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## Addictive Behaviors



Short Communication

## Biological markers of problem drinking in homeless patients

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## ABSTRACT

**Objective:** In the search for optimal biomarkers of excessive drinking, a central limitation has been the lack of sensitivity of measures. Many patients have apparently normal values of liver markers despite a considerable alcohol intake. This study aimed to test a novel combined indicator of alcohol drinking.

**Material and methods:** Concentrations of carbohydrate-deficient transferrin (%CDT),  $\gamma$  glutamyl transferase ( $\gamma$ GT), aspartate aminotransferase (ASAT), and mean corpuscular volume (MCV), together with a combined index of the %CDT and  $\gamma$ GT, the Antilla Index (AI), were studied in 104 homeless patients with ( $n = 87$ ) or without ( $n = 24$ ) problem drinking according to the Fast Alcohol Screening Test.

**Results:** Concentrations of all markers were significantly higher in the alcoholic patients than in other homeless patients. The best agreement between liver markers and self-reported status was found between the combined %CDT and  $\gamma$ GT index ( $\kappa = 0.61$ ,  $p < 0.001$ , sensitivity = 63%, specificity = 94%).

**Conclusions:** The combined AI is a relatively efficient measure of current drinking in homeless populations.

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## 1. Introduction

Alcohol problems contribute significantly to the global burden of illness, and are the 9th leading factor responsible for attributable mortality worldwide (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006).

In Western welfare states in particular, many homeless people have psychiatric illnesses, including alcohol and drug use disorders (Langle, Egarter, Albrecht, Petrasch, & Buchkremer, 2005; Nordentoft et al., 1997; O'Toole, Conde-Martel, Gibbon, Hanusa, & Fine, 2003). Homeless adults also have elevated mortality compared to the general population (Hibbs et al., 1994; Nordentoft & Wandall-Holm, 2003), and homeless alcohol abusers have high rates of alcohol-related brain damage (Gilchrist & Morrison, 2005).

A variety of biochemical parameters in circulation are altered in problem drinkers, but none has so far provided adequate diagnostic accuracy to discriminate between problem drinkers and non-drinkers or asymptomatic drinkers (Allen & Litten, 2003; Hietala, Koivisto, Anttila, & Niemelä, 2006). In a study of homeless patients seeking treatment, self-reported alcohol problems were correlated with  $\gamma$ GT, alanin

aminotransferase, and mean corpuscular volume (Hesse & Thiesen, 2007).

A sensitive biomarker of drinking problems may be attractive for several reasons. A sensitive indicator may be used for screening purposes among people who are reluctant to disclose a drinking problem. This may be the case, for example, in child custody cases or for airline pilots or medical doctors. Secondly, precise indicators may be used to provide patients with alcohol problems with more accurate information about their livers' current state. Personal feedback about the somatic effects of drinking can be a motivational factor in problem drinkers (Allen, 2003). When biomarkers lack sensitivity, there are two obvious explanations: one is that the specific biomarker actually lacks sensitivity, but the other is what most patients are told: "The numbers are fine". That is, the patient's body is unaffected by the alcohol intake. However, the other explanation is that the specific biomarker is simply inadequate as a marker of drinking.

Recently studies have suggested the use of marker combinations, which could improve assay sensitivity without sacrificing specificity (Hietala et al., 2006). A combined index using  $\gamma$ -glutamyltransferase ( $\gamma$ GT) and carbohydrate-deficient transferrin (CDT) appears to be elevated in a higher percentage of alcoholics than either  $\gamma$ GT or CDT alone (Hietala et al., 2006). In the following, we shall refer to this particular marker combination as the Antilla Index (AI). The AI is a promising indicator of problem drinker status with both a high sensitivity and a high specificity.

In order to evaluate the accuracy of diagnostic tests, it is important to know if both tests and empirically derived cut-offs remain effective

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across samples with different characteristics. For the AI, only the original article (Anttila, Jarvi, Latvala, Blake, & Niemela, 2003) and a single replication have been published (Hietala et al., 2006). The cut-offs from these studies have not been tested in any other samples.

## 2. Methods

### 2.1. Patients

The patients in the sample were 111 homeless patients referred for treatment at the Health Team for the Homeless in the City of Copenhagen. Of all patients, 19% were women, and the mean age was 43.4 (range: 23 to 74). In terms of referral, 44% were either referred for or diagnosed with an alcohol-related disorder, 6% were referred for a drug use disorder, 19% were referred for a psychiatric condition, and 41% were referred only for somatic conditions. In terms of homelessness, the patients varied widely. Some had an apartment but were unable to stay in it, many used shelters and other forms of temporary accommodations, and several used different forms of housing at different times.

Of all patients, 78% scored 3 or more on the FAST, indicating the presence of alcohol problems. Other substance use was uncommon with the exception of tobacco and cannabis use: 44% were regular cannabis users, and 74% were daily smokers.

### 2.2. Procedure

The subjects for the study were all patients from Health Team for the Homeless in the City of Copenhagen, a team providing health services approximately corresponding to those provided by general practitioners. Data were collected as part of routine clinical care, either by one of the team's four nurses or by the team's physician, H. T.

A life-history interview was conducted using a timeline to assess length of heavy drinking and drug use. The life-history interview was based on the timeline follow-back method (Fals-Stewart, O'Farrell, Freitas, McFarlin, & Rutigliano, 2000), but used whole years instead of days, and was developed for the present clinical setting. It has not been validated in research.

### 2.3. Subjects

A total of 111 patients had complete data and could be included. The majority of patients were men (81%), and the mean age was 43.4 years (range: 23 to 74). The most common reason for referral was alcohol problems (43%), followed by somatic complaints (41%). Psychiatric reasons (including behavioural problems) were cited for 19%, and illicit drug abuse for 6%.

#### 2.3.1. Measures

**2.3.1.1. Self-reported drinking.** The FAST (Hodgson, Alwyn, Bev, Thom, & Smith, 2002) is a four-item self-report measure of risk drinking. The FAST is derived from the AUDIT, and was derived by identifying the items that best discriminated patients with alcohol problems. It has been found to effectively identify problem drinkers in a range of settings. The authors of the instrument indicated that a cut-off of three or more effectively identified problem drinkers across three types of somatic samples. For this sample, the internal consistency of the FAST was Cronbach's  $\alpha = 0.82$ .

The CAGE (Ewing, 1984) is a four-item self-report measure of alcoholism. The name CAGE is an acronym for the four questions in the instrument: "Have you ever felt you should cut down on your drinking?" "Have people annoyed you by criticizing your drinking?" "Have you ever felt bad or guilty about your drinking?" "Have you ever had a drink first thing in the morning (eye-opener) to steady your nerves or to get rid of a hangover?" For this sample, the internal consistency of the CAGE based on tetrachoric correlations was Cronbach's  $\alpha = 0.94$ .

**2.3.1.2. Liver markers.** The liver markers were analyzed by the Copenhagen General Practitioners' Laboratory (CGPL) for  $\gamma$ GT, MCV, and ASAT, and by The Danish Institute for Serum Analyses (SSI) for %CDT. The CGPL analyzed the markers according to the IFCC (Bergmeyer, Horder, & Rej, 1986), and the SSI referred to International Union of Pure and Applied Chemistry code NPU10000.

The cut-offs in the liver assays were as follows:  $\gamma$ GT, men 80 U/l, women 50 U/l; %CDT, 2.6; MCV, 96 fl; AST, men 50 U/l, women 35 U/l (Hietala et al., 2006). For the Antilla index (AI), we used the cut-offs derived by Hietala and colleagues based on Receiver Operant Characteristic Curves (4.18 for men and 3.81 for women). The AI is calculated as  $AI = 0.8 \ln(GT) + 1.3 \ln(\%CDT)$ .

#### 2.3.2. Statistical analyses

We used Cohen's kappa as a measure of chance-corrected agreement. We also report sensitivity and specificity of each liver marker. For Cohen's kappa, we calculated *p*-values based on the Pearson  $\chi^2$  statistic. In order to test for multiple significance tests, we applied Bonferroni adjustment.

## 3. Results

### 3.1. Validity of the FAST

We compared subjects who were referred for an alcohol-related problem with patients who were referred for another type of problem. Of 48 patients referred for an alcohol-related problem, 1 patient (2%) scored below the cut-off of 3 or more on the FAST. Of 63 patients referred for a non-alcohol-related problem, 63% scored above the cut-off on the FAST. The  $\chi^2$  statistic for the difference in proportion was statistically significant ( $\chi^2(1) = 19.05, p < 0.0001$ ). Further, we tested the correlation between the FAST and the CAGE (Ewing, 1984). The correlation was 0.71 ( $p < 0.001$ ).

Considering that being referred for a non-alcohol problem does not rule out having an alcohol problem, we considered this preliminary evidence of the validity of the FAST, as it correlated well with an alternative self-report measure of alcohol problems and accurately identified patients referred for alcohol problems.

### 3.2. Concordance between self-reported drinking and liver markers

The concordance between self-reported drinking and liver markers is shown in Table 1. The lowest concordance was found for MCV (kappa = 0.16, NS). The best concordance was for the AI, where the kappa was 0.61. Except for MCV, all measures had specificity above 90%. Sensitivity varied substantially (33 to 63%). The best sensitivity was found for the AI.

**Table 1**  
Agreement between liver markers and FAST-positive.

		Negative	Positive	Cohen's $\kappa$	<i>p</i>	Sensitivity	Specificity
%CDT	Negative	22	2	0.41	<0.0001	45%	93%
	Positive	34	53				
$\gamma$ GT	Negative	19	5	0.35	<0.0001	39%	96%
	Positive	23	64				
AI	Negative	19	5	0.61	<0.0001	63%	94%
	Positive	11	76				
MCV	Negative	16	8	0.16	NS	30%	86%
	Positive	37	49				
ALAT	Negative	20	3	0.25	0.0027	33%	94%
	Positive	40	46				

Note: NS: Not significant.

### 3.3. Descriptive statistics stratified by hepatitis C status

Because the presence of hepatitis C virus could potentially influence the findings, we analyzed the median values by hepatitis C antibody status. In general, hepatitis C antibody status had little impact on biomarkers. Patients with positive hepatitis C status and positive FAST status had higher  $\gamma$ GT than patients with hepatitis C and FAST negative status (Mann Whitney Z: 2.02,  $p = 0.04$ ). Elevations in %CDT did not differ by hepatitis C status.

## 4. Discussion

The Antilla Index [AI] was the most precise measure of drinking problems in this sample. Unlike other measures of alcohol problems, only a minority of patients with self-reported alcohol problems have normal-range values on the AI. This has potential clinical importance, because patients who have drinking problems may receive the incorrect information that their livers are unaffected by their drinking if traditional markers are used. Even the %CDT has low specificity.

A liver marker that possesses reasonable sensitivity may be useful for both clinical and research purposes. The ability to use a single figure with pre-defined cut-off values allows researchers to compare findings, and clinicians to offer simple and unambiguous feedback to patients. However, it is important to acknowledge that even with this improvement in biomarker validity identification is not perfect. With a specificity of 63%, a substantial proportion of drinkers are not identified by the biomarker.

The present sample differs from samples in which liver markers have traditionally been studied. The patients in the study were at a homeless clinic, and presented with a variety of both psychiatric and health problems. This would include a high number of stressors, a poor nutritional status, and the presence of hepatitis C virus antibodies in a subset of the patients. The findings indicate that the AI is robust even with a sample where a number of other factors could potentially influence liver markers.

Some limitations must be acknowledged. Representativeness of homeless patients is difficult to estimate because the size of the background population is constantly changing and itself difficult to ascertain. Also, data were collected as a part of regular clinical practice. Although we planned to assess all patients as early as possible during their treatment, immediate concerns were prioritized over screening for alcohol problems, and sometimes staff had to spend some time building trust with patients before the screening could proceed.

In conclusion, the AI was a robust measure of alcohol problems, even in this group of homeless persons.

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The study was funded through intramural sources from the Centre for Alcohol and Drug Research under the University of Aarhus. The centre is funded by the Danish government based on five-year grants from the Danish National Budget.

Data collection was carried out as part of regular clinical practice, and no additional funding was available for this purpose. Neither the Centre for Alcohol and Drug Research, nor the City of Copenhagen had the right to withhold or evaluate the research prior to publication.

### Contributors

Both authors discussed the overall purpose of the study, and agreed to conduct a study over a 12-month period. Morten Hesse conducted the literature search for the study, suggested the specific instruments to be used for the study, planned and conducted the statistical analyses, and drafted the manuscript. Henrik Thiesen planned, coordinated and monitored data collection, and reviewed and revised the manuscript for critical intellectual content.

### Conflict of Interest

We declare that to the best of our knowledge, we have no conflicts of interest in relation to this manuscript.

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