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Published in:
Alcoholism: Clinical and Experimental Research

DOI:
10.1111/acer.14722

Publication date:
2021

Document version:
Accepted manuscript

Citation for published version (APA):

Go to publication entry in University of Southern Denmark's Research Portal

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Download date: 15. Sep. 2023
Residual alcohol use disorder symptoms after treatment predict long-term drinking outcomes in seniors with DSM-5 alcohol use disorder

Short title: Post-treatment alcohol use disorder symptoms

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Keywords: alcohol dependence, severity, symptom, older adults, intervention

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:10.1111/ACER.14722

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Funding & Declaration of interest

This study was funded by the Lundbeck Foundation, Denmark, which had no role in study design, collection, analysis and interpretation of data, writing of the report, and decision to submit the article for publication.

Gerhard Bühringer has received unrestricted gambling research grants from the Bavarian State Ministry of Finance (regulatory authority for and operator of the State Gambling Monopoly) via the Bavarian State Ministry of Public Health and Care Services, from the German Federal Ministry of Economics and Technology (regulatory authority for parts of the commercial gambling industry), and from public and commercial gambling providers.

Michael Bogenschutz has received research grants from the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Addiction, the Heffter Research Institute, the Multidisciplinary Association of Psychedelic Studies (MAPS), the Turnbull Family Foundation, B. More, Inc., Mind Medicine, Inc., the Fournier Family Foundation, Dr. Bronner’s Family Foundation, the Riverstyx Foundation, and private individuals.

The other authors report that they do not have a conflict of interest.
Abstract (281 words)

Background: Risk of relapse within the first months after alcohol use disorder (AUD) interventions is substantial among older adults. For this vulnerable group, little information exists on how this risk is associated with residual DSM-5 AUD symptoms after treatment.

Aims: To investigate among older adults who received short-term treatment for DSM-5 AUD 1) the prediction of drinking behaviors and quality of life 12 months after treatment initiation by six-month DSM-5 AUD symptoms, AUD severity, and AUD remission, and 2) whether these DSM-5 AUD indicators offer prognostic information beyond the information gained from six-month alcohol use (AU) status.

Methods: The international multicenter RCT ‘ELDERLY-Study’ with adults aged 60+ with DSM-5 AUD. We used data from the subsample of n=323 German and Danish participants with complete DSM-5 AUD criteria information six months after treatment initiation (61% male: mean age 65.5 years). AU was assessed with Form 90, DSM-5 AUD with the M.I.N.I., quality of life with the WHOQOL-BREF. Generalized linear models were applied to investigate associations between six-month AUD indicators and 12-month AU and quality of life.

Results: Independent of AU at six-month, having one (vs. no) residual AUD symptom at six-month predicted a 12-month ‘slip’, i.e., exceeding a blood alcohol concentration of 0.05% at least once, (OR: 3.7, 95% CI: 1.5 – 9.0), heavy episodic drinking, and hazardous use (p<0.05). AUD remission was associated with a lower risk of a ‘slip’ at 12-month (p<0.05). Failed reduction/cessation was associated with worse physical health (Coef.: -0.4, 95% CI -0.7 – -0.1).

Conclusion: For older adults, residual AUD symptoms in the first months after short-term treatment predict problematic AU outcomes within the first 12 months after treatment entry. Residual symptoms should therefore be addressed in post-treatment screenings.
1. Introduction

Treating alcohol use disorders (AUD) in older adults (OA) is an important public health challenge, given aging western societies and increasing prevalence rates of AUD among OA (Han et al., 2017). Research on OA shows that interventions for AUD and problematic AU are at least as effective in this age group as among younger adults (Satre et al., 2004, Lemke and Moos, 2003, Lemke and Moos, 2002, Oslin et al., 2002, Oslin et al., 2005). In the context of increasing need for AUD interventions in this age group, short-term outpatient AUD treatments may become increasingly important. Such treatments are feasible for OA; however, relapse rates in the first 12 months after such treatment are considerable (Andersen et al., 2020).

To prevent long-term relapse, follow-up assessments after short-term treatment completion could identify patients in need of additional support such as a stepped-care approach (Coulton et al., 2017). This calls for the identification of prognostic factors for a problematic course of AUD in the first year after treatment. Specific DSM-5 AUD symptoms, DSM-5 AUD severity, and remission could be meaningful post-treatment outcomes in addition to the commonly used indicators abstinence and drinking reduction (Søgaard Nielsen, 2018) for several reasons. As pointed out by Kiluk et al. (2018), AUD are defined by specific symptoms, not by amount of alcohol use (AU). Thus, it would be clinically meaningful to assess their status at the end of treatment. Also, specific AUD symptoms, such as craving or loss of control, could represent neurobiological changes resulting from AUD that in turn cause greater difficulty in controlling impulses to drink (Wiers et al., 2013). From a practical perspective, DSM-5 AUD symptoms can inform measurement-based care approaches. They also could be especially informative for the substantial number of patients with AUD who do not have an abstinence goal (Schippers and Nelissen, 2006, Bottlender and Soyka, 2005) but prefer interventions that permit a moderation goal. In the context of moderation as a goal, AUD symptoms could potentially provide important prognostic information. For example, some studies on the course of AU after AUD treatment find that a large proportion of patients with low risk drinking after treatment show favorable long-term outcomes (either low-risk use or abstinence) (Kline-Simon et al., 2017) and that reductions in the level of drinking are likely maintained (Witkiewitz et al., 2020, Mejldal et al., 2021). Still, studies also find variability in the course of low-risk consumption, with small to substantial proportions transitioning from ‘low risk’ or ‘controlled’ consumption to either abstinence or problematic consumption (Bottlender et al., 2007, Kline-Simon et al., 2013, Mejldal et al., 2021). One may speculate whether some transitions from low-risk drinking to abstinence take place because patients feel that maintaining consumption...
without losing control becomes too challenging. Investigating DSM-5 AUD symptoms at the end of
treatment could help identify prognostic factors that are associated with a greater risk of
problematic AU after AUD treatment. This, in turn, could help patients making informed decisions
regarding the choice of abstinence or low-risk consumption goals.

Among adults aged 18+, DSM-5 AUD severity and DSM-5 AUD symptom count at
posttreatment have been shown to predict fewer days of abstinence and more heavy drinking days at
six-month follow-up (Kiluk et al., 2018). This knowledge may not generalize to OA. OA are more
vulnerable to the detrimental effects of intense AU (Barry and Blow, 2016). They experience
prognostic factors at the end of treatment particular to their life stage (e.g., role transitions, spousal
loss, economic challenges) that differs from middle-age and early-adult life (Kuerbis, 2020). In
addition, AUD among OA may be sustained from middle age, as OA with AUD are at substantial
risk for AUD persistence (Verges et al., 2012, Dauber et al., 2018). These circumstantial factors in
OA may either raise or lower the bar for a prognostic factor to have an impact.

Of interest from a harm-reduction perspective, studies among adults aged 18+ indicate that
some treatment non-responders (i.e., individuals who still drink heavily) can have levels of
functioning comparable to treatment responders (Wilson et al., 2016). In order to gain information
on the validity of residual AUD symptoms among OA as prognostic factors at the end of treatment,
it is important to establish whether they predict not only subsequent alcohol consumption but also
psychosocial functioning (Witkiewitz et al., 2020).

We aimed to investigate in OA with DSM-5 AUD 1) the prediction of drinking behaviors
and quality of life 12 months after treatment initiation by six-month DSM-5 AUD symptoms, AUD
severity, and AUD remission, and 2) whether these DSM-5 AUD indicators offer additional
prognostic information when controlling for AU at six-month. We hypothesized that remaining
symptoms, greater AUD severity, as well as not achieving DSM-5 AUD remission at six-month
would be associated with a greater risk of drinking behaviors and lower quality of life at 12-month.

2. Methods

2.1 Study design

The ELDERLY-study is an international, multicentric, single-blinded, randomized-controlled
clinical trial (ClinicalTrials.gov database; NCT02084173 (National Institutes of Health, 2016)).
Detailed information on ELDERLY has been provided (Andersen et al., 2015, Andersen et al., 2020).

In short, the main study goal was to investigate the effects of two brief outpatient interventions in adults aged 60+ years with DSM-5 AUD. Inclusion criteria were: 1) age ≥60 years, 2) DSM-5 AUD, and 3) ability to understand the study procedures. Exclusion criteria were: 1) current psychotic symptoms, 2) acute severe major depression, 3) lifetime bipolar disorder, 4) current suicidal thoughts/behavior, 5) use of illegal opioids and/or stimulants, 6) past 30 days psychosocial alcohol treatment (pure medical detoxification allowed), and 7) having a legally authorized representative. Participants were randomized to either 1) four sessions of Motivational Enhancement Therapy (MET) or 2) up to 12 sessions, four MET-sessions plus up to eight sessions of Community Reinforcement Approach adapted for seniors (CRA-S). Both interventions were manualized and adopted from the COMBINE study (Arciniega et al., 2004). Abstinence was the main treatment goal, reduction was accepted in case participants did not want to become abstinent. ELDERLY was conducted between 2014 and 2017 by four research centers (Odense, Denmark; Albuquerque, United States; Munich and Dresden, Germany) which implemented the study at six sites in the three countries. Data were collected and managed with ‘Research Electronic Data Capture (REDCap)’ (Harris et al., 2009). ELDERLY was approved by the ethics committees at the research centers. Participants provided written informed consent before baseline.

Due to an implementation error, DSM-IV alcohol dependence instead of DSM-5 AUD was implemented as inclusion criterion at the US-site. To enable analyses based on DSM-5 AUD symptom criteria in the present study, we excluded the US-subsample (n=149) leading to a sample size of n=544 at baseline (62.7% from Denmark). Among these, response rates were 91.4% (n=497) at one-month1, 85.9% (n=467) at three-2, 75.9% (n=413) at six-, and 70.4% (n=383) at 12-month follow-up. Our main focus was on the prediction of AU-outcomes at 12-month follow-up by DSM-5 AUD severity, remission, and symptoms at six-month follow-up. Therefore, the analytical sample is based on those n=413 who participated in the six-month follow-up.

2.2 Diagnostic assessment

Baseline assessments were conducted face-to-face at research or treatment sites or participants’ homes. Six- and 12-month interviews were conducted face-to-face or by phone.

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1 End of MET
2 End of MET & CRA-S

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The Mini International Neuropsychiatric Interview (M.I.N.I.) version 5.0.0 (Lecrubier et al., 1997) was applied to assess DSM-5 AUD at baseline, six, and 12-month follow-up. Two questions on craving were added to the alcohol section for adaptation to DSM-5 (American Psychiatric Association, 2013). Information on AU-patterns were obtained with Form 90 (Miller and Del Boca, 1994), information on quality of life with the WHOQOL-BREF (The WHOQOL Group, 1998).

2.3 Variables used in the analysis

DSM-5 AUD: information on DSM-5 AUD was assessed at six-month follow-up which covered the time since last interview. The eleven single DSM-5 AUD symptoms and DSM-5 AUD remission were operationalized in accordance with DSM-5 (remission: no remaining symptom except craving) (American Psychiatric Association, 2013). DSM-5 AUD severity at six-month includes the categories no symptoms, one symptom (i.e., any one of the 11 DSM-5 AUD symptoms), mild (2-3 symptoms), moderate (4-5 symptoms), and severe (≥6 symptoms).

AU patterns were assessed for the past 30 days at six-month and at 12-month follow-up. They were operationalized as:

a) slip (exceeding a blood alcohol concentration\(^3\) of 0.05% at least once).

b) drinks per day (sum of standard drinks of 12 grams ethanol over all days with AU-information/number of days with AU-information),

c) heavy episodic drinking in seniors (≥36 grams ethanol in females; ≥48 grams in males on one day),

d) hazardous AU (exceeding the limits of an average of 12 grams ethanol per day in females and 24 grams in males) (German Federal Center for Health Education, 2017)

Quality of life: Quality of life was operationalized in agreement with the four WHOQOL-BREF domains physical health, psychological, social relationships, and environment. Higher values indicate better quality of life.

2.4 Missing values

Loss to six- and/or 12-month follow-up was not predicted\(^4\) by gender, age, country, treatment group, age at AUD onset, baseline AUD severity, employment and marital status (p≥0.05). At six-month follow-up, non-participation was less likely for those with a certificate for university entry

\(^3\) Determined by Form 90 and the Widmark formula

\(^4\) Results on missing values obtained with logistic regression for dichotomous outcomes, GLM (family specification: gamma, link function: log) for continuous outcome number of standard drinks per day.
vs. ≤ 9 years of education (p<0.05). At 12-month follow-up, non-participation was less likely for
both those with a certificate for university entry and those with 10 – 11 years of education (vs. ≤ 9
years, p<0.05). Missingness at follow-up due to non-participation was considered missing at
random (MAR).

**DSM-5 AUD criteria at six-month follow-up:** n=86/413 (21%) at six-month follow-up had at least
one missing value on DSM-5 AUD criteria. Missingness was not associated with any of the
following: gender, age, country, treatment group, AUD onset, employment, and education (p≥0.05).
Missingness was more likely for those being married or cohabitating vs. being single (p<0.05).
Missingness was associated with a lower risk of six- and 12-month heavy episodic drinking,
hazardous use, slip, and with less drinks per day. For example, at six-month, subjects with missings
on DSM-5 AUD criteria consumed 0.7 drinks per day (SD: 1.5), while those with information
consumed 3.2 (SD: 3.7). Cases with these missings were left out, leading to n=327 with more
intense AU compared to those excluded from the analyses.

**AU-information at six- and 12-month follow-up:** the maximum number of item-wise missings was
n=6.

**WHOQOL-BREF at six- and 12-month follow-up:** the maximum number of item-wise missings per
subscale was n=12 at six-month and n=16 at 12-month.

### 2.5 Statistical analysis
Analyses were conducted with the Stata Software package 16.0.
Logistic regression models were applied to predict dichotomous drinking outcomes at 12-month
follow-up by individual DSM-5 AUD symptoms, AUD severity, and AUD remission at six-month
follow-up. Generalized linear models (family: gamma; link function: log) were applied for the 12-
month outcome drinks per day. All analyses on AU outcomes were adjusted for gender, baseline
age, and country. In a separate step, we additionally adjusted for number of drinks/day at six-month
to investigate whether DSM-5 AUD indicators at six-month predicted 12-month AU independent of
six-month AU. For the outcome quality of life at 12-month, we conducted OLS and robust
regression analyses adjusted for baseline age, gender, country, and quality of life and number of
drinks/day at six-month. Results from the robust regression analysis are reported only in the cases
when it yielded different results than the OLS-models. In all analyses, treatment groups were
collapsed because the primary outcome analysis of ELDERLY did not reveal significant main
effects by treatment group (Andersen et al., 2020). Regression analyses were based on the n=327
with six-month DSM-5 criterion information; however, AUD symptoms were assessed at the six-month follow-up asking for symptoms ‘since last interview’, which was the three-month interview. To ensure identical time-periods for the assessment of the AUD symptoms, we excluded n=4 who did not participate in the preceding three-month follow-up interview from the regression analyses (n=323).

Missing values on the AU-outcomes and WHOQOL-BREF variables at 12-month (item-wise missings [up to n=14] or missings due to non-participation at follow-up [n=31/323]) were addressed by the MICE (multivariate imputation by chained equations) method of multiple multivariate imputation as recommended (Allison, 2009), since missings were assumed to be missing at random (MAR). We imputed dichotomous outcomes applying logistic regression and continuous outcomes using predictive mean matching (PMM). Furthermore, drinks per day at baseline and three-month follow-up, and demographic variables age, gender, marital status, and educational level were included as auxiliary variables in the imputation model. All auxiliary variables with missing cases were also addressed in the model, specifically missing cases of the two auxiliary variables ‘drinks per day’ at baseline and at three-month follow-up were imputed using PMM; and ordered logistic regression was utilized in the case of missing educational level. To control for regional differences each country was imputed separately. A total of 50 imputed datasets were generated and analyzed separately, and results were combined using the rules of Rubin (Rubin, 1987).

3. Results

3.1 Demographic information and DSM-5 AUD indicators at six-month follow-up

Among n=323 participants, 61.3% were male and 61.6% from Denmark. The mean age was 65.5 years (SD: 4.4; assessed at baseline). In terms of age and gender, the sample was comparable to national AUD patient data on OA from Germany and Denmark (Dauber et al., 2018, Danish Health Data Authority, 2016). At the six-month follow-up, 54.2% reported past 30 days hazardous use, 66.8% heavy episodic drinking, and 55.8% a ‘slip’. 31.6% reported no DSM-5 AUD symptoms, 10.8% one symptom, and 18.6% mild, 20.7% moderate, and 18.3% severe AUD. 35.9% fulfilled criteria for DSM-5 AUD remission. The most prevalent AUD symptoms at the six-month follow-up were lost control, failed reduction/cessation, consequences, and craving, ranging between 41.8% and 51.1% (see table 1).
3.2 Prediction of 12-month AU outcomes by six-month DSM-5 AUD features

Compared to an absence of all AUD symptoms, still having either one symptom, or mild, moderate, or severe AUD at six-month each predicted more drinks per day and a higher risk of a slip, heavy episodic drinking, and hazardous use at 12-month (p<0.05; see Table 2). Remission from DSM-5 AUD at the six-month follow-up was significantly associated with fewer drinks per day and a lower risk of a slip, heavy episodic drinking, and hazardous use at 12-month (p<0.05). Among the specific symptoms at six-month, tolerance and withdrawal predicted more drinks per day at 12-month. Interpersonal problems predicted slip, more drinks per day, and hazardous use. Lost control, failed reduction/cessation, consequences, and craving predicted more drinks per day and a higher risk of slip, heavy episodic drinking, and hazardous use\(^5\) at 12-month.

3.3 Adjustment for AU at six-month

After adjustment for number of drinks per day at six-months, DSM-5 AUD remission was still significantly associated with a lower risk for all 12-month outcomes. For DSM-5 AUD severity, all associations were retained, with one exception: for the category ‘severe AUD’ most associations were attenuated and non-significant. Regarding specific AUD symptoms, few associations (for failed reduction/cessation, craving, and physical/mental consequences) remained significant.

3.4 Prediction of 12-month quality of life by six-month DSM-5 AUD features

Six-month remission predicted better physical health at 12-month (Coef.: 0.5, 95% CI: 0.05 – 0.9; see Table 4). Failed reduction/cessation and moderate AUD (vs. no symptom) predicted worse physical health (Coef.: -0.4, 95% CI: -0.7 – -0.1; Coef.: -0.8, 95% CI: -1.3 – -0.3). Moderate AUD predicted worse social relationships (p<0.05). All other associations with quality of life were inconclusive (p>=0.05).

\(^5\) Use in hazardous situations and failure to fulfill obligations not included in the analysis because of low case numbers.
Using data from adults aged 60+ years with short-term treatment for DSM-5 AUD from two European countries, we found that DSM-5 AUD remission six months after treatment entry predicted a lower risk of 12-month problematic AU, even after adjusting for six-month AU. In contrast, reporting one DSM-5 AUD symptom, or mild, moderate or severe DSM-5 AUD six months after treatment entry was associated with a higher risk of problematic AU outcomes at 12-month. After adjustment for six-month AU, these associations remained significant for one DSM-5 AUD symptom, and for mild and moderate AUD. For severe AUD, associations were attenuated and no longer significant. Possible explanations for this surprising exception are elaborated on below. When we examined each individual AUD criterion, after adjusting for six-month AU, the majority of individual AUD symptoms at six-month did not predict 12-month AU-outcomes. Associations with quality of life were few and mostly related to physical health.

Six months after treatment entry, substantial proportions of the sample still experienced at least one residual AUD symptom, or even fulfilled criteria for mild, moderate, or severe DSM-5 AUD. Yet, compared to AUD symptom reports at baseline (Behrendt et al., 2018), symptom prevalence rates at six-month were considerably lower. From a harm reduction point of view (Witkiewitz et al., 2020), symptom reductions to, for example, as few as one symptom, can be considered a positive change. Focusing on the role of such treatment outcomes for future behaviors, our study indicates that even few symptoms that remain prevalent following treatment may propose a risk for problematic AU outcomes at 12-month.

The most prevalent symptoms at the six-month follow-up were craving, failed reduction/cessation, loss of control, and consequences. Comparable results were found in an intervention study without a focus on OA that offered interventions of comparable length (Kiluk et al., 2018).

Of note, AUD remission at six-month was associated with a reduced risk of all AU outcomes. Having one AUD symptom, mild, or moderate AUD, respectively, was associated with a higher risk of all AU-outcomes after adjusting for six-month AU; however, of note, almost all associations between severe AUD at six-month and 12-month outcomes were attenuated and non-significant after adjusting for six-month AU. It is unclear why associations for this category differ from those for the other, milder, categories. One may speculate that experiencing a high (instead of a low) symptom burden at six-month may have prompted further help seeking after six-month, and, in
consequence, further reductions in drinking up to the 12-month follow-up, which might explain this paradoxical finding. Alternatively, some OA with severe AUD may experience reversal of tolerance which can lead to reduced drinking in the presence of other symptoms (John et al., 2003).

Importantly, patients in this situation would still be in a very serious condition while actually drinking less.

Our findings indicate that AUD symptoms that are present at post-treatment are related to detrimental 12-month AU outcomes independent of the extent of post-treatment AU. Kiluk et al. (2018) showed in a sample of adults that post-treatment DSM-5 AUD criteria counts predicted fewer subsequent abstinence days and more intense subsequent AU. Our results add to this finding by demonstrating that there is an elevated risk for detrimental 12-month outcomes among OA related to not achieving remission or having even one single remaining symptom.

Epidemiological data show that a proportion of persons with prior-to-past-year DSM-IV alcohol dependence practice low-risk drinking and do not report AUD symptoms (Dawson et al., 2005). Among patients with AUD, attempting to maintain such a low risk use instead of abstinence can be stable (Kline-Simon et al., 2017), but it can also be followed by notable proportions of transitions either to abstinence or more intensive AU (Bottlender et al., 2007, Kline-Simon et al., 2013). It is largely unclear who can achieve stable low-risk AUD after treatment. Regarding our observations among OA, remaining symptoms may constitute an important predictor of disadvantageous post-treatment courses. This adds to the existing studies on AUD treatment for OA that demonstrate treatment effectiveness but also show considerable relapse rates after short-term outpatient interventions (Andersen et al., 2020, Satre et al., 2004, Lemke and Moos, 2003, Lemke and Moos, 2002). Informing older patients about remaining symptoms and associated risk could support informed decision making regarding choices between low-risk consumption or abstinence (Schippers and Nelissen, 2006).

Of interest, the most prevalent symptoms were loss of control, failed reduction/cessation, and craving. These criteria may represent neurobiological changes in AUD that underlie compulsive alcohol consumption behavior in AUD, in general (Everitt and Robbins, 2016, Kalivas and Volkow, 2005). This may explain the findings on the prediction of problematic AU outcomes by as few as one remaining symptom. Further treatment strategies aimed directly at reducing these symptoms might thus be warranted.
Associations between AUD symptoms and the WHOQOL-BREF scales were few and mostly related to physical health. The latter may be due to the greater physical vulnerability of OA (Barry and Blow, 2016). Individuals with heavy AU after treatment can differ widely in terms of functioning (Wilson et al., 2016). Here, remaining AUD symptoms predicted AU at follow-up, but, overall, did not predict quality of life. This may indicate that treatment outcome measures in AUD treatment should include AU, as well as AUD symptoms and functioning or quality of life because one measure alone may be insufficient.

Limitations

Results may not generalize to other treatment samples (e.g., inpatients, very old OA). The participation rate at the 12-month follow-up (70%) was about 14% lower than in another study on OA (Lemke and Moos, 2003); however, in our sample, attrition at 12-month was unrelated to most socio-demographic factors and multiple imputation was applied to deal with missings at 12-month as recommended (Allison, 2009). Missing information on DSM-5 AUD criteria at six-month led to exclusion of cases with less severe AU at six-month. Thus, our results show that DSM-5 AUD remission and residual symptoms can predict disadvantageous courses within a subsample with more severe consumption. Post-treatment AUD symptoms were assessed at six- but not at three-month; however, this allows for the exploration of the role of symptoms after the end of treatment, while the three-month assessment covers parts of the treatment period for MET & CRA-S. Case numbers did not permit post-hoc analysis on specific symptoms among those with only one symptom. Therefore, it remains unclear whether a specific symptom was driving the associations between this category and the AU outcomes. The assessment instruments applied here are well-established but not specifically adapted to OA (Andreas et al., 2013).

Implications

DSM-5 AUD remission and DSM-5 AUD severity (including a ‘one symptom’ category) should be adopted as additional standard outcome-measures in AUD interventions for OA that provide the option for a reduction goal. It should be acknowledged, however, that valid assessment of DSM-5 criteria in clinical practice requires appropriate training of staff in the use of a validated diagnostic instrument and would be more likely to occur if such an instrument were available free of charge for use in clinical settings. Not achieving remission, and, for some patients, having even one remaining symptom might indicate a risk of disadvantageous long-term AU outcomes. Patients

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should be informed about this risk in the context of psychoeducation and informed decision making.

Different options such as booster sessions, longer treatment, shifting from a moderation to an abstinence goal, behavioral retraining of approach tendencies, or continued support by means of internet-based or other remote interventions may offer additional support to older patients with remaining AUD symptoms (Kuerbis and Behrendt, 2020, Eberl et al., 2013, Andersen et al., 2020).

Future research needs to identify the factors that predict the occurrence of residual DSM-5 AUD symptoms at the end of interventions that accept reduction as a treatment goal. Future research could also address the long-term course of post-treatment AUD symptoms and associated levels of functioning and alcohol consumption.

5 Acknowledgement

We acknowledge the contribution of all study participants, therapists, interviewers, and student helpers.
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| Table 1: Alcohol use at six-month follow-up by DSM-5 alcohol use disorder severity, symptoms, and remission* |
|--------------------------------------------------|--------------------------------------------------|
| | % | Mean | SD |
| DSM-5 alcohol use disorder severity² | | | |
| No symptom | 31.6 | 0.9 | 1.5 |
| One symptom | 10.8 | 2.5 | 1.8 |
| Mild | 18.6 | 4.0 | 3.4 |
| Moderate | 20.7 | 4.6 | 3.8 |
| Severe | 18.3 | 5.2 | 4.8 |
| DSM-5 alcohol use disorder remission³ | | | |
| yes | 35.9 | 1.1 | 1.6 |
| no | 64.1 | 4.4 | 3.9 |
| DSM-5 alcohol use disorder symptoms | | | |
| Tolerance | 11.5 | 6.7 | 4.8 |
| Withdrawal | 22.3 | 5.3 | 5.0 |
| Lost control | 46.4 | 4.4 | 3.9 |
| Failed reduction/cessation | 47.1 | 4.5 | 3.9 |
| Much time | 14.9 | 4.8 | 4.6 |
| Activities | 17.0 | 5.1 | 4.6 |
| Physical/mental consequences | 41.8 | 4.9 | 4.2 |
| Roles | 7.1 | 4.7 | 4.4 |
| Hazardous situation | 3.7 | 4.6 | 4.3 |
| Interpersonal problems | 20.1 | 4.9 | 4.3 |
| Craving | 51.1 | 4.4 | 4.1 |

¹Follow-up prevalence at six-month follow-up (since last interview)
²In accordance with DSM-5: mild (2-3 symptoms), moderate (4-5 symptoms), severe (6+ symptoms)
³Remission of DSM-5 alcohol use disorder was defined as no symptom (craving permitted) since the last interview; out of n=116 with remission n=14 reported craving.

*based on n=323
Table 2: Associations between DSM-5 alcohol use disorder severity, symptoms, and remission at six-month and drinking behaviors at 12-month follow-up\textsuperscript{1}

<table>
<thead>
<tr>
<th>Six-month DSM-5 alcohol use disorder indicators\textsuperscript{2}</th>
<th>12-month drinking outcomes\textsuperscript{3}</th>
<th>Slip\textsuperscript{4}</th>
<th>Heavy episodic drinking\textsuperscript{5}</th>
<th>Hazardous use\textsuperscript{6}</th>
<th>Average number of drinks per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>DSM-5 alcohol use disorder remission\textsuperscript{7}</td>
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<td></td>
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<tr>
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<tr>
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<td>0.1 - 0.5</td>
<td>0.3</td>
<td>0.1 - 0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>DSM-5 alcohol use disorder severity\textsuperscript{8}</td>
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</tr>
<tr>
<td>No symptom</td>
<td>Ref.</td>
<td>Ref.</td>
<td>Ref.</td>
<td>Ref.</td>
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</tr>
<tr>
<td>One symptom</td>
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<td>1.7 - 9.9</td>
<td>4.8</td>
<td>1.8 - 12.6</td>
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<td>1.9 - 8.2</td>
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<td>2.0 - 9.2</td>
<td>5.8</td>
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<td>Moderate</td>
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<td>1.8 - 7.4</td>
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<td>1.9 - 7.9</td>
<td>4.9</td>
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<tr>
<td>Severe</td>
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<td>1.7 - 7.0</td>
<td>2.8</td>
<td>1.3 - 5.5</td>
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<td>0.6 - 2.9</td>
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</tr>
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<td>Withdrawal</td>
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<td>0.8 - 2.6</td>
<td>1.2</td>
<td>0.6 - 2.1</td>
<td>1.7</td>
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<td>Lost control</td>
<td>1.8</td>
<td>1.1 - 2.9</td>
<td>2.2</td>
<td>1.3 - 3.6</td>
<td>2.2</td>
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<tr>
<td>Failed reduction/cessation</td>
<td>2.4</td>
<td>1.4 - 3.8</td>
<td>2.9</td>
<td>1.7 - 4.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Much time</td>
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<td>0.6 - 2.3</td>
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<td>0.4 - 1.6</td>
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<td>Physical/mental consequences</td>
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<td>1.2 - 3.5</td>
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<tr>
<td>Hazardous use</td>
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<td>na</td>
<td>na</td>
<td>na</td>
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</tr>
<tr>
<td>Interpersonal problems</td>
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<td>1.008 - 3.3</td>
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<td>0.8 - 3.0</td>
<td>2.1</td>
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<tr>
<td>Craving</td>
<td>2.3</td>
<td>1.4 - 3.6</td>
<td>1.9</td>
<td>1.1 - 3.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

\textsuperscript{1} All analyses were adjusted for gender, baseline age, and country.
\textsuperscript{2} Based on n=323
\textsuperscript{3} Drinking outcomes in past 30 days before the 12-month follow-up interview
\textsuperscript{4} Defined as reaching a blood alcohol concentration of >0.05% at least once in past 30 days
\textsuperscript{5} Three or more standard drinks of 12 grams ethanol in women and four or more standard drinks in men on one occasion
\textsuperscript{6} Exceeding an average of 12 grams (women) or 24 grams (men) ethanol per day
\textsuperscript{7} Remission of DSM-5 alcohol use disorder was defined as no symptom (craving permitted) since the last interview
\textsuperscript{8} In accordance with DSM-5: mild (2-3 symptoms), moderate (4-5 symptoms), severe (6+ symptoms)
### Table 3: Associations between DSM-5 alcohol use disorder severity, symptoms, and remission at six-month and drinking behaviors at 12-month follow-up, adjusted for six-month alcohol use

<table>
<thead>
<tr>
<th>Six-month DSM-5 alcohol use disorder indicators</th>
<th>12-month drinking outcomes</th>
<th>12-month drinking outcomes</th>
<th>12-month drinking outcomes</th>
<th>12-month drinking outcomes</th>
<th>12-month drinking outcomes</th>
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</thead>
<tbody>
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<td></td>
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<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>exp(b) 95% CI</td>
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<td>0.4 0.2-0.7</td>
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<td>0.5 0.2-0.9</td>
<td>0.6 0.4-0.8</td>
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<tr>
<td>DSM-5 alcohol use disorder severity</td>
<td>3.7 1.5-9.0</td>
<td>4.0 1.5-10.6</td>
<td>3.7 1.4-9.5</td>
<td>2.2 1.2-3.7</td>
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</tr>
<tr>
<td></td>
<td>3.4 1.5-7.3</td>
<td>3.5 1.5-7.8</td>
<td>3.6 1.6-8.2</td>
<td>1.9 1.1-3.0</td>
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<tr>
<td></td>
<td>2.5 1.1-5.3</td>
<td>2.3 1.03-5.0</td>
<td>2.3 1.03-5.1</td>
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</tr>
<tr>
<td></td>
<td>2.2 0.9-4.8</td>
<td>1.4 0.6-3.2</td>
<td>2.0 0.8-4.5</td>
<td>1.9 1.1-3.1</td>
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<td>0.9 0.3-2.4</td>
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<tr>
<td>Withdrawal</td>
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<td>0.6 0.3-1.3</td>
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<tr>
<td>Lost control</td>
<td>1.4 0.8-2.3</td>
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<tr>
<td>Failed reduction/cessation</td>
<td>1.9 1.1-3.1</td>
<td>2.2 1.2-3.8</td>
<td>1.7 0.9-2.8</td>
<td>1.6 1.1-2.1</td>
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</tr>
<tr>
<td>Much time</td>
<td>0.9 0.4-1.8</td>
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<tr>
<td>Activities</td>
<td>1.0 0.4-1.9</td>
<td>0.7 0.3-1.3</td>
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<tr>
<td>Physical/mental consequences</td>
<td>1.9 1.1-3.2</td>
<td>1.3 0.7-2.3</td>
<td>1.5 0.8-2.6</td>
<td>1.5 1.1-2.0</td>
<td></td>
</tr>
<tr>
<td>Roles</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>Hazardous use</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>Interpersonal problems</td>
<td>1.3 0.6-2.5</td>
<td>1.0 0.5-2.0</td>
<td>1.3 0.6-2.5</td>
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<tr>
<td>Craving</td>
<td>1.7 1.01-2.8</td>
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<td>1.4 1.02-1.9</td>
<td></td>
</tr>
</tbody>
</table>

1. All analyses were adjusted for gender, baseline age, country, and average number of standard drinks per day at six-month follow-up
2. Based on n=323
3. Drinking outcomes in past 30 days before the 12-month follow-up interview
4. Defined as reaching a blood alcohol concentration of >0.05% at least once in past 30 days
5. Three or more standard drinks of 12 grams ethanol in women and four or more standard drinks in men on one occasion
6. Exceeding an average of 12 grams (women) or 24 grams (men) ethanol per day
7. Remission of DSM-5 alcohol use disorder was defined as no symptom (craving permitted) since the last interview
8. In accordance with DSM-5: mild (2-3 symptoms), moderate (4-5 symptoms), severe (6+ symptoms)
Table 4: Associations between DSM-5 alcohol use disorder severity, symptoms, and remission at six-month and WHOQOL-BREF at 12-month follow-up

<table>
<thead>
<tr>
<th>Six-month DSM-5 alcohol use disorder indicators</th>
<th>12-month WHOQOL-BREF outcomes</th>
</tr>
</thead>
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<tr>
<td></td>
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<td>Coef.</td>
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<tr>
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<td>0.5</td>
</tr>
<tr>
<td>No symptom</td>
<td></td>
</tr>
<tr>
<td>One symptom</td>
<td>-0.3</td>
</tr>
<tr>
<td>Mild</td>
<td>-0.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>-0.8</td>
</tr>
<tr>
<td>Severe</td>
<td>-0.2</td>
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<tr>
<td>Tolerance</td>
<td>0.2</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>0.01</td>
</tr>
<tr>
<td>Lost control</td>
<td>-0.3</td>
</tr>
<tr>
<td>Failed reduction/cessation</td>
<td>-0.4</td>
</tr>
<tr>
<td>Much time</td>
<td>0.1</td>
</tr>
<tr>
<td>Activities</td>
<td>-0.1</td>
</tr>
<tr>
<td>Physical/mental consequences</td>
<td>-0.2*</td>
</tr>
<tr>
<td>Roles</td>
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<tr>
<td>Hazardous use</td>
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<tr>
<td>Interpersonal problems</td>
<td>-0.1</td>
</tr>
<tr>
<td>Craving</td>
<td>-0.1</td>
</tr>
</tbody>
</table>

1 All analyses were adjusted for gender, baseline age, country, WHOQOL-BREF score at six-month and average number of standard drinks per day at six-month
2 Based on n=323
3 Remission of DSM-5 alcohol use disorder was defined as no symptom (craving permitted) since the last interview
4 In accordance with DSM-5: mild (2-3 symptoms), moderate (4-5 symptoms), severe (6+ symptoms)
5 Not applicable due to low case numbers
*result from robust regression; all other results from linear regression

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