significant in some populations when retrospective drinking reports, gathered up to 13 years later, are compared to the amounts and frequencies of drinking reported in

prenatal clinics [18–20]. One other study in Africa, among Ugandans, also concluded that self-reported alcohol use often lacks agreement with PEth results, particularly among women [16]. Underreporting, however, was not the case in this study from SA, for the combined biomarker results and the self-reported data indicated a similar prevalence of drinking. In this study, the percentage of alcohol users reported by the respondents is higher than that detected by individual biomarkers, but similar to that reported as positive by the two biomarkers in combination. Other studies in other populations have also shown that a combination of biomarkers [33] and/or a combination of biomarkers and self-report yield the highest prevalence of alcohol use [44–45]. We maintain that accuracy of alcohol use reporting varies by population, particularly for quantity of drinking reported among heavy or binge drinkers. There are a number of populations where studies have shown reporting to be quite accurate [17–18,43,46,47]. And for Southern African populations accurate reporting has been noted and validated. For example, one in Lesotho [12], and two in the Western Cape Province using EtG and FAEE [46,47] also found self-reported use to be significantly higher than detected by biomarkers alone. Therefore, in this study where the reporting by the respondents overall was not significantly different from that detected by the combined results from the two biomarkers is another indicator that the predominately Coloured and Black populations of Southern Africa report accurately.

Additionally, a recent longitudinal study of the Inuit in Northern Canada also indicated accurate reporting of use/no use of alcohol during pregnancy in both prenatal clinics at 11 years after delivery [18]. An additional point can be made here. Accurate reporting in any population may be a function of the nature, setting, and conduct of the interviews. In studies carried out in two separate populations, Jacobson et al. [17–18,43] reported that accuracy of reporting may more consistently accurate when interviews are conducted by well-trained, experienced, and sensitive interviewers with well-worded and well-sequenced protocols. Therefore, women may report less to nurses and physicians in less formal interview settings, particularly in antenatal clinics where disclosure of drinking may lead to critical, corrective, or judgmental rhetoric. Additionally, there were very few participants in this sample who were suspected of lying about their drinking because of a negative report of drinking and a positive biomarker result. Between 3.1% and 6.8% were classified as false positive by the biomarkers on the other hand, many more (14.5% to 32.1%) were categorized as false negatives by the biomarkers. This may be an indication that the drinking of these individuals was light to moderate (likely not heavy or consumed in a binge-like fashion) and therefore escaped detection by these biomarkers which are reported to be best in detecting binge drinking and heavy consumption. Lack of self-report in these instances could also be a result of light drinkers forgetting instances of alcohol use in the past 90 days [17].

Future analysis of these data will address the association between the specific levels of each biomarker detected in a subject, and the specific quantity and frequency of drinking that she reported. This will shed further light on the accuracy question in the future. But, from this binary analysis and the results of three previous studies comparing biomarker results with self-report in Southern Africa [12,46,47], we can conclude that alcohol use reporting in this region is generally accurate, much more so than that reported in most comparative biomarker/self-report studies from Europe [40–45] and North America [13]. There has

traditionally been a lack of stigma surrounding recreational binge drinking in this population and this may also make accurate reporting more likely [2].

4.2 The Biomarkers, When Used in Combination, Are Sensitive and Valid

Taking these two biomarker comparisons as the gold standard of validation, we might surmise that as many as 93.8% to 96.9% of the biomarker positive/self-report negative cases are truly drinkers. And one might also conclude that 14.5% to 32.1% of the drinkers have been missed (i.e. biomarker negative) because of light to moderate drinking. Or they may be individuals with particular metabolic characteristics that make detection by one or both of the specific biomarkers unlikely in a single sample collection.

Furthermore, the sensitivity analysis indicated that PEth was, in this population, the more sensitive measure when measured from bloodspots, but both PEth from bloodspots and EtG from fingernails were substantially specific. The highest sensitivity was achieved when the two biomarkers were used in combination (95%) to measure drinking in the past seven days and specificity was relatively high (76% over 90 days) with a positive predictive value of 90% and accuracy of 79% to detect drinking in the past 90 days. As utilitarian measures for antenatal clinic use, the combined results of PEth and EtG are certainly sensitive enough for most research applications for behavioral studies and in clinics to trigger preventive measures such as providing information on abstaining from alcohol during pregnancy and explanations of fetal vulnerability. They may further be utilized to justify offers of referral to alcohol treatment or case management.

Association analysis revealed that the biomarkers correlated significantly, although the magnitude of association utilizing only a binary measure of drinking detection (both self-report and biomarker results were treated as simply positive or negative) was not very strong. Again, further analysis on this topic is needed to decisively determine association by magnitude of each measure, self-report versus each biomarker.

4.3 Strengths and Limitations

The strengths of this study are these. First, we utilized a conventional technique of comparing the performance of biomarkers to self-reported alcohol use provided by the same participants. And this is one of a few studies to utilize both two different biomarkers to measure drinking in antenatal clinics and also two complimentary self-report measures to determine the accuracy of alcohol use measurement in a population believe to be candid and accurate in their reporting of alcohol consumption. Second, the two different self-report techniques were used for cross validation of the reporting. Third, of the two different biomarkers used, one was a marker for detecting recent use and the other a marker to detect moderate to heavy use over a three-month period. Each marker had its strengths and weaknesses, and the two in combination worked quite well. Using these mixed techniques in a population that has been studied previously and extensively, we were able to reliably assess or estimate both whether this was a population that is relatively accurate in their reporting, and to assess the accuracy and utility of the two biomarkers. We believe these multiple comparisons served both objectives well. The biomarkers proved to be efficacious and therefore can have utilitarian applications for both clinical and research use in

populations where moderate to heavy drinking exists among women of childbearing age. The weaknesses are these. First, similar studies should be undertaken in populations characterized by different drinking patterns, for this population is somewhat unique in the pattern of regular binge drinking on weekends. When this biomarker study was designed, we believed from prior experience and research that this was likely to be an accurate reporting population.

Therefore, testing the biomarkers against self-report in this population may render the results valid only in regards to drinking in this particular population. Second, we analyzed the data for this manuscript on a binary basis, drinking versus not drinking. We did not correlate the magnitude of the results with one another (self-report quantities versus biomarker concentrations), for such assessment requires further exploration, analysis, and discernment which is underway.

5. Conclusion

Used in combination, these two biomarkers are particularly good for confirming that this is an accurate alcohol-use reporting population and for measuring alcohol use in a binary fashion. If we use the biomarkers in combination as the standard by which to judge the accuracy of reporting, only 3.1% to 6.8% of respondents denied significant alcohol use during the prenatal period. Therefore, these biomarkers can be used for accurate estimation of moderate to heavy prenatal alcohol use in both individuals and in entire populations. Each self-report measurement and each of these two biomarkers has its particular strengths and weaknesses. But, when used in combination, they provide a strong set of tools for accurate measurement of alcohol use.

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HIGHLIGHTS

- Pregnant women in this population report alcohol use accurately.
- The AUDIT interview tool identified 67.9% as alcohol users.
- Alcohol use via reported quantity/frequency measures was 65.3%.
- PEth in blood spots identified 57% as drinkers.
- EtG in fingernails identified 38.9% as drinkers.

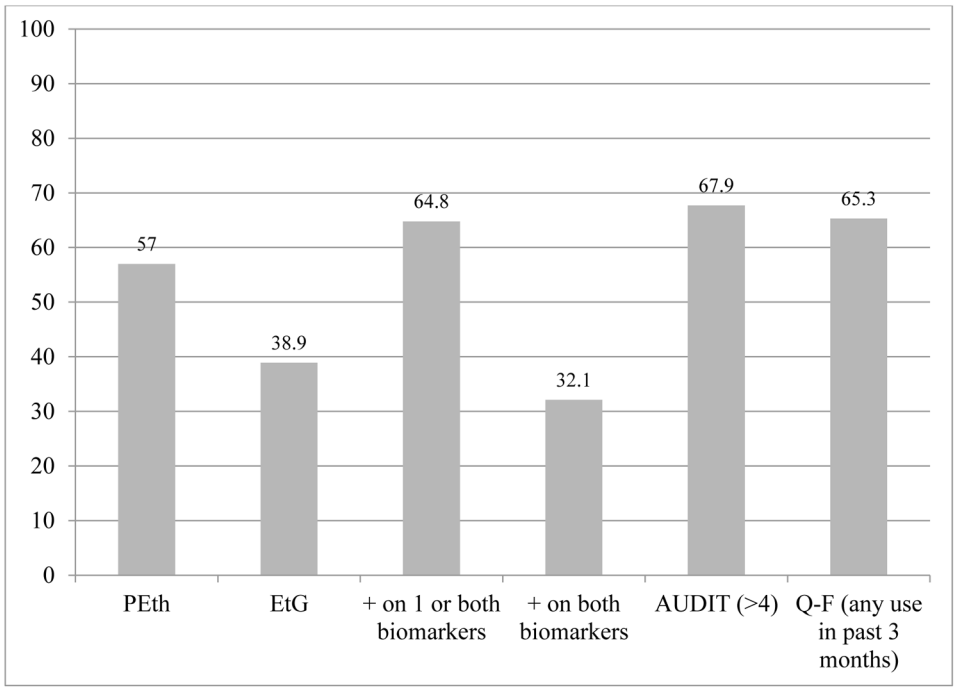

Figure 1.

positive result indicating any alcohol use by two biomarkers and two methods of self-report

Table 1

Positive Cases of Alcohol Usage as Indicated by Two Biomarkers among Females in the Antenatal Period (n=193)

Significant EtOH Usage	PEth + (≥8ng/mL)	EtG + (≥8ng/mg)	Positive cases on one or both biomarkers	Positive on both biomarkers
Positive	110 (57.0%)	75 (38.9%)	125 (64.8%)	62 (32.1%)
Negative	83 (43.0%)	118 (61.1%)	68 (35.2%)	131 (67.9%)

Table 2

Association between Self-Reported AUDIT score and Drinking Detected by PEth, EtG, and both biomarkers combined among Female Participants (*N*=193). Classification Tables and Statistics.

AUDIT score	PEth Result		EtG Result		Positive cases on one or both biomarkers	
	Negative	Positive	Negative	Positive	Negative	Positive
Negative (0–4)	46 (23.8%)	16 (8.3%)	56 (29.0%)	6 (3.1%)	42 (21.8%)	20 (10.4%)
Positive (>4)	37 (19.2%)	94 (48.7)	62 (32.1%)	69 (35.8%)	26 (13.5%)	105 (54.4%)
	χ^2=36.250, df=1, p<.001, φ=.433 (+ by PEth) / (+ by AUDIT) = 83.9% Z=4.53, p<.001		χ^2=32.742, df=1, p<.001, φ=.412 (+ by EtG)/(+ by AUDIT) = 57.3% Z= 7.40, p< .001		χ^2=42.303, df=1, p<.001, φ=.468 (+ by 1 or both biomarkers)/(+ by AUDIT) = 95.4% Z=2.37, p=.018	

Table 3

Association between Self-Reported Prenatal Drinking Prevalence among Females and Prevalence Detected by PEth and EtG (*N*=193). Classification Tables and Statistics.

Quantity- Frequency of Drinking Self-report drinking history	**PEth Result**		**EtG Result**		**Positive cases on one or both biomarkers**	
	Negative	**Positive**	**Negative**	**Positive**	**Negative**	**Positive**
Did not drink	53(27.5%)	14(7.3%)	59(30.6%)	8 (4.1%)	48 (24.9%)	19 (9.8%)
Drank in the past 7 days	5(2.6%)	55(28.5%)	21(10.9%)	39(20.2%)	3 (1.6%)	57 (29.5)
Drank in the past 30 days	15(7.8%)	36(18.7%)	32(16.6%)	19 (9.8%)	12 (6.2%)	39 (4.7%)
Drank in the past 3 months	10 (5.2%)	5 (2.6%)	6 (3.1%)	9 (5.1%)	5 (2.6%)	10 (5.2%)
	χ^2=72.320, df=3, *p*<.001, Somer's d=.549 (+ PEth)/(+Q-F) = 87.3% Z=3.94, *p* <.001		χ^2=40.568, df=3, p<.001, Somer's d=.382 (+ EtG)/(+Q-F) = 59.5% Z=6.78. *p*<.001		χ^2=65.179, df=4, *p*<.001, Somer's d=.517 (+ by 1 or both/ + by Q-F) =99.2% Z=0.825, *p*=.409	

Note: Symmetric form of Somer's d

Table 4

Comparing Positive Self-Report with Positive Biomarker Data (PEth and EtG) (*N*=193)

	Self-Report AUDIT^	Positive By 1 or Both biomarkers	Difference in Positive Cases Detected by Self- Report	Self-Report Q-F	Positive By 1 or Both Biomarkers	Difference in Positive Cases Detected by Self- Report
Negative	62 (32.1%)	68 (35.3%)		67 (34.7%)	68 (35.2%)	
Positive	131 (67.9%)	125 (64.8[a]	+6 (4.8%)	126 (65.3%)	125 (64.8%)[b]	+1 (0.8%)

^AUDIT positive: >4;

[a]Z= .664, *p*=.507

[b]Z= .103, *p*=.918

Table 5

Positive and Negative Alcohol Use Case Detection Results for Two Biomarkers (PEth and EtG) Compared with Two Self-Report Measures (AUDIT and Quantity/Frequency in the Past 90 days) as the Standard

	1 or Both biomarkers	
	Positive (≥8ng/ml)	**Negative (<8ng/ml)**
A. On 1 or Both Self-Report Measures		
Positive	112 (58.0%) (true positives)	28 (14.5%) (false negatives)
Negative	*n*=13 (6.8%) (false positives/likely deniers)	*n*=40 (20.7%) (true negatives)

	On Both biomarkers	
B. On both Self-Report Measures	**Positive (≥8ng/ml)**	**Negative (<8ng/ml)**
Positive	55 (28.4%) (true positives)	62 (32.1%) (false negatives)
Negative	6 (3.1%) (false positives/likely deniers)	70 (36.3%) (true negatives)

Z-test of proportions comparing positive on 1 or both biomarkers (64.8%) to positive on 1 or more self-report measures (72.5%) : Z=1.630, *p*=.103 based on A portion of table.

Table 6

Sensitivity and Specificity of Alcohol Use Biomarkers: Detection by individual test and with combined results by time period measured

	Sensitivity	Specificity	Positive Predictive Value (Yield)	Accuracy
PEth *				
7 days	0.9167	0.5865	0.5000	0.6891
90 days	0.7214	0.8302	0.9182	0.7513
EtG **				
7 days	0.6500	0.7293	0.5200	0.7047
90 days	0.5071	0.9245	0.9467	0.6218
Positive by 1 or both biomarkers				
7 days	0.9500	0.4887	0.4560	0.6321
90 days	0.8000	0.7547	0.8960	0.7876

* Measured in blood spots

** Measured in fingernail clippings

Table 7

Summary of Associations Among Biomarker Results and Self-Reported Drinking over the Past Three Months

Variables	φ^2 (strength of association*
PEth vs AUDIT	.187
EtG vs AUDIT	.170
PEth vs EtG	.154
PEth vs Q-F	.301
EtG vs Q-F	.146
1 or both biomarkers vs 1 or both self-report	.268
Both biomarkers vs Both Self-Report	.169

*All $p < .001$