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Comparison of self-reported alcohol consumption and ethyl glucuronide in hair in a sample of 60+ year -olds treated for DSM-5 alcohol use disorder

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Abstract

There is a lack of evidence for the consistency between self-reported alcohol consumption (SRAC) and concentrations of ethyl glucuronide in hair (hEtG) among elderly patients treated exclusively for alcohol use disorder (AUD). Hence, this study assessed the consistency between these two measures in these patients. A total of 190 patients with AUD were assessed for SRAC using Form 90 and hEtG, 14 or 22 weeks after treatment conclusion. Patients were grouped according to SRAC (g/day) and corresponding hEtG concentrations (pg/mg): 0 and <5 (abstinence), 0.1–14.3 and 5.0–9.9 (low consumption), 14.4–21.4 and 10.0–15.9 (moderate consumption), 21.5–59.9 and 16.0–30 (high consumption) and ≥60 and >30 (excessive consumption). The extent of underreporting and overreporting was examined by crosstabulations, and inter-rater reliability was reported by kappa correlations. Associations and effect modification were examined by conditional logistic regression. Due to multitesting, *p*-values ≤0.01 were considered significant. Underreporting was found in 96 patients (50.5%) and overreporting in 41 patients (21.6%). The kappa coefficients varied between 0.19 and 0.34. HEtG was more likely to detect low, moderate and high alcohol consumption compared with SRAC (ORs between 5.1 and

12.6, all p-values <0.01), but SRAC and hEtG did not differ significantly with respect to identification of abstinence (OR = 1.9, $p = 0.05$). Inconsistency between the outcome measures was found in a considerable number of the patients. More studies examining the consistency between SRAC and specific direct biomarkers of alcohol in this population seem warranted.

KEYWORDS
aged, alcohol drinking, biomarkers, hair, outcome assessment, self-report

1 | BACKGROUND

Alcohol use disorders (AUD) are highly prevalent and represent a significant risk factor for several diseases.[1–4] In the context of sociodemographic changes in Western societies, the prevalence of AUD is increasing in older patients,[5–7] and effective treatment targeting this patient segment is therefore important.[8,9]

The outcome of treatment is usually measured by self-reported alcohol consumption (SRAC), which is regarded as a reliable and valid method when applying standardised assessment instruments.[10,11] One such instrument is Form 90, which combines the techniques of Timeline Follow-Back methods[12] and average consumption grids[13] and thereby assesses both episodic and more stable patterns of alcohol consumption.[14] Test–retest reliability of Form 90 has been shown to be good to excellent in assessing alcohol consumption,[14–16] and there are also indications of criterion and construct validity.[16]

Albeit the favourable psychometric properties, there is evidence of inconsistency between psychometric assessment instruments and biomarkers in AUD treatment settings.[17] This inconsistency mostly constitutes underreporting, but high alcohol consumption is not necessarily reflected by elevated concentrations of biomarkers[18–26] and may therefore appear as overreporting. Biomarkers of alcohol consumption have different time frames of detection and varying sensitivity and specificity.[27,28] Ethyl glucuronide (EtG) in hair (hEtG) is considered a reliable and valid biomarker of long-term alcohol exposure,[29,30] allowing for a retrospective evaluation of a period of several months.[27] Small amounts of ingested alcohol, that is, less than 1%, are metabolised into EtG by enzymatic ethanol glucuronidation mostly in the liver.[31,32] In blood and urine, EtG is detectable during a short time span (a few hours to a few days), whereas keratinised sample matrices store EtG for months.[27,31]

So far, hEtG has been used to examine alcohol consumption or validate self-reported consumption among university and college students,[33–35] in teenage populations (aged 14–15 years)[36] and in a population study of young men.[37] Also, hEtG has been applied in child custody cases,[38] as well as in examinations of prenatal alcohol exposure.[39–43] Further, hEtG has been used in somatic treatment settings[44–46] and is widely utilised in forensic[47,48] and criminal justice[49–52] settings.

Despite the wide use of hEtG, this method has only been applied to a limited extent in elderly samples (aged 60 + years), for example, to evaluate nursing staff's reports of patients' alcohol consumption and to assess alcohol consumption among nursing home residents. Although some of the nursing home residents may have been treated for AUD during the study or may have received treatment for AUD previously, the study did not take place in a treatment setting that addressed AUD.[53] In AUD treatment settings, underreporting has been examined by means of EtG in several studies, mostly by means of urine as sample matrix,[54–61] but none of them exclusively examined elderly patients. Furthermore, these studies did not exclude patients who also used illicit drugs which may pose a problem due to the effect of these drugs on cognitive performance[62,63] and thereby SRAC.

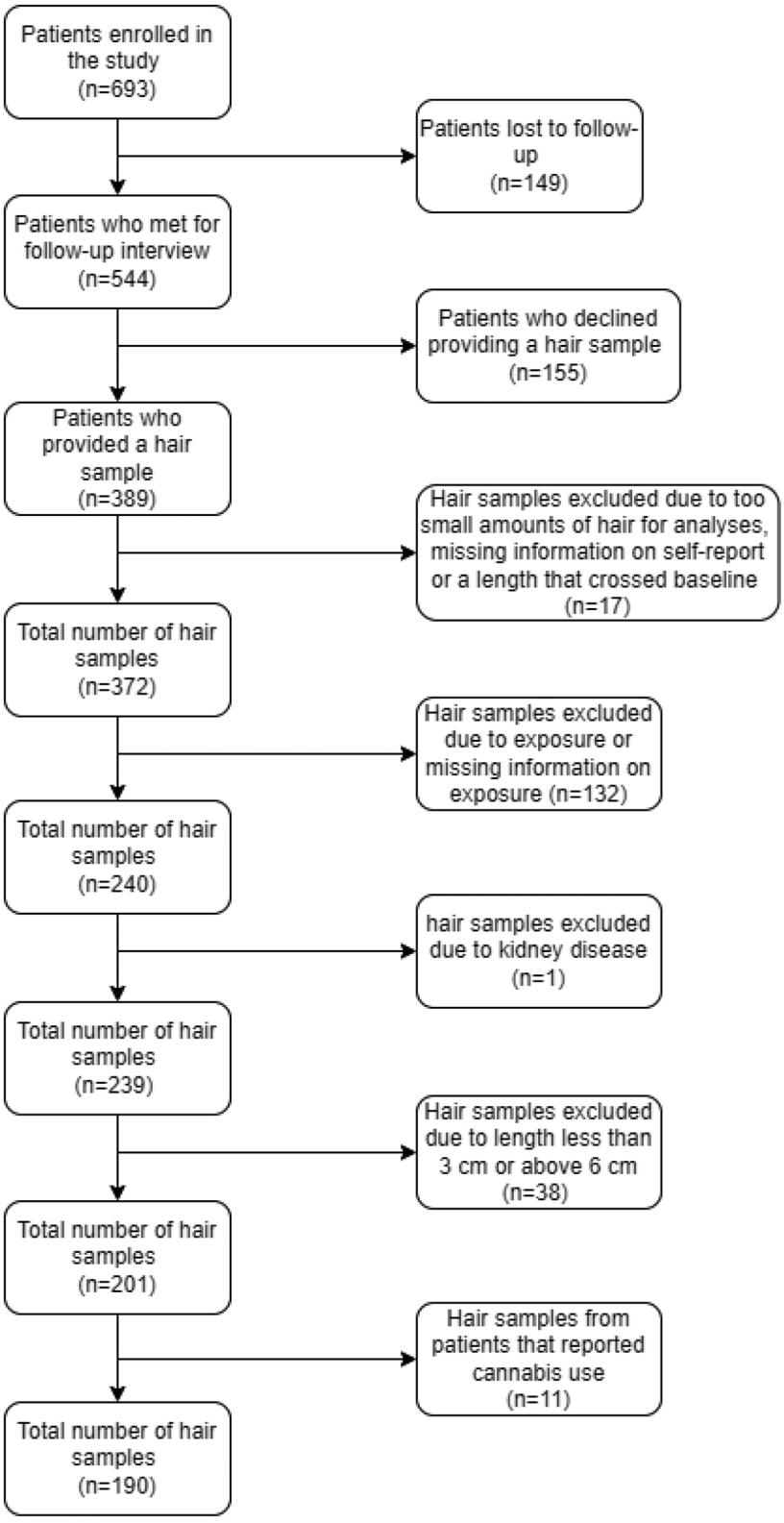
To date, only two studies have assessed EtG in patients treated for AUD with no other substance use aside from possible use of nicotine, and both used urine sample as matrix. In these studies, middle-aged patients (mean age approximately 50 years) were asked if they were abstinent and underreporting was found in 5%–50%.[20,21] The reason for the large discrepancy in rates of underreporting between the two studies is probably due to differences in the study samples. The study that found an underreporting rate of 5%[20] was conducted with a usual treatment sample, whereas the study that found an underreporting rate of 50%[21] was conducted among patients on a waiting list for a liver transplant.

Due to the increasing number of elderly individuals with AUD and because hEtG is considered an asset for identifying alcohol consumption in both clinical and forensic toxicology settings,[30] it is important to have accurate information on alcohol consumption when evaluating the effects of treatment and also because older patients are more sensitive to alcohol consumption[64] and physical circumstances, comorbidity and medical interactions may increase the negative consequences of alcohol. However, to our best knowledge, no study has yet examined consistency between SRAC and hEtG in elderly patients treated for AUD with no other substance use aside from possible nicotine use. The aim of this study, therefore, was to examine consistency between SRAC and hEtG in this patient population. We hypothesised that alcohol consumption would be identified to a larger extent by means of hEtG than by SRAC.

2 | METHODS

Data for the present study stem from the Elderly Study, which has been described in detail elsewhere.[8] Briefly, the Elderly Study was an international multicentric RCT-study (Denmark, Germany, and

FIGURE 1 Flowchart of the exclusion process



the United States) that compared the effects of two interventions on alcohol consumption outcomes: (1) short-term Motivational Enhancement Treatment (MET) and (2) MET with an add-on of up to eight sessions based on the Community Reinforcement Approach (CRA) targeting specific problems among older adults (CRA-S). The patients were interviewed by an independent study interviewer. Data for the present study were obtained at the time of treatment enrollment (baseline) and 26 weeks after baseline. In the Elderly study, patients were randomised to either four (MET) or up to 12 (MET + CRA-S) weeks of treatment, and the 26-week follow-up interview therefore took place 14 or 22 weeks after treatment completion.

2.1 | Sample

A total of 693 patients were included in the Elderly study, and 544 patients met for the follow-up interview. Of these 544 patients, 155 patients declined to provide a hair sample, and 389 patients accepted. However, not all hair samples were included in further analyses.

Hair samples were excluded if (1) the amount of hair was too small for analyses or if information on SRAC was missing, (2) the hair had been exposed to treatment or information on treatment was missing, (3) the patient had renal disease, (4) the length of hair was not between 3 and 6 cm as recommended by The Society of Hair Testing,[65] (5) the length of hair included time prior to the baseline interview and 6) the patient reported cannabis use at the follow-up interview.

A total of 190 hair samples were included in the analyses. For an overview of the exclusion process, please see Figure 1.

2.2 | Measures

2.2.1 | Sociodemographic information, comorbidity and biometrics

At baseline, we obtained data on age, gender, marital status, employment status and prior AUD treatment. Also, The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) AUD and other psychiatric disorders were assessed using the Mini-International Neuropsychiatric Interview (M.I.N.I.) version 5.0.0 (adapted to DSM-5 AUD)[66] and somatic disorders using the Charlson Comorbidity Index (CCI).[67]

Concentrations of EtG in hair are not affected by liver disease, age, gender and ethnicity but due to renal excretion of EtG and the distribution of alcohol in nonadipose tissue, kidney function and body mass index (BMI) should be taken into consideration.[31,68] Moderate and severe kidney disease decreases the elimination rate of EtG and thereby causes higher concentrations of EtG.[69,70] Renal disease was identified by CCI.[67]

For examining potential effect modification of BMI on the association between hEtG as an outcome and exposure to alcohol, we used information on the patients' height and weight from the Form 90.[15,71]

2.2.2 | SRAC, level of dependence and cannabis use

SRAC and cannabis use were assessed by means of Form 90.[15,71] At baseline, the patients were asked about their consumption during the previous 90 days. In the follow-up interview, patients were asked about their consumption since the last interview. Level of dependence was defined by means of the Alcohol Dependence Scale (ADS).[72,73]

2.2.3 | EtG concentrations in hair and biochemical considerations

Hair samples were collected during the follow-up interview conducted 26 weeks after the baseline interview. It has been shown that when hair samples are collected, an average of 0.8 ± 0.1 cm is left on the scalp and the growth rate of hair is on average 1.06 cm per month.[74] Based on the average length of hair left and growth rate, data on SRAC during the previous 23 days leading up to the follow-up interview were disregarded and day 24 was considered as time zero. Days of SRAC that matched the time span covered by the hair samples were included; that is, if a hair sample had the length of 3 cm, a time span of 2.8 months was investigated for SRAC, based on Form 90 information obtained at 26 weeks follow-up and, if necessary, also at 12 weeks follow-up. To get the least variation of hair growth, hair was cut from the posterior vertex region of the head and as close to the scalp as possible. When possible, a length of 3 to 6 cm of hair was provided, as this is considered the optimal length for analysing hEtG according to The Society of Hair testing,[65] and only EtG concentrations obtained from hair samples with a length between 3 and 6 cm were included in the statistical analysis. Scalp hair was preferred, although body hair, excluding axillary and pubic hair, is also usable.[32,75–77] When scalp hair was not available, hair samples from the chest, beard or extremities were used. hEtG is considered not to be affected by natural hair colour, but levels may decrease due to hair dyeing, bleaching, and perming.[31,68,78] Some hair products (sprays, lotions and perfumes) containing EtG or high concentrations of alcohol may lead to elevated hEtG despite no alcohol consumption.[79–81] To avoid false concentrations of hEtG, we excluded hair samples that had been exposed to treatment. Patients were asked about exposure, but in some cases, exposures were only identified during the analysis process.

EtG concentration was measured as pg/mg in hair. Based on recommendations from the Society of Hair Testing, a value of 5 pg/mg was set as the cut-off for abstinence as this level does not contradict self-reported abstinence.[65] However, there is a risk of false negative results because daily consumption of smaller amounts of alcohol does not necessarily lead to hEtG exceeding 5 pg/mg.[82,83] A value of 30 pg/mg was set as the cut-off for excessive alcohol consumption. A meta-analysis that studied the cut-off of 30 pg/mg corresponding to heavy drinking (≥60 g/day) found an overall sensitivity and specificity of 0.96 and 0.99, respectively,[84] but the included study samples did not consist exclusively of elderly patients.

There are no recommended cut-offs for hEtG that correspond to low or moderate alcohol consumption.[65] Because some patients reported alcohol consumption that did not exceed excessive consumption, modified cut-offs were provided based on previous research. In a controlled alcohol-dosing study, it was possible to discriminate between low (100 g alcohol weekly, avg. 14.3 g daily) and moderate (150 g alcohol weekly, avg. 21.4 g daily) consumption.[83] Except for one case, EtG values did not exceed concentrations above 10 and 16 pg/mg, respectively. Therefore, these cut-offs were used

as indicators of low and moderate consumption, respectively, though they may be considered rather conservative compared with other suggested cut-offs.[82,85]

Although natural hair colour and age are considered not to affect hEtG, hair texture changes and loses pigmentation with increasing age.[86] The influence of hair texture on hEtG has not been investigated sufficiently,[31] but because grey hair is hollow,[86] we investigated potential effect modifications of a natural hair colour of grey on the association between hEtG as an outcome and exposure to alcohol. Natural hair colour was identified either by the research assistant or during the analysis process. A description of the analysis of hEtG is provided in the supporting information.

2.2.4 | Data analysis

Baseline characteristics were compared between patients who provided hair samples and those who did not by means of the chi-square test for dichotomous categorical covariates, Mann–Whitney test for continuous covariates and gamma test for ordinal scale covariates.

Patients were grouped according to level of SRAC (g/day) and corresponding hEtG level (pg/mg) (see Table 1): 0 g/day and <5 pg/mg (abstinence). 0.1–14.3 g/day and 5.0–9.9 pg/mg (low consumption). 14.4–21.4 g/day and 10.0–15.9 pg/mg (moderate consumption). 21.5–59.9 g/day and 16.0–30 pg/mg (high consumption) and ≥ 60 g/day and >30 pg/mg (excessive consumption).[65,83]

Conditional logistic regression was used to assess the association between categories of SRAC and corresponding categories of hEtG as well as potential effect modifications of BMI and natural hair colour on the association between hEtG as an outcome and exposure to alcohol. The dependent variable was level of alcohol consumption, that is, presence or absence of abstinence or low- moderate- or high alcohol consumption. The independent variable was the method of assessment of alcohol consumption, that is, SRAC or hEtG. Due to multitesting, *p*-values were Bonferroni corrected, and *p*-values ≤0.01 were considered significant.[87]

Percentages of underreporting and overreporting between corresponding categories of SRAC and hEtG were reported with a confidence interval of 95%, and inter-rater reliability was calculated as Cohen's kappa. Kappa values correspond to the following levels of agreement: <0.2: none, 0.21–0.39: minimal, 0.4–0.59: weak, 0.6–0.79: moderate, 0.8–0.9: strong and >0.9 almost perfect.[88]

All analyses were performed with the STATA Software package 16.0,[89] and the codes were internally peer reviewed before the manuscript was submitted for external review and publication.

TABLE 1 Level of consumption and corresponding self-reported alcohol consumption and concentrations of EtG in hair

Level of consumption	Corresponding self-reported alcohol consumption (g/day)	Corresponding concentration of EtG in hair (pg/mg)
Abstinence	0.0	<5.0
Low consumption	0.1–14.3	5.0–9.9
Moderate consumption	14.4–21.4	10.0–15.9
High consumption	21.5–59.9	16.0–30.0
Excessive consumption	≥60.0	>30.0

Note: Reference: L Crunelle, C., Cappelle, D., Yegles, M., De Doncker, M., Michielsen, P., Dom, G., van Nuijs, A.L., Maudens, K.E., Covaci, A., Neels, H., 2016. Ethyl glucuronide concentrations in hair: A controlled alcohol-dosing study in healthy volunteers. Analytical and Bioanalytical Chemistry 408, 2019–2025. Society of Hair Testing, 2020. Consensus for the use of alcohol markers in hair for supporting the assessment of abstinence and chronic alcohol consumption.
Abbreviations: EtG, ethyl glucuronide; g, gramme(s); pg/mg, picogramme(s)/mg.

3 | RESULTS

The rate of participation in the follow-up interview was 78.5% (544/693). Baseline characteristics did not differ significantly between patients who provided hair samples ($n = 389$) and those who did not ($n = 155$). Of the 389 hair samples, 190 were considered optimal for analysing and 199 were excluded. Sample characteristics are summarised in Table 2.

3.1 | Patient characteristics and hair sample information

Of the 190 hair samples included in the primary analyses, information on current psychiatric comorbidity was available for 165 patients, of which 31 (18.8%) had psychiatric comorbidity constituted by mood and anxiety disorders. Information on BMI was available for 165 patients. For an overview, see Table 3.

Most of the hair samples were taken from the scalp ($n = 180$, 94.7%) and few samples were provided from beard or body hair ($n = 10$, 5.3%). Natural hair colour of grey and white was found in 137 patients (72.1%), and of these patients, 13 still had some of their original hair colour left. The length of the included hair samples ranged from 3 to 6 cm, with a median of 3 cm and a 75th quartile of 4 cm.

3.2 | SRAC, EtG concentrations in hair and effect modification

High alcohol consumption (≥60 g/day) was 12.6 times more likely to be registered by means of EtG in hair only than by self-report only. For low (14.3–21.3 g/day) and moderate (21.4–59.9 g/day) alcohol consumption, the odds ratios were 6.1 and 5.1, respectively (all *p*-values <0.01), and for abstinence, the odds ratio was 1.9 ($p = 0.05$). Of the total number of pairs ($n = 190$), the number of discordant pairs

TABLE 2 Comparison of demographic and clinical characteristics during the 30 days prior to requesting hair samples between patients who provided a hair sample and those who did not ($n = 544$)

	Provided a hair sample	Did not provide a hair sample	
N	**389**	**155**	***P*-value**
Age (years)			
Median [min - max] (Q1, Q3)	64 [60–86] (62, 68)	64 [60–79] (62, 68)	0.45
Gender			0.62
Males *n* (%)	232 (59.6)	96 (61.9)	
Living with partner			
Yes	185 (47.6)	79 (51.0)	0.47
Employment status			
Work full/part time *n* (%)	78 (20.1)	33 (21.3)	0.27
Retired *n* (%)	246 (63.2)	95 (61.3)	
Unemployed *n* (%)	36 (9.3)	9 (5.8)	
Other *n* (%)	29 (7.5)	18 (11.6)	
Previous treatment for AUD			
Yes *n* (%)	160 (41.1)	79 (51.0)	0.04
Level of Dependence[a]			
None/mild[b] *n* (%)	278 (71.8)	104 (67.3)	0.18
Moderate[b] *n* (%)	94 (24.3)	34 (22.1)	
Severe[b] *n* (%)	15 (3.9)	16 (10.4)	
Somatic comorbidity[c]			
Yes *n* (%)	157 (40.4)	71 (45.8)	0.25
Psychiatric comorbidity[d,e]			
Yes *n* (%)	59 (17.9)	25 (17.4)	0.88
Self-reported alcohol consumption during the previous 30 days, assessed at time of follow-up interview (g/day)[f]			
Median [min - max] (Q1, Q3)	18.4 [0–230.4] (0.3, 52.2)	11.3 [0–198.4] (0, 43.1)	0.07

Note: *n* is smaller for 'level of dependence', see (a); 'psychiatric comorbidity', see (e); and 'self-reported alcohol consumption the previous 30 days' see (f). Abbreviations: AUD, alcohol use disorder; g, gramme(s); pg/mg, picogramme(s)/milligramme; Q1, 25th percentile; Q3, 75th percentile; SD, standard deviation.

[a]$n = 387/154$.

[b]Based on the four quartiles in Alcohol Dependence Scale: none/mild (first quartile), moderate (second quartile), severe (third and fourth quartiles). Skinner, H.A., Horn, J.L., 1984. Alcohol dependence scale (ADS): User's guide. Addiction Research Foundation.

[c]According to Charlson Comorbidity Index. Charlson, M.E., Pompei, P., Ales, K.L., MacKenzie, C.R., 1987. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J. Chronic Dis. 40, 373–383.

[d]Current major depressive episode, current dysthymia, current panic disorder, current agoraphobia, current social anxiety disorder, current obsessive–compulsive disorder and current generalised anxiety disorder.

[e]$n = 329/144$.

[f]$n = 382/152$.

varied between 46 (abstinence) and 82 (high consumption), and the number of concordant pairs varied between 108 (high consumption) and 144 (abstinence). There was no significant age difference between the group with elevated hEtG compared with SRAC and the rest of the patients. For details, see Table 4.

Kappa values for agreement between the consumption categories varied between 0.19 and 0.34 (see Table 5). The lowest value represented hEtG≥30 pg/mg (excessive consumption), suggesting no agreement. In hair samples representing abstinence or low or moderate alcohol consumption, the kappa values indicated minimal level of agreement.

In patients who reported abstinence at 26 weeks follow-up ($n = 34$), underreporting was observed in 16 of them (47.1%) (Table 5).

Among patients who reported a level of alcohol consumption between 0.1 and 59.9 g/day ($n = 122$), underreporting was observed in 80 of them (65.6%).

Overreporting was found in 41 patients (21.6%). For details, see Table 5.

There was no significant effect modification of natural hair colour (defined as grey/white or nongrey/white hair) or BMI in the logistic regression model.

4 | DISCUSSION

This study is the first to assess the consistency between SRAC and hEtG among elderly patients in outpatient treatment for AUD with no other substance use aside from possible nicotine use. Of the total number of patients ($n = 190$), 96 (50.5%) underreported their alcohol consumption. Overreporting was found in 41 patients (21.6%), and kappa coefficients varied between 0.19 and 0.34. Detection of low, moderate, and high alcohol consumption was significantly more likely by means of hEtG than by SRAC (OR = 5.1–12.6, $p < 0.01$), but the two methods did not differ significantly with respect to identifying abstinence ($p = 0.05$).

The rate of underreporting in our study is similar to that reported in a previous study conducted among patients treated for AUD on a waiting list for a liver transplant (50%).[21] However, the rate of underreporting in our study was much higher than that found in another previous study (5.5%)[20] conducted on a sample that is more similar to ours, that is, patients in a standard AUD treatment setting. However, our study cannot be directly compared with these previous studies due to differences in age, sample matrix as well as time point of the assessment.[20,21]

Regarding SRAC, although there is evidence for the reliability of the Form 90,[14–16] caution is warranted in using self-report for several reasons. First, social desirability may pose a problem,[90] which aligns with our finding that those who drank the most also tended to underreport more frequently. When it comes to social desirability among the elderly, their own perception of drinking must also be taken into consideration. Recent research has shown that some drinking habits among the elderly may be associated with stigma and considered inappropriate among the elderly themselves,[91] which may lead to underreporting. Second, alcohol consumption may cause poor episodic memory and cognitive impairment,[92,93] and some patients may suffer from minimal hepatic encephalopathy, which may aggravate cognitive functions.[94–96] However, in the present study, patients with moderate or severe cognitive impairment were excluded at the baseline assessment. Third, anxiety and mood disorders may also affect cognitive performance[97,98] and thereby lead to discrepancy between SRAC and hEtG. Also, patients in this study were asked about their alcohol consumption covering a time span of several weeks and it may be challenging to recall the amounts consumed several weeks ago. Lastly, some patients may exaggerate their alcohol consumption.

TABLE 3 Characteristics of the included patients ($n = 190$)

Age (years)	
Median [min - max] (Q1, Q3)	64.0 [60–81] (62.0, 68.0)
Gender	
Males *n* (%)	115 (60.5)
BMI[a] (kg/m^2)	
Median [min - max] (Q1, Q3)	24.9 [16.5–43.4] (22.6, 29.0)
Self-reported daily alcohol consumption in the time corresponding to the length of the hair sample (gramme)	
Median [min - max] (Q1, Q3)	13.9 [0.0–193.4] (1.3, 38.7)
EtG concentrations in hair (pg/mg)	
Median [min - max] (Q1, Q3)	34.3 [0.0–1201.8] (4.3, 99.7)
Current psychiatric comorbidity[b]	
n (%)	31 (18.8)

Note: *n* is smaller for 'BMI', see (a) and for 'current psychiatric comorbidity', see (b).
Abbreviations: BMI, body mass index; Q1, 25th percentile; Q3, 75th percentile; pg/mg, picogramme/milligramme.
[a]$n = 184$.
[b]$n = 165$.
[c]Since last interview (26-week follow-up interview).

TABLE 4 Association between self-reported average alcohol consumption (g/day) and hEtG and kappa values ($n = 190$)

hEtG	Self-reported avg. alcohol consumption		Kappa	OR (99.0% CI)
Abstinence	>0 g/day	0 g/day		
≥5 pg/mg	$n = 126$	$n = 16$	0.29	1.9 (0.99–3.7)[ns]
<5 pg/mg	$n = 30$	$n = 18$		
Low consumption	<14.3 g/day	≥14.3 g/day		
<10 pg/mg	$n = 43$	$n = 9$	0.34	6.1 (2.99–14.1)**
≥10 pg/mg	$n = 55$	$n = 83$		
Moderate consumption	<21.4 g/day	≥21.4 g/day		
<16 pg/mg	$n = 50$	$n = 12$	0.27	5.1 (2.8–10.5)**
≥16 pg/mg	$n = 62$	$n = 66$		
High consumption	<60 g/day	≥60 g/day		
<30 pg/mg	$n = 80$	$n = 6$	0.19	12.6 (5.6–35.6)**
≥30 pg/mg	$n = 76$	$n = 28$		

Note: The length of the hair samples was 3–6 cm.
Abbreviations: CI, confidence interval; g, gramme(s); hEtG, ethyl glucuronide concentration in hair; ns, not significant; OR, odds ratio; pg/mg, picogramme(s)/milligramme.
**p-value < 0.01.

TABLE 5 ($n = 190$) Number of patients distributed in groups according to level of consistency between self- and hair-reported alcohol consumption

	hEtG[a]					
Self-reported level of alcohol consumption [g/day] (*n*)	Abstinent (<5 pg/mg) *n* (%)	Low (5–9.9 pg/mg) *n* (%)	Moderate (10–15.9 pg/mg) *n* (%)	High (16–30 pg/mg) *n* (%)	Excessive (>30 pg/mg) *n* (%)	Total hEtG>SRAC *n* (%)[b] [95% CI]
Abstinent (34)	18 (52.9)[c]	1 (2.9)[d]	3 (8.8)[d]	1 (2.9)[d]	11 (32.4)[d]	16 (47.1) [29.7;64.8]*
Low [0.1–14.3] (64)	23 (35.9)[e]	1 (1.6)[c]	2 (3.1)[d]	9 (14.1)[d]	29 (45.3)[d]	40 (62.5) [49.5;74.3]*
Moderate [14.4–21.4] (14)	2 (14.3)[e]	0 (0.0)[e]	0 (0.0)[c]	4 (28.6)[d]	8 (57.1)[d]	12 (85.7) [57.2;98.2]*
High [21.5–59.9] (44)	4 (9.1)[e]	1 (2.3)[e]	5 (11.4)[e]	6 (13.6)[c]	28 (63.6)[d]	28 (63.6) [47.7;77.6]*
Excessive [≥ 60.0] (34)	1 (2.9)[e]	1 (2.9)[e]	0 (0.0)[e]	4 (11.8)[e]	28 (82.4)[c]	N/A
Total SRAC>hEtG *n* (%)[f] [95% CI]	30 (62.5) [47.3;76.0]*	2 (50.0) [6.8;93.2]*	5 (50.0) [18.7;81.3]*	4 (16.7) [4.7;37.4]*	N/A	N/A

Abbreviations: CI, confidence interval; EtG, ethyl glucuronide; g, gram(s); hEtG, EtG concentration in hair; N/A, not applicable. pg/mg = picogram(s)/milligram; SRAC = self-reported alcohol consumption.
[a]The length of the hair samples was 3 – 6 centimeters.
[b]The percentage of patients of the respective self-reported alcohol consumption group.
[c]Consistency between self-report and hEtG.
[d]Underreporting.
[e]Overreporting.
[f]The percentage of patients of the total sample.
*p<0.001.

This is mostly seen at the time of enrolment into treatment, for example, if the patient thinks that a certain level of drinking is a prerequisite to be accepted into treatment.[23] Since the patients in this study were interviewed at follow-up, lapse of memory seems more likely, but exaggerated alcohol consumption cannot be ruled out as a contributing reason behind overreporting.

Regarding the timeline where day 24 was considered as time zero for SRAC, hair representing a period of drinking may still have been included in the present study. As the 24 days represents the average length of hair left on the scalp after providing the sample, one must consider that even experienced research assistants may leave up to 1.6 cm of hair,[74] which is equivalent to 52 days growth. Length of hair equivalent to 28 days growth or more must be considered as a potential risk of contamination, which may explain at least some of the inconsistency between the outcome measures. In the present study 5.3% of the hair samples were either beard or body hair. Although cut-offs for EtG concentrations are the same for scalp and nonscalp hair, there may be differences in the physiology of hair growth[65] that have not been accounted for, which may explain some of the inconsistency observed.

There is evidence that hEtG is not affected by natural hair colour,[31,68,99,100] but due to the large number of patients with a natural hair colour of grey (72.1%) in the present study, we examined if there was any effect modification of natural hair colour on hEtG, which was not detected. One issue that may be of importance is that pigmented and white/grey hair have different growth rates. The growth rate of pigmented hair decreases with ageing, whereas the growth rate of depigmented hair remains steady over time.[86] This means that EtG in a hair sample with a length of, for example, 3 cm has been compared with SRAC covering 2.8 months, although the time span should have been longer. The consequences of this may be that we have missed information on consumed alcohol detected by SRAC and only identified alcohol consumption by the hair samples.

In the present study, no significant effect modification was found of BMI. Increased BMI may be of significance due to the distribution of ethanol in nonadipose tissue. One study found significant differences in EtG concentrations between patients with a BMI > 25 kg/m2 and those with a lower BMI,[101] but the study did not lead to a recommendation for using differentiated cut-offs depending on BMI level. However, the suggested cut-off for abstinence at that time was 7 pg/mg[101] and not 5 pg/mg as it is currently.[65]

The present study found no significant difference in age between the group with elevated hEtG compared with SRAC and the rest of the patients. Studies so far have shown that age does not impact hEtG,[31,68,102] but it is possible that the patients in the present sample, due to their age, had somatic comorbidity of significance for the EtG concentrations, for example, unrecognised kidney disease. Further, although age should not affect hEtG,[31,68] it cannot be ruled out that hEtG may be increased in an exclusively elderly sample compared with a younger sample. However, in a controlled alcohol-dosing study ($n = 30$), none of the patients aged 62–68 years ($n = 7$) exceeded the corresponding concentrations of EtG in hair.[83] In the present study, 75% of the patients did not exceed the age of 68 years. Therefore, it seems unlikely that age alone would explain the inconsistencies observed.

Some patients did not exceed the cut-off levels for EtG, although they reported an equivalent or higher level of alcohol consumption. For the patients who did not exceed 5 pg/mg EtG in hair, the reason may be that this concentration is not necessarily exceeded if small amounts of alcohol are consumed on few occasions. Another

explanation may be that if the patients reported alcohol consumption just once, they were no longer categorised as abstinent. Regarding the other cut-off levels for EtG, the results may either suggest conservative cut-offs[82,85] or a tendency of overreporting. However, as mentioned above, this is mostly seen at the time of enrollment into treatment[23] but cannot be ruled out as an explanation for inconsistency in this study.

In the present study, we conducted the main analyses on a relatively small number ($n = 190$) of hair samples that were provided ($n = 389$). The relatively large number of excluded samples may affect the use of hEtG as an outcome measure, both in clinical practice and in research. This may be even more pronounced in seniors because with increasing age alopecia and hair thinning occur more frequently,[86] reducing the probability of obtaining optimal hair samples. Further, our findings show that hair treatment is very common in this age group, limiting the use of hair samples even more.

The present study takes its primary focus on the discordant pairs, and we have discussed possible explanations for overreporting and underreporting, respectively. However, the number of concordant pairs should also be noted because although they do not add information to the analyses on associations, they still provide information on the degree of consistency in the total sample. In this study, the number of concordant and thereby consistent pairs varied between 108 (high consumption) and 144 (abstinence) out of a total of 190 pairs, that is, consistency on the group level varied between 56.8% (high consumption) and 75.8% (abstinence).

5 | STRENGTHS AND LIMITATIONS

This study has several notable strengths. Data stem from a population that so far hardly has been investigated, the self-reported information on alcohol consumption is detailed and the data allowed us to control for potential effect modification of BMI and hair colour on hEtG. Also, the length of the hair that was left on the scalp when the hair samples were collected was taken into consideration. Although only 389 of 544 patients (71.5%) provided hair samples, no significant differences in baseline data were found between participants who provided and declined to provide a hair sample, and thus, the sample examined may be deemed representable for the whole sample.

However, some limitations should be mentioned. First, the follow-up rate at 26 weeks was 78.5%. Second, not all samples were scalp hair. Third, 199 samples were excluded. Fourth, although we applied the most reliable and valid self-report instrument and biomarker available for assessing alcohol consumption, both methods have limitations that may compromise detection of the true rate of alcohol consumption in treatment-seeking patients. Fifth, we only screened for use of illicit drugs by self-report. The optimal strategy would have been to assess illicit drugs use by use of biological matrix, such as urine samples. However, urine samples are usually not routinely performed in Danish alcohol treatment settings, and we expected that many patients would have decline to participate in this study if it had been mandatory to provide urine samples. Further, it would have been interesting to assess alcohol consumption by EtG in urine frequently as this would have provided the possibility of detecting alcohol consumption more precisely.[58] For future validation studies on SRAC, the use of phosphatidyl ethanol (PEth) as a biomarker would be of interest. Though some precautions should be considered, this biomarker is not sensible to external contamination and therefore has some advantages compared with hEtG. The detection time of PEtH is shorter than for hEtG, but PEth would provide the possibility of detecting episodic/binge drinking.[103,104] However, for PEtH to be able to detect episodic drinking, frequent testing would be required, which would not have been feasible in this study. Another limitation is that our data were derived from a RCT which may compromise external validity.[105,106] Lastly, although age and natural hair colour are not considered to affect hEtG, the impact of these factors on hEtG has not been investigated in an exclusively elderly sample, and we may therefore have failed to identify all the problems that should be taken into consideration when interpreting the results.

6 | CONCLUSION AND FUTURE DIRECTIONS

The present study found underreporting of alcohol consumption in a considerable number of elderly patients treated for DSM-5 AUD. The two methods performed equally well in identifying abstinence, but detection of low, moderate and high alcohol consumption was more likely by means of hEtG than SRAC. Further, there was no significant effect modification of natural hair colour (defined as grey/white or nongrey/white hair) or BMI on the association between hEtG as an outcome and exposure to alcohol.

More research is needed examining the extent of underreporting in elderly patients with and without AUD. Moreover, it is of interest to examine consistency by means of different time assessments of self-report, including both retrospective and successive registration.

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CONFLICT OF INTEREST

No competing interests to declare.

AUTHOR CONTRIBUTIONS

Authors DGN, AIM, ASN and KA designed the study. Author FN performed the hair analyses. Authors KA, GB and MB were principal investigators on the Danish, German and American sites, respectively. RB and SB were co-PIs at the Danish site and Dresden sites,

respectively. DGN wrote the first draft of the manuscript, and all authors contributed to and approved the final manuscript.

ETHICS STATEMENT

All patients provided informed consent and had to pass an informed consent quiz. The study was approved by local ethical committees. In Denmark by The Regional Scientific Ethical Committees for Southern Denmark, (project-ID S-2013138); In Germany by the Ethics Committee, Technische Universitäet, Dresden, (project-ID EK 389102013) and Ethical Board of the German Society of Psychology (DGPs, Reg.-No. EKAntrag Pfeiffer-Gerschel/Bühringer 12/2013, Munich); and USA, New Mexico (project-ID University of New Mexico HRRC #13–580).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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