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Estimating Driver Risk Using Alcohol Biomarkers, Interlock BAC Tests and Psychometric Assessments: Initial Descriptives

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Abstract

Aim—To identify alcohol biomarker and psychometric measures that relate to drivers' blood alcohol concentration (BAC) patterns from ignition interlock devices (IIDs).

Design, Setting, Participants, Measurements—In Alberta, Canada, 534 drivers, convicted of driving under the influence of alcohol (DUI), installed IIDs and agreed to participate in a research study. IID BAC tests are an established proxy for predicting future DUI convictions. Three risk groups were defined by rates of failed BAC tests. Program entry and followup blood samples (n=302, 171) were used to measure phosphatidyl ethanol (PETH), carbohydrate deficient transferrin (%CDT), gamma glutamyltransferase (GGT) and other biomarkers. Program entry urine (n=130) was analyzed for ethyl glucuronide (ETG) and ethyl sulfate (ETS). Entry hair samples were tested for fatty acid ethyl esters (FAEE) (n=92) and ETG (n=146). Psychometric measures included the DSM-4 Diagnostic Interview Schedule Alcohol Module, Alcohol Use Disorders Identification Test (AUDIT), the Timeline Followback (TLFB), the Drinker Inventory of Consequences (DRINC), and the Temptation and Restraint Inventory (TRI).

Findings—Except for FAEE, all alcohol biomarkers were significantly related to the interlock BAC test profiles; higher marker levels predicted higher rates of interlock BAC test failures. PETH, the strongest with an overall ANOVA F ratio of 35.5, had significant correlations with all nine of the other alcohol biomarkers and with 16 of 19 psychometric variables. Urine ETG and ETS were strongly correlated with the IID BAC tests.

Conclusions—The findings suggest several alcohol biomarkers and assessments could play an important role in the prediction and control of driver alcohol risk when relicensing.

Keywords

alcohol; driver; ignition interlock; biomarkers; assessment; DUI; phosphatidyl ethanol (PETH)

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INTRODUCTION

Alcohol-related Risk on the Roadways

In the United States, alcohol use is associated with the road death of approximately 17,000 people annually. Annually, over the past 10 years, 21–22% of all fatal crashes have had a driver with a BAC (blood alcohol concentration) of more than .08 g/dL (the USA legal limit) [1]. Alcohol ignition interlocks (IIDs), which require a breath test before an engine start, were devised to prevent alcohol-impaired driving by requiring a driver convicted of DUI (driving under the influence of alcohol) to blow a low BAC air sample (usually set to lock the ignition at .02 – .04 g/dL) before a car can be started.

Interlocks have been studied in North American for 20 years. Ten studies with different subgroups and durations show a 40 to 90% reduction in recidivism while the IID is installed on the vehicle [2;3;4]. A meta-analysis by Willis, Lybrand, and Bellamy [5] estimated that IIDs reduced the relative risk of DUI recidivism by 64%. Once the IID is removed from the vehicle, recidivism increases to control rates.

Interlock BAC Test Patterns

In addition to blocking vehicle starts by a driver with an elevated BAC, the IID also logs a cumulative record of BAC tests. Studies of the IID BAC test records have been reported on 2000+ DUI offenders in Alberta, Canada (1995–1999 [6,7,8]), 7500+ offenders in Quebec, Canada (2000–2003 [9]), and 7000+ offenders in New Mexico (2003–2008). This data from over 16,000 DUI offenders show a consistent pattern of behavior in which the rate of positive (and generally locked out/failed) BAC tests in the IID record reliably predicts post-interlock repeat DUI. That is, attempts to start a car with positive BAC predict subsequent recidivism (after IID removal). The positive BAC tests occur most frequently during the first start up of the day (7 to 9 AM on working weekdays, 10 AM to noon on weekends) and likely reflect drinking the night before resulting in a BAC that has still not fallen below .02 g/dL by morning. The morning pattern was confirmed in Texas with another 11,000 offenders providing 20 million additional tests [10]. In all three sites, the most vehicle starts Monday-Friday occur around 5 PM.

Alcohol Biomarkers for Triangulating Driver Risk

Additional predictors of driver alcohol-related risk are still warranted for forensic purposes. The IID is a vehicle sanction; others are permitted to drive the car and, possibly, contribute breath-test results to the log file. More importantly, some high-risk drivers defy the IID requirement and drive cars without interlocks. Alcohol biomarkers can provide driver-specific information. While biomarkers seem to have not had systematic use in North America as an aid in road safety, they are increasingly used in Europe for driver re-licensing decisions.

In North America, biomarkers are most commonly used to supplement diagnostic assessments among alcohol-dependent patients participating in treatment or in clinical trials [11]. Because clinical diagnosis is part art, part science, using it as a criterion for validating markers is unsatisfying. There is no gold standard in the clinic, but interlock data can provide a useful high-sensitivity criterion. Together, alcohol biomarkers and interlock BAC test profiles may prove to be useful independent methods for quantifying the risk posed by convicted DUI offenders.

Indirect Markers: CDT, GGT, MCV, ALT, AST—The indirect alcohol markers primarily reflect organ responses to repeated ethanol exposure. The most widely used are carbohydrate deficient transferrin (CDT) and gamma glutamyltransferase (GGT), both of

which can be measured in serum for several days to several weeks after high levels of regular drinking. GGT is dependable, widely used, and inexpensive but less specific than CDT; GGT can be elevated for reasons having to do with hepatic or biliary disease unrelated to alcohol [12]. GGT was reported to be elevated in one-fourth to one-half of those arrested for alcohol-related driving infractions [13].

Regarding CDT, transferrin is a glycoprotein made in the liver that transports iron throughout the body. Each molecule has several carbohydrate chains with sialic acid end groups, some of which are lost after heavy drinking. As heavy drinking progresses, more end groups are deficient in their carbohydrate residue. The percent deficiency (%CDT) renders it a very specific alcohol exposure marker. Consumption of five or more drinks per day (60 g ethanol), for a week or more, is widely cited as sufficient to elevate CDT. Age-related or gender-related factors may affect CDT measurement [14]. Among the widely used indirect markers, macrocytic (red cell) volume (MCV), although moderately specific to ethanol, is far less sensitive than other markers.

Several European nations include indirect alcohol biomarkers, especially CDT, GGT, and MCV as part of their re-licensing decisions. In Luxembourg, Appenzeller, Schneider, Maul, and Wennig [15] found that drivers with arrest BAC levels in the ranges of .25–.30, .30–.35 and .35+ g/dL had CDT levels higher than 3% at rates of 22%, 47% and 67% of the sample, respectively. Gilg, Bucholtz, and Huth [16] in Germany found 24% of drivers arrested for DUI had elevated CDT, 26% had elevated GGT, but only 7% had both. The method of combining and the types of markers can improve sensitivity or specificity. Korzec et al. [13] found 74 and 82% of his driver sample were heavy drinkers based on the biomarker evidence, but a dependence diagnostic instrument identified just 4% as alcoholic. A Norwegian study [17] found that GGT was more likely to be elevated in arrested males older than age 29. GGT levels were at least twice as high in those with arrest BACs ≥ .25 g/dL than in those between .05 and .15 g/dL. There is no standard protocol for selecting biomarkers or cutoff levels. Sweden, for example, has a medical review program for DUI offenders that links reductions of alcohol markers to successful completion of their interlock program [18;19]. Relicensing decisions are made using GGT, CDT, and MCV but also the nonspecific liver enzymes AST (aspartate aminotransferase) and ALT (alanine aminotransferase) in a Boolean “OR” combination to maximize sensitivity. Specificity of driver fitness decisions are improved by looking for markers at or above the 97.5 percentile of national mean population levels. Bjerre and colleagues have reported that this monitoring program reduces sick leave and hospital utilization [20].

Direct Markers: PETH, FAEE, ETG, ETS—Markers that directly reflect acute alcohol ingestion have had little study with DUI drivers. Unlike many indirect markers that reflect end-organ response to alcohol, the direct markers are both very specific and very sensitive.

This class of markers includes phosphatidyl ethanol (PETH), a membrane phospholipid found in the erythrocyte fraction of whole blood and formed only in the presence of ethanol [21]. PETH’s half-life is about 4 days, and no substances besides alcohol cause positives on PETH [22;23;24]. Hartmann et al. [25] reported that PETH is detectable in blood for 2 weeks after sustained ethanol intake.

Minor pathways of ethanol metabolism synthesize ethyl glucuronide (ETG) (via conjugation with glucuronic acid) or ethyl sulfate (ETS) (via sulfation). ETG and ETS can be found in serum, urine, or hair, and ETG concentrations are 1/1000 that of ethanol. Both ETG and ETS can be measured up to 2 days in the urine [26] after dosing to .08 g/dL, or longer in clinical samples of heavy drinkers [27]. Wurst and others [28;29] suggest that ETS may be a more stable indicator of ethanol exposure than ETG, as ETS is less likely to be altered by

bacteria if there is a urinary tract infection at the time of sampling [30]. Kip et al. [31] reported that in the emergency room, ETG and PETH are more reliable indicators of drinking than the Alcohol Use Disorders Identification Test (AUDIT).

Fatty acid ethyl esters (FAEE), another direct alcohol marker found in both serum and hair, has shown promise as an indicator of alcohol use proclivity [32]. Pragst and Yegles [32] reported that fatal alcohol crash victims had an average combined FAEE level 10 times higher than social drinkers. A cutoff of 0.5 ng/mg is thought to distinguish moderate to heavy drinking. To detect high-risk drinkers for diagnostic purposes, the investigators suggest using the combined FAEE cutoff value of 1.0 ng/mg and/or a positive hair ETG result of 25 pg/mg [33]. Kintz et al. [34] recommended 50 pg/mg cutoff for judging hair ETG as high.

Significance

The convergence of information in interlock BAC test records, alcohol psychometric assessments, and alcohol biomarkers holds promise for objectifying the often-difficult decisions related to driver licensing. This research study was designed to examine how well these indicators converge, whether they can be usefully combined, and to determine levels of the marker types most associated with high-risk BAC profiles in the interlock record. This initial paper provides simple descriptive summaries and cross-relationships between the markers, the interlock BAC tests, and the psychometric measures. Alcohol dependence is not a precondition for DUI; better tools can improve the evaluation of public risk exposure to drinking drivers.

METHODS

This research was conducted by the Pacific Institute for Research and Evaluation (PIRE) in the Washington DC area; subjects were recruited in Alberta, Canada (province population ~ 3.3 million), at the Guardian Interlock Systems (GIS) service center in Edmonton (city population ~ 730,000). This project—a three-partner collaboration of the Alberta Transportation Safety Board (ATSB) of the provincial Transport Ministry, GIS, and PIRE—is the second interlock research collaboration since 1994 for these organizations.

DUI offenders from central Alberta who want an IID installed do so at the GIS service center in Edmonton. The interlock business and this interlock research were completely separate activities managed by different people. For DUI offenders participation was voluntary, confidential, and had no bearing on the offender's relationship with the government. All subjects signed informed-consent documents, and all research staff completed the National Institutes of Health training protocols for human subjects' research. This research was reviewed and approved annually by the PIRE East IRB under FWA00003078. Intake proceeded continuously as prospective subjects became available between the dates of December 2003 and May 2007.

Procedures: Subjects and Measures

At the time of IID installation, 942 DUI offenders were asked to participate in the research: 58% of first offenders (n=346) and 53% of multiple offenders (n=183) agreed. Among multiple offenders, 125 were second offenders, and 58 had three or more prior DUI convictions; 6 could not be matched. The "look-back" period for defining prior offenses in Alberta driver records is 10 years. The 534 participants were 87% male, mean age 38.7 ±11.5 ranging from ages 19 to 74. Participants reported Caucasian ancestry (91%) with the remaining 9% split among nine ethnic categories, none more than 2.5%. The most prevalent income group was the highest (24%), earning more than $90,000 Canadian Dollars (CDN)

per year (likely reflecting Alberta's booming oil industry); Canada's 2004 median income was $70,000/year. Just 44% of participants lived in or near Edmonton; the others were from rural towns or farms (39%), and 16% were from small urban areas beyond Edmonton.

Participants reported on general demographics, the Timeline Followback (past 30 days of drinking) [35], DSM-IV (Diagnostic and Statistical Manual IV) Module R (alcohol abuse and dependence) via the Computerized Diagnostic Interview Schedule (C-DIS) interview [36], the (AUDIT) [37], the Drinkers Inventory of Consequences (DRINC) [38], and the Temptation and Restraint Inventory (TRI) [39]. The research coordinator, who administered the C-DIS, had trained on C-DIS during a week in St. Louis with the Washington University staff. Thirty-nine percent of the study subjects met DSM-IV criteria for alcohol dependence, 12% met criteria for alcohol abuse. Nearly half (49%) were either negative or could not be definitively diagnosed by the software; 13% (69 of 536) were fully negative for both diagnoses (e.g., without inconclusive diagnoses).

Most subjects were asked to provide blood samples twice, both at the start and near the end of their IID requirement. The lag between the initial and subsequent blood samples was about 8 months (mean=8.4 and median=7.8). About 55% of those asked provided a second blood sample; the drop off may have reflected the inadequacy of the participant fees relative to the time burden for reporting to the blood lab.

After the research began, informed consent was adjusted and approved so hair samples and urine samples could be collected. Table 1 shows the count of different markers that were measured by source collected and whether they were baseline or followup samples. The smaller number of urine (prefix "u") and hair (prefix "h") samples reflects their late addition to the protocol. Samples for PETH, CDT, uETG, and uETS were held at −80C for long-term storage, and then were batched and packed in dry ice for shipment. Hair was sampled from the scalp near the inion, packed in aluminum foil and shipped for measurement of hFAEE and/or hETG.

Analytic Methods—Alcohol Markers

Heparinized whole blood was collected, stored at −80C, and shipped in three batches over 4 years of sample collection. In Lund, Sweden, in the laboratory of Drs. Christer Alling, Steina Aradottir, and Therese Hansson, phosphatidyl ethanol was extracted and measured by high performance liquid chromatography (HPLC) via published protocols [23;24;40;41]. The limit of quantitation (LOQ) was 0.22 μmol PETH/L; 31.5% of baseline samples and 40.7% of the followup samples were below the LOQ. Samples were analyzed with control samples on two levels (low control 0.63 μmol/L, and high control 0.82 μmol/L) as a quality check above and below typical clinical cutoff values of 0.70 μmol/L. High variability is found below 0.70 μmol/L.

CDT was measured in the laboratory of Dr. Martin Javors at the University of Texas in San Antonio with the use of Axis-Shield (Oslo, Norway) immunoassay "%CDT" kits, which measure the percentage of total transferrin in serum that consists of asialo-, monosialo-, and disialo-transferrin isoforms. Javors determined that the Axis-Shield kit has high-test/retest reliability through analysis of 197 human samples randomly selected from approximately 20% of all samples to verify reliability. Results showed $r^2 = .78$, with x and y intercepts not statistically different from zero [42].

ETG and FAEE in hair [32] were determined, respectively, at the laboratories of Dr. Michel Yegles at the University of Luxembourg and Dr. Fritz Pragst at Humbodlt University in Berlin, Germany. When there was sufficient material, a sample of hair was used for both measurements. Methods for extraction and analysis of ETG in hair are found in Yegles et al.

[33]. The analytic procedures for FAEE extraction and measurement in hair were documented in Pragst et al. [43].

Urine samples, collected in years 3 and 4, were frozen and shipped for measurement of ethyl glucuronide and ethyl sulfate at the United States Drug Testing Laboratory (USDTL), a commercial facility near Chicago, Illinois. The specimens were analyzed for creatinine and ethanol; uETG and uETS determinations were performed using standard protocols on an API 2000 high-flow liquid chromatographic-tandem mass spectrometry (LC-MS/MS) (Applied Biosystems, Foster City, CA, USA). The limit of detection for uETG and uETS was 38.7 ng/mL and 7.2 ng/mL, respectively. High values were clipped at 10,001 ng/mL.

The measurement of GGT, AST, ALT, and MCV was conducted with standard clinical chemistry protocols at the Dynacare Kasper Medical Laboratory in Edmonton promptly following blood collection.

Interlock Data

The IID installation duration and vehicle usage vary across subjects. To account for differences, interlock usage (tests taken) is set as a denominator and failed interlock BAC tests are expressed as a rate relative to all tests taken by each subject. Study subjects used the interlock car an average of 277 days; subjects performed a mean 2800 BAC tests during the study. This reflects a median of 9.9 (mean 10.7) BAC tests per day that the car was used, reflecting a mix of startup tests and the required running retests. The overall mean number of BAC tests during the full time the IID was installed was 9.8 tests per day of which 5.8 were startup tests; accordingly, 63% of all tests were startup tests. The target for analysis is startup tests because startup tests have a higher density of positive BAC than retests (e.g., all retests must be preceded by a passed startup test). In Alberta, the ignition locks out at .04 g/dL

Statistical Methods

All analyses were done with SPSS ver. 15. Procedures include order and interval correlations, one-way analyses of variance (ANOVAs), and when appropriate square root and log normalizing transformations. All tables are based on raw values to allow readers to compare levels across studies.

RESULTS

Results are organized to show (1) alcohol biomarker interrelationships, (2) the relationship between alcohol biomarker and interlock BAC test results, (3) the relationship between psychometric or diagnostic assessments and the interlock BAC test results, and (4) the relationship between biomarkers and the psychometric measures.

Marker Interrelationships

Table 2 shows biomarker cross correlations calculated for both Pearson (interval correlations on the right above the diagonal) and Spearman (ordinal correlations shaded on the left below the diagonal tests). PETH levels were significantly correlated with all other blood markers in both Pearson and Spearman at $P<.0005$. The exception to the generally significant correlations between PETH and other markers was its Pearson correlation with hair ETG. FAEE showed weak positive correlations using Pearson and strongly significantly correlations using Spearman. Spearman correlations are not influenced by outliers or other departures from distributional normality, as is Pearson's test.

Statistical significance of correlations can be a misleading criterion, especially when there are several hundred xy pairs. With large samples, even small correlations can be statistically significant. The correlation itself, the r value, is an effect size indicator for judging the strength of the relationship between two variables. Although all the markers have positively skewed distributions, strong correlations in both Pearson and Spearman minimizes the possibility that a few outliers account for spurious relationships or that the effect sizes are biased. The strongest relationships for PETH are with GGT, %CDT, uETG, and uETS, with r values in the range of 0.4 for both types of correlations. The sensitivity of PETH is underscored by its strong relationship with urine ETG (r>.4) and urine ETS, both of which, like PETH, are direct markers that reflect recent drinking. We found, as others often report, there was no correlation between GGT and %CDT.

Interlock BAC Measures

Interlock results were aggregated at 2-month intervals to examine change over time. At the group level, the mean vehicle use over time during each of three 2-month intervals varied very little for either first-time DUI offenders or multiple offenders. The (mean, median) vehicle startup tests were stable, in each 2-month period: 0–2 months (355, 308), 2–4 months (345, 288) and 4–6 months (346, 288). While driving per se did not change, there were reductions in the rates of positive BAC tests across those intervals. For example, relative to BAC test rates during months 0 to 2, rates of positive BAC tests in months 4 to 6 declined to about half (49% lower for first offenders, 45% lower for multiple offenders). Because total driving holds steady (as indicated by start tests), the decline in positive BAC tests suggests that over time interlock offenders learn to separate their drinking and driving. A similar finding reported in an earlier study [6] also showed a reduction over time in the proportion of all tests that were elevated. Is the decline in failed interlock BAC tests over time related to a decline in drinking, or just drinking and driving? A partial answer to this question comes from biomarker evidence.

Baseline and Followup Markers

Table 3 shows the initial and average 8 months later sample of the six markers that could be paired. In Table 3, the follow-up marker results end with a “2.” On the right of Table 3 are paired t statistics showing that only MCV (168 pairs) was significantly lower in the second sample (P=.014), but the mean levels of MCV of less than 91.25 are within the normal range. No marker, other than MCV, showed change from the first to the second samples. This failure to find much evidence of change in the drinking level may partly explain why, even though IID programs reduce impaired driving by an average of 64% during the installed period [5], control levels of recidivism resume once the IID is removed from the car. The alcohol biomarkers’ levels at the start and at follow up show little evidence that overall drinking declined. Program participants may be learning to alter drinking and driving without reducing overall drinking. There was no treatment intervention concurrent with the IID.

Biomarkers and Interlock BAC Fail Groups

Categorization of interlock BAC test rates into a small number of bins facilitates presentation of the results. Because ignition lockout rate (in Alberta when BAC ≥ .04 g/dL) is a discrete indicator of drinking control, the 136 participants who had zero lockouts are defined as one subset of the overall group and represent 26.8% of the sample. At the other extreme, the high-rate group was set by inspection of the data series. The rate interval of failed tests began to widen at about the 80th percentile, so the definition of the high rate group was set at a fail rate above .0145 (fail starts to all starts). There were 20.5% of the subjects above this cut. The remaining cases between the zero group and the high group define the middle group representing 52.8% of the total. In summary, the zero group

included n=136, a low group had n=268, and a high group had n=104. The total sample with useable interlock data was N=508.

The data in Table 4 show the descriptive summaries of initial biomarkers broken out by the interlock BAC categories. One-way ANOVA of these results, with Scheffe post hoc tests, shows that, with the exception of hair markers (hFAEE and hETG), there were differences (all at least P<.001) in which the high-BAC group was always unique. The overall F value is shown for each analysis and the subgroups are flagged with an asterisk.

To ensure that the strong significant relationships in Table 4 for all the blood and urine biomarkers and the interlock BAC groups were not a secondary consequence of skewed outliers in the biomarker data series, all markers were subjected to both square root and natural log transformations to force them into more normally distributed data series. The ANOVA and post hoc analyses of these transformed data determined that the statistical significance and the interlock subgroup separation were at least as strong as found with the raw data. Moreover, after log transformation of the strongly skewed hair ETG data, it also yielded a statistically significant split between the high to low BAC groups.

Most alcohol biomarker studies categorize responses as above or below some cutoff level. This is not the tactic adopted here because the subject population of DUI offenders is heterogeneous and overlaps a more socially normative drinking population. Accordingly, cutoff levels derived from clinical samples do not serve our purpose. The alcohol biomarkers are used here as a tool to characterize DUI drivers. The mean levels of markers for the high risk group shown in Table 4 could be used as cutoff estimates for other DUI risk studies. The biomarker means for the 3 interlock BAC subgroups matched our assumption that more BAC lockouts on the interlock would be associated with higher marker levels. To make this point graphically, a Z score (standard deviation [SD] unit) chart allows for direct comparison of markers by interlock group in a way that is free of underlying measurement units; figure 1 shows the breakout of the biomarker Z scores (mean=0, SD=1). All the biomarkers of the high BAC interlock group are much higher than the two lower risk groups.

Alcohol Assessments and Interlock BAC Fail Groups

The three interlock BAC test bins were evaluated against baseline psychometrics measures via ANOVA with Scheffe post hoc Scheffe tests to determine subgroup differences. Psychometric assessments shown in Table 5 include the full AUDIT, the AUDIT-C (the first three consumption items), four questions from the 30-day TLFB (maximum drinks in one day, total drinks in the month, longest abstinence period, longest drinking period); DRINC total score plus the five subscales (physical, interpersonal, intrapersonal, social responsibility, impulse control), the five basic subscales from the TRI are included (govern, restrict, emotion, preoccupation, concern); and DIS-C DSM-IV abuse and dependence are scored categorically as positive or negative (those that could not be definitively diagnosed as positive for abuse or dependence are scored as negative). The results show that, with the exception of the DSM abuse and dependence variables and two TRI variables, the rest of the assessments were significantly related in the predicted direction to the interlock BAC positive subgroups. In most cases, the Scheffe post hoc tests found the high-BAC interlock subgroup was uniquely different from the other two, and is shown in Table 5 with asterisks.

Alcohol Biomarkers and Alcohol Assessments

Although the primary focus of this paper is on the interlock BAC relationships, review of the bivariate correlations of the markers and the psychometric assessments is warranted as

these are commonly reported by others. The same assessment variables found in Table 5 were correlated with the markers shown in Table 4, and the results are found in Table 6.

The traditional markers—MCV, ALT, and AST—relative to the other biomarkers, correlate poorly with the self-report psychometric variables. Of all the psychometrics, the four TLFB variables were the most consistently correlated with biomarkers. The TLFB and AUDIT variables had the strongest correlations with the direct markers (PETH, FAEE, ETG, and ETS), whether measured in blood, hair, or urine. GGT and CDT were correlated less strongly, but nonetheless positively, with the TLFB and AUDIT measures.

PETH was strongly correlated with all but 3 of the 19 assessment variables. Hair ETG was well correlated with AUDIT and TLFB and with the DSM-IV dependence variable. In all cases, the TLFB variable of "longest abstinence" period was negatively correlated with the biomarkers, as it should be. The TLFB 30-day longest drinking and total drinks variables were, among all self-report assessments, the ones most strongly related to the markers with Spearman correlations as high as r=.56 and several with r>.40. The TRI subscales were not related to any biomarkers other than PETH. Other than ETG or ETS the DSM variables were unassociated with other biomarkers, much as they were unassociated with the interlock BAC risk bins.

Finally, because not all of the participants would give blood samples, we evaluated whether those who provided blood for analysis were different from those who did not. Subsets splits based on whether blood was provided were evaluated on the most consistent psychometric measures. Results from independent group t tests for AUDIT, TLFB, and DRINC scales showed that the blood donor and nondonor subgroups were either not different on those measures or, when different, the blood group had the higher risk. Based on these results, the blood donors are not a lower-risk subset of the total and therefore the results probably do not underestimate the biomarker levels of interlock-using DUI drivers.

DISCUSSION

The public risk exposure to alcohol-impaired drivers is significant. For example, nearly all U.S. states have drivers with 10–20 or more DUI convictions on their records. California alone has more than 300,000 drivers with three or more prior DUI convictions [44]. In the United States, there is a daily average of about 22 fatal crashes in which a driver's BACs was ≥.08 g/dL [1]. Our ability to deter drinking drivers is very limited, as is our ability to intervene effectively. Better, more objective, tools are needed to make licensing decisions.

This study tested the relationships of three categories of alcohol-risk measures. These included: nine alcohol biomarkers in three matrices (blood, urine, and hair), an average of approximately 2800 alcohol interlock BAC tests per vehicle reflecting about 8 months of driving, and self-report data captured on five standard psychometric assessments.

Interlock BAC test profiles reflect actual attempts to drive with an elevated BAC. Published biomarker cutoffs that have been used as criteria for making severity judgments in alcohol treatment populations may not be the appropriate ones for DUI samples. For example, the evidence in this paper shows PETH to be a strong correlate of BAC positive tests and IID lockouts. The mean ±SD for PETH of the high-risk group (shown in Table 4) is 1.45 ±1.17 μmol/L. Although this is significantly greater than, and more than twice the level of, the middle risk group, it is less than the 2.47± 2.2 found among alcohol-dependent patients reported by Hartmann et al. [25] or the 3.4 ± 2.6 μmol/L for outpatients reported by Aradottir et al. [40]. The clinical problem and the public roadway safety problem are not identical and the biomarker cutoff levels should not be identical.

PETH is a remarkably strong, general alcohol risk indicator. It is significantly rank correlated with all of the other alcohol biomarkers tested (Table 2), with 16 of 19 psychometric assessments (Table 6) and has an overall F ratio of 35.5 against the three interlock risk groups (Table 4). The strong relationships among the consumption measures (TLFB, AUDIT-C), the direct markers from blood and urine (ETG, ETS, PETH), and the interlock BAC tests makes considerable sense because all reflect actual drinking rather than indirectly reflecting possible disease status as do indirect markers. This constitutes support for using direct markers when assessing public health risk posed by alcohol impaired drivers. ETG, requiring only a urine sample, is appealing on a cost basis. PETH requires whole blood but may be the gold standard. The PETH results in this study are in accord with Wurst and colleagues's conclusion from clinical evidence that this marker is both highly specific and highly sensitive. That conclusion seems to hold as well for this mixed population of DUI offenders who vary widely on both drinking levels and dependence severities.

It is also noteworthy that the more traditional, indirect alcohol markers (GGT, ALT, AST, and MCV) and %CDT related less strongly to the psychometric assessments than did the direct markers. This does not have any particular implication for the adequacy of these markers for assessment of alcohol dependence, but it suggests the sensitivity of indirect markers is less adequate when the target to be estimated is recent consumption. Drinking indicated by the direct markers appears to be compatible with the 30-day TLFB and the 28-day AUDIT.

The salience of the FAEE and ETG markers in hair is more difficult to judge. There were fewer cases for analysis than for other markers, the variance was high, and there was no followup sample to judge within-subject stability. Nonetheless, the group means in Table 4 and Figure 1 for both hair markers formed a sequence from low to high that matched the low to high interlock BAC risk subgroups, and once log transformed, the hair ETG levels were significantly predictive of the interlock BAC groups. Also, from Table 2, the Spearman correlation of 62 pairs of hair FAEE and blood PETH was .521 ($P<.0001$). This is nearly identical to the $r=.527$ Spearman correlation of hFAEE and PETH reported by Wurst et al. [45] from 17 alcoholic inpatients.

The hair ETG marker was well associated with the TLFB, AUDIT, and AUDIT-C and had the strongest relationship to DSM dependence and abuse. Hair ETG did less well paired against other markers. The 92 pairs of hair ETG and hair FAEE had a weak but significant Spearman correlation $r=.27$ ($P=.007$). Hair ETG and urine ETG/ETS were not related by Spearman correlation.

Psychometric assessments require subject cooperation, yield potentially self-incriminating disclosures, and are expected to perform more poorly as risk indicators in nonresearch situations. In this study, all subjects were given signed confidentiality assurances. The reasonably good relationships between many alcohol self-report measures and the objective biomarker and interlock results might be different without those assurances.

The most widely used markers today are GGT and %CDT. Comment on their performance is warranted. As is evident in Table 4, both GGT and %CDT distinguished the three interlock risk groups well and did so with large F ratios. For the interlock high-risk group, the mean GGT was 91.6 U/L, and the high-risk group %CDT mean was 3.28%, both above widely used clinical cutoffs of 75 U/L and 2.7%, respectively. As expected, these two markers are not correlated with each other (via either Pearson or Spearman) and, therefore, probably discriminate different types of alcohol problems. In a panel of markers, it is beneficial if each test can provide unique rather than redundant information.

The Table 3 biomarker data show little evidence for change within subjects and suggest why IIDs are routinely found to only temporarily suppress re-convictions for impaired driving. It appears that overall drinking does not change while the IIDs are installed. The evidence for IID suppression of DUI convictions from more than 10 studies is very strong, and the evidence is equally strong that the effect is lost when the devices are removed. Because we know that the rate of failed tests declines during the period of installation even while the total number of tests taken holds steady, it seems evident that the offenders learn to separate drinking and driving without reducing drinking per se. Treatment interventions may be needed to change the behavior of some drivers. For DUI samples, motivational approaches [46] have had some success. Marques et al. [47] reported on a motivational approach with interlock using DUI offenders in Texas built around a structured intervention with provider and participant manuals [48;49]

Finally, when the last driver records were retrieved from Alberta in mid-2008, about 6% of the offenders who provided blood had later been reconvicted for DUI, not enough for conclusive analyses. A usual rate of repeat offense accumulation is 4 to 6% per year. By the end of 2010, 75 or more offenders will likely have been reconvicted, allowing for a more conclusive binary logistic regression and survival analyses.

Implications

Recent technological innovations bring promise that we can do a better job of managing alcohol risks on the roads. Monitoring drivers with ignition interlocks and monitoring alcohol consumption with biomarkers could remove some of the subjectivity in deciding which drivers warrant greater or lesser degrees of control. Few if any states or provinces in North America use alcohol biomarkers as a routine part of this driver license decision-making process, and only a few programs use the alcohol IID record as a criterion in relicensing decisions. Used by skilled treatment providers, and close monitoring by the authority, these tools may help improve public health and safety by bringing more and better science to practice.

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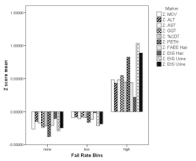

Figure 1.
Z score representation of 10 baseline alcohol biomarkers by fail-rate bins of elevated interlock BAC tests

Table 1

Alcohol biomarkers measured

Marker	Source/unit	Initial sample n=	Followup sample n=
Macrocytic volume (MCV)	Red cell fL	300	170
Alanine aminotransferase (ALT)	Serum U/L	302	171
Aspartate Aminotransferase, (AST)	Serum U/L	302	171
Gamma glutamyltransferase (GGT)	Serum U/L	302	171
Carbohydrate deficient transferrin (CDT)	Serum % isoforms to total	298	165
Phosphatidyl ethanol (PETH)	Whole Blood µmol/L	298	167
Fatty acid ethyl esters (hFAEE)	Hair ng/mg	92	0
Ethyl glucuronide (hETG)	Hair pg/mg	146	0
Ethyl glucuronide (uETG)	Urine ng/ml	130	0
Ethyl sulfate (uETS)	Urine ng/ml	130	0

Table 2

Initial alcohol biomarker correlations: Pearson (top right, above diagonal) and Spearman (shaded bottom left, below diagonal)

		MCV	ALT	AST	GGT	%CDT	PETH	Hair_FAEE	Hair_ETG	Urine_ETG	Urine_ETS
MCV	r	1	.05	.15(**)	.16(**)	.20(**)	.26(***)	.13	.13	.18(*)	.10
	n	300	300	300	300	297	297	62	101	129	129
ALT	r	−.02	1	.85(***)	.57(***)	−.03	.34(***)	.22	−.04	.29(**)	.24(**)
	n	300	302	302	302	298	298	63	102	130	130
AST	r	.08	.74(***)	1	.59(***)	.08	.41(***)	.26(*)	.02	.34(***)	.30(***)
	n	300	302	302	302	298	298	63	102	130	130
GGT	r	.03	.66(***)	.47(***)	1	−.02	.44(***)	.09	.18	.35(***)	.34(***)
	n	300	302	302	302	298	298	63	102	130	130
%CDT	r	.17(**)	−.10	.04	−.09	1	.39(***)	.10	.01	.17	.17
	n	297	298	298	298	298	297	62	101	130	130
PETH	r	.30(***)	.22(***)	.27(***)	.42(***)	.36(***)	1	.26(*)	.18	.41(***)	.38(***)
	n	297	298	298	298	297	298	62	101	129	129
Hair_FAEE	r	.19	.13	.19	.35(**)	.08	.52(***)	1	.01	.40	.03
	n	62	63	63	63	62	62	92	92	4	4
Hair_ETG	r	.12	.08	.19	.18	.07	.20(*)	.28(**)	1	.25	.43(**)
	n	101	102	102	102	101	101	92	146	42	42
Urine_ETG	r	.27(**)	.18(*)	.29(**)	.12	.29(**)	.47(***)	.40	.13	1	.90(***)
	n	129	130	130	130	130	129	4	42	130	130
Urine_ETS	r	.24(**)	.21(*)	.30(***)	.19(*)	.25(**)	.47(***)	.20	.14	.93(**)	1
	n	129	130	130	130	130	129	4	42	130	130

* Correlation is significant at P< 0.05 level (2-tailed).

** Correlation is significant at P < 0.01 level (2-tailed).

*** Correlation is significant at P < .0005 level (2-tailed).

Table 3

Initial and follow-up alcohol marker pairs

		Mean	N	Std. Dev.	r	t	df	Sig (2-tailed)
Pair 1	MCV	91.22	168	4.02				
	MCV2	90.85	168	3.78				
	MCV pairs				.88	2.49	167	.01
Pair 2	ALT	33.75	169	20.22				
	ALT2	34.59	169	26.40				
	ALT pairs				.78	−.66	168	.51
Pair 3	AST	28.36	169	13.46				
	AST2	28.02	169	16.42				
	AST pairs				.77	.42	168	.67
Pair 4	GGT	53.20	169	91.58				
	GGT2	51.38	169	76.41				
	GGT pairs				.88	.55	168	.58
Pair 5	%CDT	2.58	161	.91				
	%CDT2	2.56	161	1.04				
	%CDT pairs				.60	.38	160	.70
Pair 6	PETH	.70	163	.72				
	PETH2	.69	163	.78				
	PETH pairs				.65	.22	162	.82

Table 4

Initial alcohol biomarkers by interlock BAC fail-rate bins

	Fail rate bins	Mean	N	Minimum	Maximum	Std. deviation
MCV	None	90.21	75	84	97	3.33
	Low	90.90	152	79	101	3.86
	High*	93.16	58	84	105	4.20
F=10.7, df=2/282, P=.000	Total	91.18	285	79	105	3.93
ALT	None	28.87	75	10	103	16.31
	Low	30.43	154	11	107	17.62
	High*	42.31	58	11	241	36.99
F=7.1, df=2/284, P=.001	Total	32.42	287	10	241	23.09
AST	None	24.83	75	14	87	10.61
	Low	25.74	154	13	55	7.56
	High*	33.86	58	15	142	23.56
F=9.7, df=2/284, P=.000	Total	27.14	287	13	142	13.49
GGT	None	28.28	75	7	116	20.98
	Low	41.14	154	6	374	43.17
	High*	91.60	58	10	955	159.15
F=11.8, df=2/284, P=.000	Total	47.98	287	6	955	81.68
%CDT	None	2.50	73	1.3	5.49	0.84
	Low	2.65	152	1.06	10.27	1.08
	High*	3.28	58	0.81	10.92	1.56
F=8.6, df=2/280, P=.000	Total	2.74	283	0.81	10.92	1.17
PETH	None	0.43	74	0.22	2.67	0.51
	Low	0.61	151	0.22	3.28	0.61
	High*	1.45	58	0.22	5.49	1.17
F=35.5, df=2/280. P=.000	Total	0.74	283	0.22	5.49	0.83

	Fail rate bins	Mean	N	Minimum	Maximum	Std. deviation
FAEE hair	None	0.46	13	0.05	2.23	0.69
	Low	0.56	50	0.03	3.05	0.74
	High	1.11	22	0.07	5.79	1.57
F=2.7, df=2/82, P=.075	Total	0.69	85	0.03	5.79	1.03
ETG hair	None	43.02	29	0.7	357	76.56
	Low	49.95	78	0.7	487	76.64
	High	68.68	30	5.8	411	94.79
F=0.8, df=2/134, P=.435	Total	52.59	137	0.7	487	80.80
ETG urine	None	846.15	34	38.7	10001	2250.89
	Low	1095.43	65	38.7	10001	2489.12
	High*	5232.45	22	38.7	10001	4471.87
F=19.3, df=2/118, P=.000	Total	1777.57	121	38.7	10001	3299.00
ETS urine	None	465.44	34	7.2	10001	1744.10
	Low	625.35	65	7.2	10001	1940.78
	High*	3496.09	22	7.2	10001	3998.85
F=13.5, df=2/118, P=.000	Total	1102.37	121	7.2	10001	2632.96

*Subgroup significantly different from the others.

Table 5

Initial alcohol assessments by interlock BAC fail-rate bins

	Fail rate bins	Mean	N	Std. deviation
AUDIT total	None	7.76	135	4.86
	Low	9.00	268	5.09
Total F=15.3, df=2/504, P=.000	High*	11.34	104	4.90
AUDIT_C	None	4.27	135	1.79
	Low	4.59	268	1.69
Total F=11.1, df=2/504, P=.000	High*	5.29	104	1.54
TLFB max drinks one day	None*	6.87	120	5.69
	Low	9.04	243	6.90
Total F=8.5, df= 2/459, P=.000	High	10.37	99	6.12
TLFB total drinks	None	34.34	120	34.45
	Low	41.47	243	51.04
Total F=7.9, df=2/459, P=.000	High*	59.10	99	50.44
TLFB longest abstinence	None	9.86	120	7.38
	Low	10.28	243	7.08
Total F=5.7, df=2/459, P=.003	High*	7.49	99	6.04
TLFB longest drinking	None*	4.72	120	7.03
	Low	3.90	243	6.15
Total F=3.9, df=2/459, P=.000	High*	6.21	99	8.58
DRINC total score	None*	4.75	126	6.22
	Low*	7.28	248	8.70
Total F=18.7, df=2/473, P=.000	High*	12.44	102	14.01
DRINC physical	None	1.00	129	1.44
	Low	1.49	261	2.03
Total F=16.5, df=2/490, P=.000	High*	2.54	103	2.72
DRINC interpersonal	None	0.91	129	1.74
	Low	1.59	259	2.51
Total F=16.3, df=2/487, P=.000	High*	2.96	102	4.05
DRINC intrapersonal	None	0.85	133	1.77
	Low	1.58	263	2.76
Total F=13.3, df=2/496, P=.000	High*	2.80	103	4.12
DRINC social responsibility	None	0.61	132	1.33
	Low	0.81	257	1.50

	Fail rate bins	Mean	N	Std. deviation
Total F=10.9, df=2/489, P=.000	High*	1.61	103	2.52
DRINC impulse control	None	1.47	132	1.60
	Low	1.91	263	2.10
Total F=8.4, df=2/495, P=.000	High*	2.61	103	2.71
TRI govern	None*	6.52	133	5.01
	Low*	8.85	266	6.46
Total F=12.3, df=2/498, P=.000	High*	10.44	102	6.76
TRI restrict	None	11.26	133	7.32
	Low	11.86	265	7.43
Total F=2.4, df=2/497, P=.093	High	13.33	102	7.24
TRI emotion	None	6.19	134	4.11
	Low	6.97	267	4.83
Total F=12.5, df=2/500, P=.000	High*	9.31	102	6.01
TRI cognitive preocc	None	4.10	133	2.96
	Low	4.66	266	3.80
Total F=5.6, df=2/498, P=.004	High*	5.76	102	4.55
TRI concern drink	None	7.63	133	5.85
	Low	7.41	267	5.37
Total F=1.6, df=2/498, P=.192	High	8.59	101	5.79
DSM abuse	None	0.28	136	0.45
	Low	0.40	268	0.49
Total F=3.1, df=2/505, P=.047	High	0.38	104	0.49
DSM dependence	None	0.32	136	0.47
	Low	0.39	268	0.49
Total F=2.1, df=2/505, P=.126	High	0.45	104	0.50

*Subgroup significantly different from others

Table 6

Spearman correlation of initial alcohol assessments by initial biomarker level

	MCV	ALT	AST	GGT	%CDT	PETH	Hair_FAEE	Hair_ETG	Urine_ETG	Urine_ETS
Range (n) =	**264–300**	**266–302**	**266–302**	**266–302**	**263–298**	**263–298**	**89–92**	**140–144**	**125–130**	**125–130**
AUDIT total	0.09	0.05	0.10	.14(*)	.16(**)	.35(***)	0.11	.23(**)	.34(***)	.39(***)
AUDIT_C	.11(*)	0.08	.12(*)	.15(*)	.20(***)	.38(***)	0.14	.27(**)	.47(***)	.50(***)
TLFB max drinks 1 day	0.04	.13(*)	0.11	.19(**)	.13(*)	.30(***)	0.12	.23(**)	.31(***)	.34(***)
TLFB total drinks	.17(**)	.12(*)	.16(**)	.21(***)	.23(***)	.49(***)	.31(**)	.30(***)	.52(***)	.56(***)
TLFB long. abstinence	−.23(***)	−0.11	−.18(**)	−.17(**)	−.28(***)	−.44(***)	−.29(**)	−.22(**)	−.47(***)	−.52(***)
TLFB longest drinking	.25(***)	0.09	.13(*)	.13(*)	.23(***)	.41(***)	.33(**)	.29(**)	.46(***)	.48(***)
Drinc total score	0.06	0.01	0.09	.12(*)	0.10	.30(***)	0.16	.24(**)	.27(**)	.30(**)
Drinc physical	0.03	0.01	0.08	.12(*)	.16(**)	.32(***)	0.20	.30(***)	.21(*)	.23(**)
Drinc interpersonal	0.04	0.07	.15(*)	.13(*)	0.05	.25(***)	0.05	.20(*)	.19(*)	.21(*)
Drinc intrapersonal	0.07	0.02	0.09	.13(*)	0.08	.27(***)	0.14	0.15	.20(*)	.21(*)
Drinc social responsible	0.09	−0.02	0.07	0.05	0.09	.20(***)	0.09	0.07	0.17	.21(*)
Drinc impulse control	0.06	0.07	0.06	0.05	−0.00	.15(**)	0.06	0.10	.22(*)	.25(**)
TRI govern	0.08	−0.07	−0.05	0.07	.14(*)	.25(***)	0.12	.21(*)	0.11	0.13
TRI restrict	−0.01	0.01	−0.04	0.11	−0.01	0.09	0.03	0.15	−0.01	−0.00
TRI emotion	0.05	−0.03	−0.03	0.09	0.01	.24(***)	0.02	0.15	0.10	0.09
TRI cognitive preocc	.12(*)	−0.00	0.01	0.02	0.06	.22(***)	0.14	0.04	0.13	0.12
TRI concern drink	0.03	0.01	−0.03	0.01	0.02	0.08	0.07	0.04	−0.04	−0.07
DSM abuse	0.07	−0.01	−0.04	0.06	−0.00	0.04	0.06	.24(**)	0.11	0.11
DSM dependence	−0.01	0.04	0.07	0.09	.13(*)	.17(**)	0.01	.29(***)	.27(**)	.29(**)

*Correlation is significant at P< 0.05 level (2-tailed).

**Correlation is significant at P< 0.01 level (2-tailed).

***Correlation is significant at P< .0005 level (2-tailed)