Controlled drinking – non-abstinent versus abstinent treatment goals in alcohol use disorder:

A Systematic Review, Meta-Analysis and Meta-Regression

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Abstract

Background and Aims: The proportion of untreated patients with alcohol use disorder (AUD) exceeds that of any other mental health disorder and treatment alternatives are needed. A widely discussed strategy is to depart from the abstinence paradigm as part of controlled drinking approaches. This first systematic review with meta-analysis aims to assess the efficacy of non-abstinent treatment strategies compared with abstinence-based strategies.

Methods: CENTRAL, PubMed, PsycINFO, and Embase databases were searched until February 2019 for controlled (randomized and non-randomized) clinical trials (RCTs and non-RCTs) among adult AUD populations, including an intervention group aiming at controlled drinking and a control group aiming for abstinence. Following PRISMA and Cochrane guidelines, literature search, data collection and risk of bias assessment were carried out independently by two reviewers (PROSPERO Registration-No.: CRD42019128716). The primary outcome was the proportion of participants consuming alcohol at or below the recommended threshold. Secondary outcomes were social functioning, drinking reductions, abstinence rates and dropouts. Using random effects models, RCTs and non-RCTs were analyzed separately. Sensitivity and subgroup analyses accounted for methodological rigor, inclusion of goal-specific treatment, length of follow-up and AUD severity.

Results: Twenty-two studies (including five RCTs) with 4,204 patients were selected. There was no statistically significant difference between both treatment paradigms in RCTs [odds ratio: 1.32 (95%CI: 0.51-3.39)]. Nonrandomized studies of free goal-choice favored

abstinence-orientation [0.60 (0.40-0.90)], unless goal-specific treatment was provided [0.79 (0.40-1.56)] or in studies of low risk of bias [0.73 (0.49-1.09)] or with long follow-up [1.49 (0.78-2.85)]. Effect sizes were not clearly dependent on AUD severity. Abstinence- and controlled drinking interventions did not clearly differ in their effect on social functioning and drinking reductions.

Conclusions: Available evidence does not support abstinence as the only approach in the treatment of alcohol use disorder. Controlled drinking, particularly if supported by specific psychotherapy, appears to be a viable option where an abstinence-oriented approach is not applicable

Keywords

Alcohol Use Disorder, Abstinence, Controlled Drinking, Meta-Analysis, Meta-Regression

Introduction

Alcohol use disorders (AUD) and alcohol-related harm are among the most burdensome diseases both at individual and at societal levels[1]. With proportions of only around 20% of patients receiving treatment, the treatment gap for AUD exceeds that of any other mental health disorder[2–4]. This major unmet medical need, along with the limited efficacy of treatments applied, is emphasized in several National Treatment Guidelines for Alcohol-Related Disorders[5–7].

Reasons for a lack of successful treatment outcomes may include the severe nature of AUD but also the strong focus on abstinence in current treatment strategies. Given a rather small proportion of patients capable of, and/or willing to, achieve abstinence[5,8,9], it is imaginable that, under an abstinence paradigm, some patients and clinicians lose confidence in the effectiveness of treatments and are discouraged by the perception that abstinence is the

only viable goal. In what we sense as a gradual paradigm-shift in treatment recommendations in AUD, non-abstinence oriented treatment options, namely dose-reduction strategies, have been included as intermediate treatment goals into the UK National Institute for Health and Care Excellence (NICE) guidelines[6] and recommendations by the European Medicine Agency[10]. In addition to pharmaceuticals fostering abstinence (e.g. anti-craving drugs[11]), new pharmacological approaches, directed at reducing alcohol consumption (e.g. nalmefene), have been developed and absence of heavy drinking has now been accepted as an additional primary outcome for phase 3 pharmacotherapy trials of AUD by the US Food and Drug Administration (FDA)[12].

Since the beginning of the debate on non-abstinent AUD treatments, “controlled drinking (CD)” has been a controversial term[13]. We pragmatically choose “CD” to generally specify a treatment goal where patients are *aiming* for a sustained pattern of drinking within rationally pre-defined limits of low-risk consumption. This is beyond merely striving for “moderation” or “reduced drinking”. And, rather than assuming that any AUD-patient can return to such a sustained pattern of drinking, we emphasize that these interventions merely accept CD as a potential outcome and a valid goal alongside abstinence.

Serious concerns about CD approaches have repeatedly been put forward and acceptability among clinicians remains low[14,15]. This applies in particular to recommending CD as a final rather than intermediate goal, and to patients with alcohol dependence as opposed to harmful drinkers[16]. It is feared that CD may be against the best interests of individuals with AUD, harboring the risk of self-deception and the risk of undermining treatment attempts by offering and implementing an alternative to abstinence treatment, even though the latter is currently known to be associated with the least risk of harm for the patient[17,18]. At the same time, a number of clinical trials showed improvements and rates of remission to low-risk drinking with non-abstinent treatment strategies[19–21]. From a medical viewpoint it is also evident that drinking reductions decrease the risk of adverse consequences[9,17,22–26].

So far, it is unclear how useful a treatment goal of CD is relative to approaches aiming for abstinence: trials yielded contradictory results[19,27] and, in part, are circular since defining abstinence as primary outcome favors abstinence-oriented treatments. The American Psychiatric Association (APA) has recently emphasized the lack of evidence regarding the comparison of CD and abstinence approaches and, related, regarding goal-choice paradigms in general[7]. To our knowledge, no systematic review including meta-analysis has been published. The present work therefore is the most comprehensive attempt *aiming to* estimate the comparative efficacy of CD approaches in relation to abstinence paradigms with regards to 1.) alcohol consumption measures, as well as 2.) drinking-related and social outcomes, while 3.) accounting for treatment and patient characteristics, namely disorder severity, goal-specificity of treatment and definition of treatment goal.

Methods

This is a systematic literature review and meta-analysis. We registered the study protocol on the International prospective register of systematic reviews PROSPERO (CRD42019128716). Methods followed guidelines by the Cochrane Collaboration for the conduction of systematic reviews[28] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[29].

Eligibility criteria – participants, intervention and control groups

We included prospective follow-up studies comparing the efficacy of non-abstinent versus abstinent treatment regimens, using samples of adult patients (≥18 years) with alcohol dependence or alcohol abuse/harmful use diagnosed according to standard operationalized criteria (i.e. Research Diagnostic Criteria, DSM-III, DSM-III-R, DSM-IV, DSM-IV-TR, DSM-5, or ICD-10). All treatment interventions aiming at controlling alcohol consumption (CD paradigms) on a non-abstinent basis were eligible.

We excluded studies that did not include a comparison group that aimed for abstinence. Concomitant pharmacological interventions were not an exclusion criterion, as long as these were given to both intervention- and comparator-groups.

Following recommendations by the Cochrane Collaboration[28], two reviewers independently carried out the screening of the references retrieved from the electronic databases (JH, MM), applying the pre-defined inclusion/exclusion criteria (see above), first by considering all information provided in title and abstract, and then reading the full text of relevant studies.

Outcomes

By definition, intervention and comparison groups are aiming for different outcomes (abstinence (AB) vs. CD) and outcomes for this study had to reflect both treatment goals. The primary outcome was defined as the difference in the probability of achieving CD between the subjects in the CD-oriented and AB-oriented study arms, with CD defined as low-risk drinking within recommended limits (following author's most rigorous definition), *including abstinence*. As recommended limits for low-risk drinking may differ, we decided on adopting trials author's most rigorous, standardized definition that was most comparable to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) low-risk (non-binge) drinking levels[30] and WHO low- or medium-risk drinking levels[31]. This outcome can equally be reached by both interventions. However, health benefits may be higher with larger proportions of abstinent patients. In order to present the broader picture, we defined clinically relevant secondary outcomes, considering measures of social functioning, measures of alcohol consumption and drinking reductions, measures of abstinence and dropouts.

When a study provided data for more than one measure of treatment outcome, data for our primary outcome were considered using the following hierarchy: no drinking above recommended low-risk limits; no violations of a non-harmful, low-risk drinking goal (adopting trial author's definition); controlled, non-harmful drinking days.

Secondary outcomes were defined as: i) treatment difference in efficacy on social functioning (considering, in hierarchical order: legal problems, accidents, occupational status/employment, relationships, inventories of drinking problems/consequences), ii) treatment difference in efficacy on substantial improvement in drinking reduction (adopting trial author's definition), and iii) treatment differences in number of patients maintaining abstinence and abstinent days, in rates of subjects with relapse to heavy drinking and heavy drinking days (HDD), in drinks per drinking day (DDD), and in dropouts.

Literature Search

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) until February 18th, 2019. CENTRAL is focused on randomized and non-randomized controlled studies. It comprises, among other sources, articles indexed in MEDLINE, PsycINFO, and Embase databases as constantly screened by the Cochrane Drugs and Alcohol Group (CDAG), following the Cochrane Highly Sensitive Searches. Additionally, we searched MEDLINE, PsycINFO and EMBASE from October 2018 onwards, as recommended by the CDAG (personal communication) to identify studies that could have been missed due to a possible time lag in CDAG's screening schedule. In these searches, we used generic search terms for alcohol-use and drinking, combined with generic terms for abstinence and non-abstinent or controlled-drinking approaches (for explicit search entry, see Supplement Figure S1). We supplemented the search by carrying out reference searches of all eligible articles, relevant review articles, and the "Mesa Grande Project" database, which was systematically updated on clinical trials for AUDs up to 2001[32,33]. No further restrictions (e.g., for language or time period) were applied.

Data collection

Two researchers abstracted data from the original studies (JH, HC). Unclear cases were solved by discussion with the senior author (CB). We retrieved data on the association between treatment goal and achieving successful treatment outcomes (e.g. odds ratio (OR), or success rates and total N per group), with respective measures of statistical dispersion. If

a trial provided data for more than one timepoint per outcome, the longest follow-up was included for every outcome in our main analyses. For nonrandomized studies, we primarily extracted outcome data based on a goal-choice at study-*entry*, if available. If data were presented in figures only, values were extracted using Engauge Digitizer 11.2 MacOSX (M.Mitchell). Additionally, information on the following characteristics were retrieved from each of the included studies: randomization procedure, goal-choice and switching of goals throughout follow-up, treatment intervention and goal-specificity of treatment, definition of the CD goal, proportion of patients with alcohol dependence in the study sample, additional psychopharmacological treatment and the proportions of female and male participants.

Risk of bias assessment

In accordance with the Cochrane Handbook[34], methodological rigor of studies was assessed using the Cochrane risk of bias tool for randomized controlled trials (RCTs) and the Newcastle Ottawa Scale[35] for nonrandomized studies. Judgments for each study were duplicated (JH, HC). Additionally, a global rating for each study was conducted, considering those studies in the highest third of summary rating scores to be of "lower" risk of bias.

Data analysis

Analyses are based on intention-to-treat (ITT) populations. If no ITT data were available, we included results on completer- or per-protocol populations, in this order. Study arms characterized by an imposed goal of abstinence due to baseline factors (such as particularly severe AUD) were excluded from our comparisons (applicable for Booth et al. 1984[36]).

Summary effect estimates were calculated on the odds ratio scale (OR and 95%-CI) using random-effects models (DerSimonian and Laird method), as the studies differed in several methodological aspects, such as diagnostic criteria and specific interventions employed. Effect sizes from different, non-overlapping subgroups of populations within a study were pooled using a fixed-effect model, as recommended in the Cochrane Handbook[34] (three-level meta-analytic approach). Heterogeneity among studies was quantified with the I^2

statistic. An α of .05 was considered statistically significant for the primary outcome. For all other analysis, *p* values are presented in an exploratory sense. Number Needed to Treat (NNT) was calculated for primary outcome analyses, using success rates of abstinence-oriented treatment arms as an approximation to the patient's expected event rate.

For the primary and the secondary outcomes, RCTs and non-randomized studies were analyzed separately. For the primary outcome, non-randomized studies were further analyzed in three consecutive steps, considering 1. all non-randomized studies, 2. those presenting data based on a goal-choice of CD within actually defined low risk limits, and 3. those providing goal-specific treatment intervention.

Sensitivity Analyses

For the primary outcome we conducted an additional sensitivity analysis in which, if not otherwise stated or accounted for within the trial, cases lost to follow-up were considered as treatment failures (i.e. "worst-case analysis").

Pre-specified subgroup and sensitivity analyses referred to: studies of higher methodological rigor; studies based on a CD goal within recommended (low risk) limits (as opposed to self-defined reduction or no specific goal at all); and studies offering goal-specific therapeutic intervention for patients in each group, respectively. To avoid undue reliance on single trials, in primary outcome sensitivity analyses, we removed all studies one by one from the analysis (leave-one-out analyses).

Meta-Regression and Moderator Analysis

In random-effects meta-regression for our primary outcome, we investigated associations of the studies' effect estimates (log OR) with baseline severity of AUD (rating each study by the proportions of dependent patients and "problem drinkers"/patients with harmful alcohol use), gender (percentage of female patients), and length of follow-up.

Publication bias

Possible publication bias for the primary outcome analysis was inspected assessing funnel plot asymmetry using Egger's test and by visually inspecting the funnel plot.

Analyses were conducted according to the Cochrane Collaboration Handbook[28] and using Comprehensive Meta-Analysis V3 (Biostat, Engelwood, New Jersey).

Results

After screening of titles and abstracts of 6,134 articles, 123 full-texts were assessed for eligibility. Of these, 22 studies, published between 1973 and 2017, were eligible for systematic review (Figure 1). Overall, the studies included 4,204 patients, 2,251 aiming for abstinence and 1,953 aiming for CD. 5 studies were RCTs[21,37–40], and one trial used a partially randomized design[41]. Sixteen studies allowed patients to choose their goal; 8 of these also allowed for switching of goal during treatment. All 5 RCTs and 9 of the nonrandomized trials provided goal-specific treatment interventions, i.e. abstinence-fostering treatment for patients aiming for abstinence and CD-fostering treatment for patients aiming for CD. The remaining trials merely assessed patients' personal goal but provided no specific or abstinence-oriented treatment only. Four studies did not define a goal of CD as aiming for drinking within defined limits and included patients without a specific goal or those aiming for any drinking reduction into the CD-oriented groups[19,42–44]. Seven studies included patients with alcohol dependence only; the remaining included patients with harmful use in varying degrees. Four trials included psychopharmacological treatment[42,44–47]. One study included women only[48], one men only[27] (Table 1). Individual definitions of the primary outcome for each study are presented in Supplement Table S2.

Primary Outcome

Defining treatment success as abstinence as well as controlled, low-risk drinking within recommended limits, the following effect sizes resulted when comparing patients in abstinence-oriented treatment arms with patients aiming for CD:

In all following analyses, an OR>1 favors CD-oriented study-arms.

a) Two RCTs were summarized to an effect size of OR: 1.32 (95%CI: 0.51-3.39; I^2: 0%). Quantitatively summarizing all of the five RCTs is impossible due to substantial methodological heterogeneity, and only two provided data suitable for our primary outcome. However, generally speaking, the remaining three RCTs showed no statistically significantly stronger effect for either treatment approach, but showed point estimates consistent with better outcomes in CD concerning alcohol consumption levels[39,40] and the percentage of patients that reduced their drinking[37]. Differential findings from all five RCTs are included in our secondary outcome analyses below.

b) 1. Of the nonrandomized (observational) studies assessing goal-choice, twelve provided data for our primary outcome and were summarized to an effect size of OR: 0.60 (95%CI: 0.40-0.90; I^2: 65.2%).

2. Among these, 10 studies based analyses on a goal-choice of CD within actually defined low risk limits (as opposed to no goal or any drinking reduction). These amounted to an OR of: 0.68 (95%CI: 0.43-1.08; I^2: 60.0%).

3. Of these, eight studies provided goal-specific treatment intervention (i.e. CD-fostering for CD groups and abstinence-fostering for AB groups), which were summarized to an effect size of OR: 0.79 (95%CI: 0.40-1.56; I^2: 68.0%).

Risk of bias

Summary ratings of methodological rigor of each study are presented in Table 1. the nonrandomized studies with the highest ratings (7 out of 18, with a score of 6 (range: 4-6)) were considered “lower” risk of bias (Supplement Figure S3).

Subgroup- and sensitivity analyses

In all following analyses, an OR>1 favors CD-oriented study-arms.

Single trials did not greatly influence the calculations as indicated by leave-one-out analyses.

In all nonrandomized studies of higher methodological rigor (i.e. lower risk of bias), the summary OR was 0.73 (95%CI: 0.49-1.09; I^2: 57.7%) (7 studies). Among nonrandomized studies providing goal-specific treatment intervention, those of lower risk of bias were summarized to an OR of 0.98 (95%CI: 0.44-2.20, I^2: 69,7%) (5 studies).

Broken down by group, and based on “worst-case”-analyses, 44.1% (95%CI: 30.3%-58.9%) of abstinence-oriented patients, and 34.0% (95%CI: 25.7%-43.3%) of CD-oriented patients successfully exercised low-risk drinking (13 studies). Taking into account studies that defined a CD-goal within limits and provided goal-specific interventions, success rates amounted to 39.9% (95%CI: 24.7%-57.2%) for abstinence-oriented patients, and 36.1% (95%CI: 28.5%-44.4%) for CD-oriented patients. Among nonrandomized studies of higher methodological rigor (low RoB only) providing goal-specific treatment intervention, success rates were: 37.6% (95%CI: 13.0%-70.9%) of abstinence-oriented patients, and 39.2% (95%CI: 33.8%-44.9%) of CD-oriented patients.

Meta-Regressions and Moderator Analyses

Length of follow-up

Meta-regression among studies (N=14) providing outcome data for subsequent lengths of follow-up yielded a statistically significant decrease in differences between abstinence-orientation and CD-approaches over time (primary outcome), and effects sizes tended in

favor of controlled drinking approaches with longer follow-up (statistically significant correlation (slope=0.0428; df=1; p-value(2-sided)=0.0204; R^2=0.25) between effects size and length of follow-up (Supplement Figure S4)). Among investigations of follow-up periods of more than 12 months (i.e. 24-42 months), the summary OR was 1.49 (95%CI: 0.78-2.85; I^2: 0%) (4 studies). No interaction between length of follow-up and AUD severity at baseline was observed. Attrition rates were not substantially different between studies of shorter and longer follow-up.

AUD Severity at Baseline

In trials including patients with alcohol dependence only, goal-choices did not differ statistically significantly in our primary outcome: OR 0.61 (95%CI: 0.29-1.27; I^2: 68.9%) (5 studies). Likewise, meta-regression of our primary outcome analysis did not indicate interaction of effect size and AUD severity (Supplement Figure S5).

Gender

Gender distribution in primary studies (as measured in percentage of female patients per study population) did not affect effect size (Supplement Figure S6).

Numerical results from primary outcomes, subgroup and sensitivity analyses are summarized in Table 2.

Secondary Outcomes

All secondary outcomes are presented in Figure 3.

i) In abstinence- and CD-oriented study arms, measures of social functioning improved equally. ii) Equal proportions of patients achieved substantial improvement in drinking reduction. Broken down by group, 58.8% (95%CI: 51.2%-65.9%) of abstinence-oriented patients, and 58.3% (95%CI: 51.1%-64.2%) of CD-oriented patients substantially improved regarding drinking severity. iii) Briefly, there were no clear-cut differences between abstinence-oriented and controlled drinking approaches. Dropouts tended to occur more

frequently in abstinence arms, whereas abstinence was observed more often, but not exclusively, in abstinence arms. By group, 21.2% (95%CI: 15.5%-28.3%) of abstinence-oriented patients, and 9.7% (95%CI: 5.9%-15.4%) of CD-oriented patients maintained abstinence at follow-up.

Publication Bias

Regarding indication of small study effects, there was no obvious funnel plot asymmetry upon visual inspection and using Egger's test (p=0.462; 2-tailed) (Supplement Figure S7).

Discussion

Our analyses yielded main results: *1.* With regard to controlled, low-risk use of alcohol, there was no statistically significant difference between abstinence- and CD-oriented approaches, based on data from the limited number of small RCTs. *2.* In nonrandomized studies analyzing free goal-choice behavior, no statistically significant difference was found when patients received goal-specific treatment interventions and the two approaches were observed to be of equal efficacy in the limited number of studies of higher methodological quality. With no specific or abstinence-based treatment intervention only, however, patients were more likely to achieve low-risk drinking when aiming for abstinence. *3.* Results on social parameters, improvements in drinking severity, relapse into heavy drinking, and drinks per drinking day indicated equal efficacy of either treatment modality. Additional findings suggest that achieving controlled, low-risk drinking is more likely when patients aim for drinking within recommended, low-risk limits than when they follow a self-defined reduction. Effect sizes in observational trials were dependent on length of follow-up and CD-oriented treatment were more effective in studies with a follow-up of two years and longer.

Implications

While one obvious inference of this investigation is the pressing need for high-quality RCTs in the future, clinicians and patients are *currently* facing clinical decision uncertainty regarding abstinence versus CD in the management of AUD. How can our results inform these decisions?

Our findings provide evidence to address some of the concerns that have been raised against the CD-paradigm. First, our results indicate that offering a goal of CD does not *per se* undermine patients' insight into necessary changes in behavior, as one third of patients returning to low-risk drinking in CD-oriented arms maintained abstinence. More generally, a substantial proportion of individuals initially choosing CD switched to a goal of abstinence in trials allowing for realignment. Accordingly, with CD, patients seem to be open to proposals for change, and previous work found that patient participation in drinking goal choice increases goal-commitment and self-efficacy[56], and goal-acceptance seems to be correlated to a positive outcome[57]. Second, there is no indication from our meta-regression that severity of AUD predicts whether a patient will do better under an abstinence-oriented or a CD treatment regimen, as the results did not change between patients with alcohol dependence and hazardous/harmful drinkers. Therefore, our results do not confirm the conventional wisdom that CD is only acceptable in non-dependent patients.

In general, neither RCTs nor observational studies provide clear-cut support for a focus on abstinence-oriented or on CD-oriented treatment approaches. Wide CIs, contradictory signals from summary effects, substantive heterogeneity in several of our analyses as well as only few and dated RCTs mean that the case is still out as to whether CD or abstinence-orientation are similar in efficacy.

To be sure, more often than not, abstinence is desirable from a medical point of view[17]. And clearly, patients are more likely to maintain abstinence with AB-oriented interventions. Even beyond that, our "worst case scenario" analysis indicates that a larger proportion of patients

will achieve controlled, low-risk drinking with a goal of abstinence (44% as opposed to 34% in CD-oriented arms). This analysis, however, entails patients in CD-oriented arms that were not aiming for low-risk drinking or that were offered no or abstinence-oriented treatments only, and 95%-CIs were overlapping. The more patients are provided with a goal-specific treatment, the more CD-orientation becomes a similarly effective approach. Still, 34% may be regarded a sizeable success rate in CD-arms with respect to the current low treatment rates in AUD. Even beyond that, if low-risk drinking levels are not achieved, numerically equal proportions of patients in AB-goal and CD-goal treatment arms will benefit from treatments by improvements in drinking severity. Consistent with our findings, accumulating evidence confirms the achievability of non-abstinent recovery and – importantly – the associated improvements in physical and mental health[26], mortality[17], psychiatric co-morbidity and quality of life[58,59], and social functioning[60,61]. Our findings seem particularly relevant to the field given the low acceptability of non-abstinent treatment goals among clinicians in several countries[14,15,62,63].

The unsatisfactory success of current abstinence-oriented treatments points to the need for refinement of, or alternatives to, such approaches. Our results suggest that CD, when accompanied by CD-fostering treatment intervention, is not inferior. In light of the remaining uncertainty and the experience in the field with the abstinence paradigm, CD may be seen as an option after abstinence has not been achieved or if patients are not at all willing to stop drinking altogether.

Strengths and Limitations

This study has several strengths, but it is also not without limitations. *First*, selection bias is unlikely to have affected our review, as our search strategy followed the recommendations by the CDAG, and beyond database screening we searched reference lists of reviews and previous systematic search efforts (e.g., “Mesa Grande Project”). We must acknowledge, however, the potential for studies to have been missed. *Secondary*, all steps of this review were duplicated, following best practice methods. We also put substantial effort in contacting

authors of relevant studies and received an unusual amount of feedback, including previously unpublished data. As a result, to our knowledge, this is the most comprehensive review on the topic to date. *Thirdly*, choice of the primary outcome was a challenge. Although reasonably pragmatic, it may still slightly be biased against abstinence strategies, because there may be more health benefit in groups with higher proportions of abstinent patients. Therefore, only with our secondary outcome analyses, we believe that our analyses present the full picture. *Fourthly*, our conclusions are limited by the limitations of primary studies. Many of them, especially the RCTs, date back more than 30 years. Several studies carried a high risk of bias, particularly nonrandomized studies. Those trials, however, allow to approximate the effect of goal-*choice* in a naturalistic setting and offer the opportunity to study treatment details in a hypothesis-generating fashion. *Fifthly*, our analyses include patients with various degrees of severity of AUD. Meta-regression and moderator analyses, however, adjusted for illness severity, because high disorder severity has been discussed as contra-indication to controlled drinking. Interestingly, this was not confirmed by our findings. *Sixthly*, we found moderate to substantial between-study heterogeneity in our main analysis (except for RCTs). Therefore, we used random effects, carried out numerous sensitivity and subgroup analyses of more homogeneous samples, and verified the robustness of results after leaving each study out. Even beyond that, our meta-regressions and moderator analyses pointed to the robustness of our findings. *Seventhly*, declining differences in efficacy with longer follow-up may be caused by higher dropout-rates in both treatment arms over time, resulting in decreased relative effect sizes between the two paradigms. Reassuringly, however, dropout-rates were not substantially different between studies of longer and those of shorter follow-up.

Conclusions

The present evidence does not unequivocally favor abstinence-based approaches in the treatment of AUDs. In fact, the few, and methodologically limited, RCTs point to equal efficacy of either strategy. While summary effects of nonrandomized controlled trials tended

to favor abstinence-based approaches short-term, CD-orientation proved to be non-inferior with specific treatment intervention, with ongoing follow-up and in studies of higher methodological rigor. The results, however, are marked by wide CIs and heterogeneity, indicating a need for sufficiently powered RCTs to guide clinical decision making. For now, CD, particularly if accompanied by specific psychotherapy support seems to be a viable option where an abstinence-oriented approach is not applicable.

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References

1. Organization WH. *Global Status Report on Alcohol and Health 2018*. World Health Organization; 2018. Accessed September 11, 2019. https://apps.who.int/iris/handle/10665/274603

2. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*. 2015;72(8):757-766. doi:10.1001/jamapsychiatry.2015.0584

3. Kohn R, Saxena S, Levav I, Saraceno B. The treatment gap in mental health care. *Bull World Health Organ*. 2004;82(11):858-866. doi:/S0042-96862004001100011

4. Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. *The Lancet*. 2019;394(10200):781-792. doi:10.1016/S0140-6736(19)31775-1

5. Mann K, Batra A, Hoch E, al. e. S3-Leitlinie "Screening, Diagnose und Behandlung alkoholbezogener Störungen" AWMF-Register Nr. 076-001. 2016. Published online 2016.

6. NICE - National Institute for Health and Care Excellence. Alcohol-use disorders: diagnosis, assessment and management of harmful drinking (high-risk drinking) and alcohol dependence | Guidance | NICE. Accessed September 13, 2019. https://www.nice.org.uk/guidance/cg115

7. American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder*. American Psychiatric Association Publishing; 2018. doi:10.1176/appi.books.9781615371969

8. Finn SW, Bakshi A-S, Andréasson S. Alcohol Consumption, Dependence, and Treatment Barriers: Perceptions Among Nontreatment Seekers with Alcohol Dependence. *Substance Use & Misuse*. 2014;49(6):762-769. doi:10.3109/10826084.2014.891616

9. Falk DE, O'Malley SS, Witkiewitz K, et al. Evaluation of Drinking Risk Levels as Outcomes in Alcohol Pharmacotherapy Trials: A Secondary Analysis of 3 Randomized Clinical Trials. *JAMA Psychiatry*. 2019;76(4):374-381. doi:10.1001/jamapsychiatry.2018.3079

10. EMA (European Medicines Agency). *Annual Report 2010 (Adopted by the Management Board June 28, 2011). EMA/306870/2011*.

11. Bschor T, Henssler J, Müller M, Baethge C. Baclofen for alcohol use disorder-a systematic meta-analysis. *Acta Psychiatr Scand*. 2018;138(3):232-242. doi:10.1111/acps.12905

12. Center for Drug Evaluation and Research. Alcoholism: Developing Drugs for Treatment. U.S. Food and Drug Administration. Published September 2, 2015. Accessed January 9, 2020. http://www.fda.gov/regulatory-information/search-fda-guidance-documents/alcoholism-developing-drugs-treatment

13. Marlatt GA, Larimer ME, Baer JS, Quigley LA. Harm reduction for alcohol problems: Moving beyond the controlled drinking controversy. *Behavior Therapy*. 1993;24(4):461-503.

14. Davis AK, Rosenberg H. Acceptance of non-abstinence goals by addiction professionals in the United States. *Psychol Addict Behav*. 2013;27(4):1102-1109. doi:10.1037/a0030563

15. Luquiens A, Reynaud M, Aubin HJ. Is controlled drinking an acceptable goal in the treatment of alcohol dependence? A survey of French alcohol specialists. *Alcohol Alcohol*. 2011;46(5):586-591. doi:10.1093/alcalc/agr083

16. Rosenberg H, Davis AK. Differences in the acceptability of non-abstinence goals by type of drug among American substance abuse clinicians. *Journal of Substance Abuse Treatment*. 2014;46(2):214-218. doi:10.1016/j.jsat.2013.07.005

17. Roerecke M, Gual A, Rehm J. Reduction of alcohol consumption and subsequent mortality in alcohol use disorders: systematic review and meta-analyses. *J Clin Psychiatry*. 2013;74(12):e1181-1189. doi:10.4088/JCP.13r08379

18. Batra A, Müller CA, Mann K, Heinz A. Alcohol Dependence and Harmful Use of Alcohol. *Dtsch Arztebl Int*. 2016;113(17):301-310. doi:10.3238/arztebl.2016.0301

19. Enggasser JL, Hermos JA, Rubin A, et al. Drinking goal choice and outcomes in a Web-based alcohol intervention: Results from VetChange. *Addictive Behaviors*. 2015;42:63-68.

doi:10.1016/j.addbeh.2014.10.036

20. Sanchez-Craig M, Annis HM, Bornet AR, MacDonald KR. Random assignment to abstinence and controlled drinking: evaluation of a cognitive-behavioral program for problem drinkers. *J Consult Clin Psychol*. 1984;52(3):390-403.

21. Graber RA, Miller WR. Abstinence or controlled drinking goals for problem drinkers: A randomized clinical trial. *Psychology of Addictive Behaviors*. 1988;2(1):20-33. doi:10.1037/h0080474

22. Hasin DS, Wall M, Witkiewitz K, et al. Change in non-abstinent WHO drinking risk levels and alcohol dependence: a 3 year follow-up study in the US general population. *Lancet Psychiatry*. 2017;4(6):469-476. doi:10.1016/S2215-0366(17)30130-X

23. Witkiewitz K, Kranzler HR, Hallgren KA, et al. Drinking Risk Level Reductions Associated with Improvements in Physical Health and Quality of Life Among Individuals with Alcohol Use Disorder. *Alcohol Clin Exp Res*. 2018;42(12):2453-2465. doi:10.1111/acer.13897

24. Nutt DJ, Gual A, Anderson P, Rehm J. Why Less Is Always More in the Treatment of Alcohol Use Disorders. *JAMA Psychiatry*. 2019;76(4):359-360. doi:10.1001/jamapsychiatry.2018.2807

25. Kline-Simon AH, Litten RZ, Weisner CM, Falk DE. Posttreatment Low-Risk Drinking as a Predictor of Future Drinking and Problem Outcomes Among Individuals with Alcohol Use Disorders: A 9-Year Follow-Up. *Alcohol Clin Exp Res*. 2017;41(3):653-658. doi:10.1111/acer.13334

26. Charlet K, Heinz A. Harm reduction—a systematic review on effects of alcohol reduction on physical and mental symptoms. *Addiction Biology*. 2017;22(5):1119-1159. doi:10.1111/adb.12414

27. Caddy GR, Addington HJ, Perkins D. Individualized behavior therapy for alcoholics: A third year independent double-blind follow-up. *Behaviour Research and Therapy*. 1978;16(5):345-362. doi:10.1016/0005-7967(78)90004-9

28. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Accessed September 12,

2019. http://handbook-5-1.cochrane.org/

29. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097

30. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Drinking Levels Defined. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Published September 14, 2011. Accessed January 10, 2020. https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking

31. World Health Organization. International guide for monitoring alcohol consumption and related harm. 2000;(WHO/MSD/MSB/00.4). https://apps.who.int/iris/handle/10665/66529

32. Miller WR, Wilbourne PL. Mesa Grande: a methodological analysis of clinical trials of treatments for alcohol use disorders. *Addiction*. 2002;97(3):265-277. doi:10.1046/j.1360-0443.2002.00019.x

33. Miller WR, Walters ST, Bennett ME. How effective is alcoholism treatment in the United States? *J Stud Alcohol*. 2001;62(2):211-220. doi:10.15288/jsa.2001.62.211

34. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook. Accessed October 21, 2019. https://training.cochrane.org/handbook/current

35. GA Wells, B Shea, D O'Connell, J Peterson, V Welch, M Losos, P Tugwell,. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Accessed September 12, 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

36. Booth PG, Dale B, Ansari J. Problem drinkers' goal choice and treatment outcome: A preliminary study. *Addictive Behaviors*. 1984;9(4):357-364. doi:10.1016/0306-4603(84)90035-2

37. Pomerleau O, Pertschuk M, Adkins D, Brady JP. A comparison of behavioral and traditional

treatment for middle-income problem drinkers. *J Behav Med*. 1978;1(2):187-200.

38. Sanchez-Craig M, Lei H. Disadvantages to Imposing the Goal of Abstinence on Problem Drinkers: an empirical study. *British Journal of Addiction*. 1986;81(4):505-512. doi:10.1111/j.1360-0443.1986.tb00362.x

39. Lee HS, Mericle AA, Ayalon L, Areán PA. Harm reduction among at-risk elderly drinkers: a site-specific analysis from the multi-site Primary Care Research in Substance Abuse and Mental Health for Elderly (PRISM-E) study. *International Journal of Geriatric Psychiatry*. 2009;24(1):54-60. doi:10.1002/gps.2073

40. Stimmel B, Cohen M, Sturiano V, Hanbury R, Korts D, Jackson G. Is treatment for alcoholism effective in persons on methadone maintenance? *Am J Psychiatry*. 1983;140(7):862-866. doi:10.1176/ajp.140.7.862

41. Orford J, Keddie A. Abstinence or controlled drinking in clinical practice: a test of the dependence and persuasion hypotheses. *Br J Addict*. 1986;81(4):495-504.

42. Adamson SJ, Heather N, Morton V, Raistrick D. Initial Preference for Drinking Goal in the Treatment of Alcohol Problems: II. Treatment Outcomes. *Alcohol Alcohol*. 2010;45(2):136-142. doi:10.1093/alcalc/agq005

43. Mowbray O, Krentzman AR, Bradley JC, Cranford JA, Robinson EAR, Grogan-Kaylor A. The effect of drinking goals at treatment entry on longitudinal alcohol use patterns among adults with alcohol dependence. *Drug Alcohol Depend*. 2013;132(0):182-188. doi:10.1016/j.drugalcdep.2013.01.018

44. Berger L, Brondino M, Fisher M, Gwyther R, Garbutt JC. Alcohol Use Disorder Treatment: The Association of Pretreatment Use and the Role of Drinking Goal. *J Am Board Fam Med*. 2016;29(1):37-49. doi:10.3122/jabfm.2016.01.150143

45. Bujarski S, O'Malley SS, Lunny K, Ray LA. The effects of drinking goal on treatment outcome for alcoholism. *Journal of Consulting and Clinical Psychology*. 2013;81(1):13-22.

doi:10.1037/a0030886

46. Dunn KE, Strain EC. Pretreatment alcohol drinking goals are associated with treatment outcomes. *Alcohol Clin Exp Res*. 2013;37(10):1745-1752. doi:10.1111/acer.12137

47. Mann K, Lemenager T, Hoffmann S, et al. Results of a double-blind, placebo-controlled pharmacotherapy trial in alcoholism conducted in Germany and comparison with the US COMBINE study. *Addiction Biology*. 2013;18(6):937-946. doi:10.1111/adb.12012

48. Al-Otaiba Z, Worden BL, McCrady BS, Epstein EE. Accounting for Self-Selected Drinking Goals in the Assessment of Treatment Outcome. *Psychol Addict Behav*. 2008;22(3):439-443. doi:10.1037/0893-164X.22.3.439

49. Simon J. Adamson JDS. Drinking goal selection and treatment outcome in out-patients with mild—moderate alcohol dependence. *Drug and Alcohol Review*. 2001;20(4):351-359. doi:10.1080/09595230120092670

50. Booth PG, Dale B, Slade PD, Dewey ME. A follow-up study of problem drinkers offered a goal choice option. *J Stud Alcohol*. 1992;53(6):594-600.

51. Haug S, Eggli P, Schaub MP. Drinking Goals and Their Association With Treatment Retention and Treatment Outcomes Among Clients in Outpatient Alcohol Treatment. *Subst Use Misuse*. 2017;52(3):313-321. doi:10.1080/10826084.2016.1225764

52. Hodgins DC, Leigh G, Milne R, Gerrish R. Drinking goal selection in behavioral self-management treatment of chronic alcoholics. *Addict Behav*. 1997;22(2):247-255.

53. Meyer A, Wapp M, Strik W, Moggi F. Association Between Drinking Goal and Alcohol Use One Year After Residential Treatment: A Multicenter Study. *Journal of Addictive Diseases*. 2014;33:234-242. doi:10.7892/boris.60149

54. Öjehagen A, Berglund M. Changes of drinking goals in a two-year out-patient alcoholic treatment program. *Addictive Behaviors*. 1989;14(1):1-9. doi:10.1016/0306-4603(89)90011-7

55. Vollmer H, Krämer S, Schneider R, Feldhege FJ, Schulze B, Krauthan G. Ein verhaltenstherapeutisches Programm zur Behandlung junger Alkoholabhängiger unter besonderer Berücksichtigung der Therapiemotivation. *Suchtgefahren*. 1982;28(1):1-15.

56. Lozano BE, Stephens RS. Comparison of participatively set and assigned goals in the reduction of alcohol use. *Psychology of Addictive Behaviors*. 2010;24(4):581-591. doi:10.1037/a0021444

57. Heather, Raistrick, Godfrey. A summary of the Review of the Effectiveness of Treatment for Alcohol Problems. Accessed November 3, 2019. https://scholar.googleusercontent.com/scholar?q=cache:1y1muVyp5pUJ:scholar.google.com/&hl=en&as_sdt=0,5

58. Hulse GK, Tait RJ. Five-year outcomes of a brief alcohol intervention for adult in-patients with psychiatric disorders. *Addiction*. 2003;98(8):1061-1068. doi:10.1046/j.1360-0443.2003.00404.x

59. Shaw GK, Waller S, Latham CJ, Dunn G, Thomson AD. THE DETOXIHCATION EXPERIENCE OF ALCOHOLIC IN-PATIENTS AND PREDICTORS OF OUTCOME. *Alcohol Alcohol*. 1998;33(3):291-303. doi:10.1093/oxfordjournals.alcalc.a008393

60. Gual A, Bravo F, Lligoña A, Colom J. Treatment for Alcohol Dependence in Catalonia: Health Outcomes and Stability of Drinking Patterns over 20 Years in 850 Patients. *Alcohol Alcohol*. 2009;44(4):409-415. doi:10.1093/alcalc/agp032

61. Kraemer KL, Maisto SA, Conigliaro J, McNeil M, Gordon AJ, Kelley ME. Decreased Alcohol Consumption in Outpatient Drinkers Is Associated with Improved Quality of Life and Fewer Alcohol-related Consequences. *Journal of General Internal Medicine*. 2002;17(5):382-386. doi:10.1046/j.1525-1497.2002.10613.x

62. Higuchi S, Maesato H, Yoshimura A, Matsushita S. Acceptance of controlled drinking among treatment specialists of alcohol dependence in Japan. *Alcohol Alcohol*. 2014;49(4):447-452. doi:10.1093/alcalc/agu036

63. Davis AK, Nickelsen T, Zucker RA, Bonar EE, Walton MA. Acceptability of nonabstinent treatment outcome goals among addiction treatment providers in Ukraine. *Psychol Addict Behav*. 2018;32(4):485-495. doi:10.1037/adb0000354

Figure 1: PRISMA Flow Chart

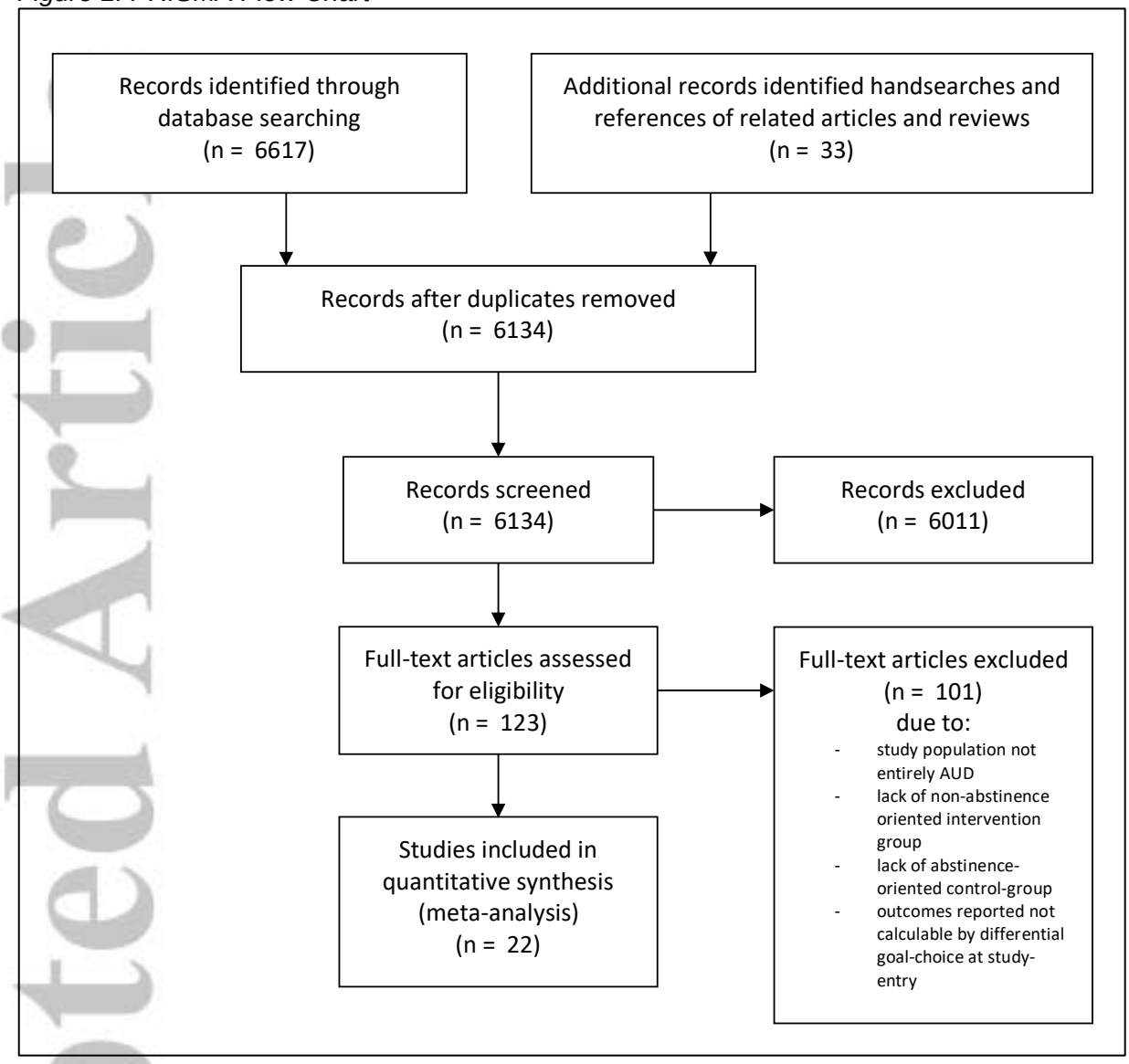


Figure 2: Forest Plot, Primary Outcome – Effect size between abstinence and CD oriented strategies, with treatment success defined as controlled, low-risk drinking within recommended limits, including abstinence.

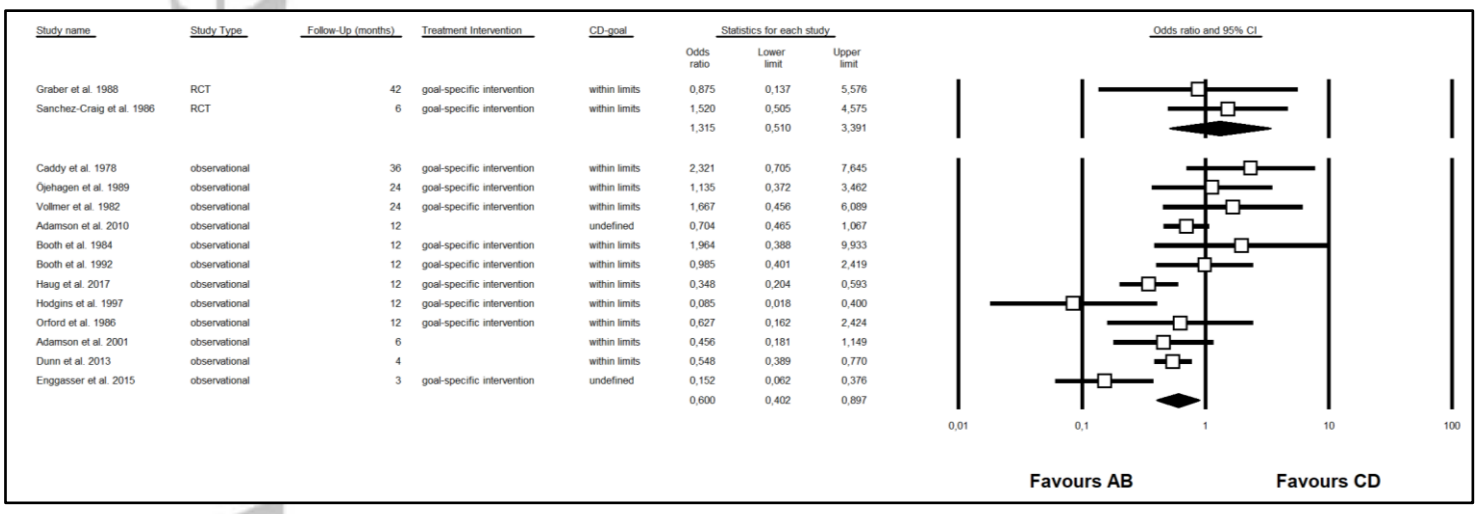
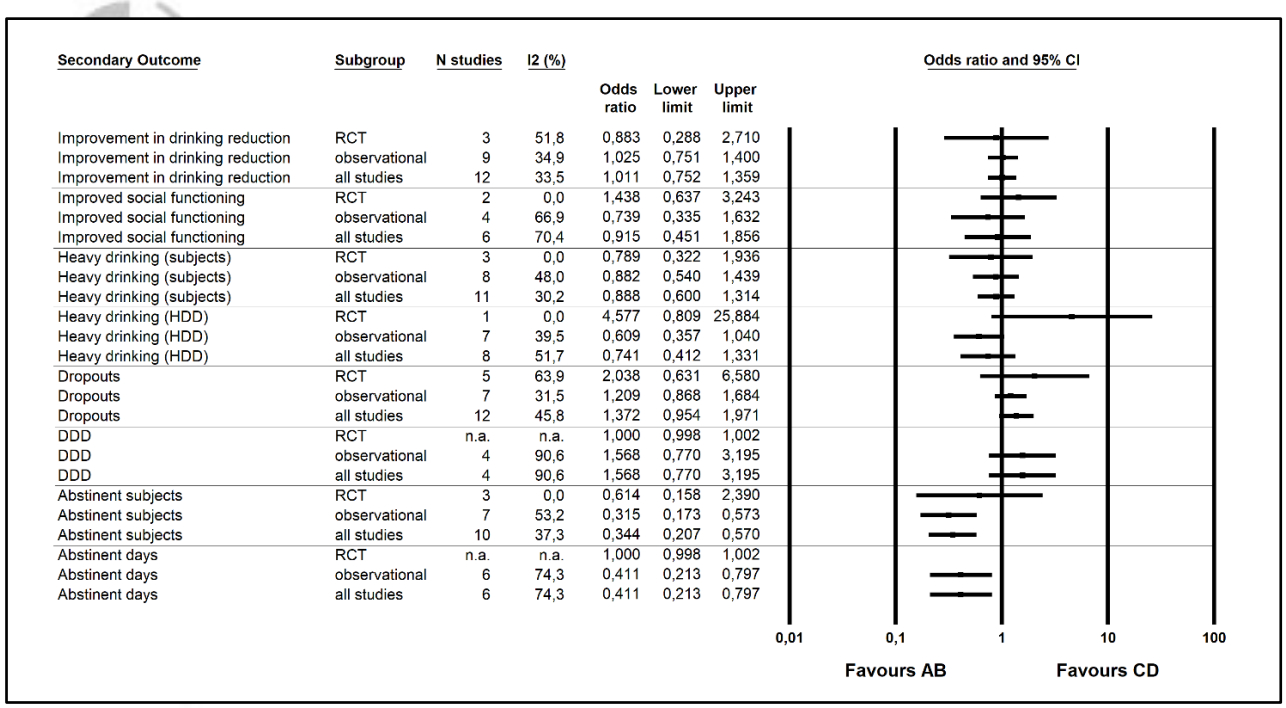


Figure 2: Studies grouped by study type (RCT, nonrandomized studies of free goal-choice(observational)), ordered by length of follow-up. Pooled effect sizes calculated per study type group. AB=abstinence, CD=controlled drinking, CI=confidence interval, RCT=randomized controlled trial. OR>1 in favor of CD arms.

Figure 3: Secondary Outcomes – Effect sizes for drinking-related outcomes between abstinence- and CD-oriented strategies



Secondary Outcome	Subgroup	N studies	I2 (%)	Odds ratio	Lower limit	Upper limit
Improvement in drinking reduction	RCT	3	51,8	0,883	0,288	2,710
Improvement in drinking reduction	observational	9	34,9	1,025	0,751	1,400
Improvement in drinking reduction	all studies	12	33,5	1,011	0,752	1,359
Improved social functioning	RCT	2	0,0	1,438	0,637	3,243
Improved social functioning	observational	4	66,9	0,739	0,335	1,632
Improved social functioning	all studies	6	70,4	0,915	0,451	1,856
Heavy drinking (subjects)	RCT	3	0,0	0,789	0,322	1,936
Heavy drinking (subjects)	observational	8	48,0	0,882	0,540	1,439
Heavy drinking (subjects)	all studies	11	30,2	0,888	0,600	1,314
Heavy drinking (HDD)	RCT	1	0,0	4,577	0,809	25,884
Heavy drinking (HDD)	observational	7	39,5	0,609	0,357	1,040
Heavy drinking (HDD)	all studies	8	51,7	0,741	0,412	1,331
Dropouts	RCT	5	63,9	2,038	0,631	6,580
Dropouts	observational	7	31,5	1,209	0,868	1,684
Dropouts	all studies	12	45,8	1,372	0,954	1,971
DDD	RCT	n.a.	n.a.	1,000	0,998	1,002
DDD	observational	4	90,6	1,568	0,770	3,195
DDD	all studies	4	90,6	1,568	0,770	3,195
Abstinent subjects	RCT	3	0,0	0,614	0,158	2,390
Abstinent subjects	observational	7	53,2	0,315	0,173	0,573
Abstinent subjects	all studies	10	37,3	0,344	0,207	0,570
Abstinent days	RCT	n.a.	n.a.	1,000	0,998	1,002
Abstinent days	observational	6	74,3	0,411	0,213	0,797
Abstinent days	all studies	6	74,3	0,411	0,213	0,797

Figure 3: Effect sizes between abstinence and controlled drinking strategies. AB=abstinence, CD=controlled drinking, CI=confidence interval, RCT=randomized controlled trial, observational=nonrandomized studies of free goal-choice, DDD= drinks per drinking day. OR>1 favors CD study-arms.

Table 1 – Characteristics of Trials

RCT

Author, year of publication (study name)	Study participants	Allocation of the intervention	Switching	N CD	N AB	Follow-up (months)	Interventions	Comment	Risk of bias
Graber et al. 1988[21]	Problem Drinkers, DSM-III alcohol abuse, all but 4 patients diagnosed alcohol dependence at some point in their lives	random		12	12	42	goal-specific PT, BSCT		RCT, some concerns
Lee et al. 2009[39]	Elderly at-risk drinkers	random		14	20	6	PT, per site: integrated care, moderation-based, MI, indivual versus enhanced referral, group, 12-step AB-based	no data on primary outcome; study authors' definition of outcomes: n. of drinks, n. of binge episodes	RCT, some concerns
Pomerleau et al. 1978[37]	Poblem drinkers	random		18	14	12	specific, per group	no data on primary outcome; study authors' definition of outcomes: percentage abstinent/reduced/unimproved	RCT, some concerns
Sanchez-Craig et al. 1984/86[38]	Problem drinkers, socially stable, but high intake consumption levels	random	AB to CD only	35	35	6	goal-specific PT, per group		RCT, low concerns
Stimmel et al. 1983[40]	Methadone maintenance patients being "active alcoholic" (Nat.Council on Alcoholism criteria (Am J Psych 1972))	random		42	42	(3-30)	specific, per group	no data on primary outcome; study authors' definition of outcomes: 1-/2-day alc. consumption, blood alc. level, clinic behavior	RCT, unknown/high concerns

Nonrandomized studies

Author, year of publication (study name)	Study participants	Allocation of the intervention	Switching	N CD	N AB	Follow-up (months)	Interventions	Comment	Risk of bias
Orford et al. 1986[41]	17 of 30 men and 9 of 16 women "definitively alcoholic" according to Rand criteria (approx. "alc dependence"), further 6 men and 5 women "border line alcoholic"	free goal-choice, randomization for those without strong preference		27	16	12	specific PT-intervention per group, brief vs. Intensive	strict criterion for success (cat. I only) for primary outcome	unknown/high
Adamson et al. 2001[49]	Mild-moderate alcohol dependence, exclusion of: severe dependence, history of withdrawal syndrome, sign. raised liver enzymes	free goal-choice	no diff. In retention during treatment, tendency towards CD afterwards up to 6 months	71	37	6	PT, MET(short-term) for 1/3 of patients, unspecific for CD or AB	additional treatment group not aiming for controlled drinking within recommended non-abusive limits was excluded from analyses	unknown/high
Adamson et al. 2010[42] (UKATT) (alt. reports: Heather et al. 2010, UKATT 2001)	Diagnosis of alcohol dependence or abuse according to DSM-IV criteria (American Psychiatric Association, 1994). Alcohol had to be the client's main problem for which help is sought.	free goal-choice; CD-goal without defined limits		339	403	12	PT, part MET(short-term), part SBNT, unspecific for CD or AB; disulfiram or acamprosate allowed - sign. differences in intake between goal-choice groups,	CD goal was not defined as within non-abusive limits	low
Al-Otaiba et al. 2008[48]	DSM-IV alcohol abuse or dependence, women only, 98% of samples alcohol dependence	CD gaol: 1 drink per week only		22	35	18	PT, abstinence-oriented treatment only	women only	unknown/high
Berger et al. 2016[44]	DSM-IV alcohol dependence, exclusion of withdrawal seizures and delirium tremens in history	goal: self-defined reduction in consumption, CD-goal without defined	(may have taken place, but pretreatment goal for outcomes)	62	37	3, representing post-discharge, no further follow-up	brief behavioral counseling, unspecific/individual for CD or AB, acamprosate or PLC	CD goal: self-defined reduction in consumption, no defined limits	unknown/high
Booth et al. 1984[36]	Problem drinkers, on average 2 out of 4 dependence score points	free goal-choice		12	15	12	PT, inpatient BSC individual	additional treatment group with severe symptoms being assigned to a goal of abstinence excluded from analyses	low
Booth et al. 1992[50]	Problem drinkers, most experienced withdrawal some more severe symptoms of physical dependence	free goal-choice	AB-goal 64% at baseline, 59% at discharge	41	59	12	PT, inpatient BSC individual		low
Bujarski et al. 2013[45] (COMBINE)	DSM-IV Alcohol dependence, patients drinking heavily for the 90-day period preceding study enrollment, no sign. signs of alcohol withdrawal	free goal-choice		346	506	4, representing post-discharge, no further follow-up	pharmacotherapy (naltrexone, acamprosate, PLC), MM alone or MM+CBI, abstinence-oriented treatment only	COMBINE study sample, MM alone vs. MM+CBI, pharmacotherapy	unknown/high

Author, year of publication (study name)	Study participants	Allocation of the intervention	Switching	N CD	N AB	Follow-up (months)	Interventions	Comment	Risk of bias
Caddy et al. 1978[27] (alt. reports: Sobell et al., Maisto et al.)	Gamma alcoholics, alcohol addiction, male only	free goal-choice		40	30	36 months	randomization to TAU, abstinence-oriented (control) or PT Behavioral Treatment (intervention)	men only; outcome data primarily extracted from the Caddy et al. report of the study (latest follow-up, independent author report)	low
Dunn et al. 2013[46] (COMBINE)	DSM-IV Alcohol dependence, pat. Who had been drinking heavily for the 90-day period preceding study enrollment, no sign. signs of alcohol withdrawal	free goal-choice		340	340	4, representing post-discharge, no further follow-up	pharmacotherapy (naltrexone, acamprosate, PLC), MM alone or MM+CBI, abstinence-oriented treatment only	COMBINE study sample, matched pairs	low
Enggasser et al. 2015[19]	Returning veterans, problem drinking, AUDIT-score between 8 and 25 for men and 5 and 25 for women (i.e. harmful or hazardous drinking but not likely to be heavily alc dependent)	free goal-choice; self-defined reduction in consumption, CD-goal without defined limits	71% retained goal AB, 76% retained goal CD,	265	40	3	Web-based cognitive behavioral intervention	subgroups initial goal-choice unchanged vs. initial choice switched; outcome is drinking within guideline-limits, but goal in moderation-arms: reduction irrespective of limits	unknown/high
Haug et al. 2016/17[51]	Outpatient alcohol treatment clients, alcohol consumption was main reason for treatment, at least 3 counselling sessions provided during treatment, mixed sample, partly aftercare following detoxication	free goal-choice		375	350	12	specific individual PT, MI, CBT, BSCM; outpatient treatment	separate outcome analyses for at-risk/non at-risk at baseline, partly non at-risk possibly more severely ill but detoxication prior to study entry	low
Hodgins et al. 1997[52]	Adults seeking treatment for alcohol problems, alcohol is the major problem substance with at least 10 years of alc problems, appropriateness for outpatient therapy; "clearly chronic alcoholics, long history + high MAST scores"	free goal-choice	89% retained goal AB, 51% retained goal CD,	34	69	12	individual PT, SM, individual self management training, outpatient treatment		unknown/high
Meyer et al. 2014[53]	Alcohol Use Disorder, ADS-Score on average 19 out of 36	free goal-choice	73% retained goal AB, 54% retained goal CD	53	99	12	PT, inpatient treatment, abstinence-oriented treatment only		unknown/high
Mowbray et al. 2013[43]	DSM-IV alcohol dependence	free goal-choice; CD-goal without defined limits: abstinence yes, no, maybe, don't know		54	217	12	specific intervention per treatment site, but independent of patients' goal choice (87% received abstinence-oriented treatment)		unknown/high
Mann et al. 2013[47] (PREDICT) (alt. report: Gueorguieva et al. 2014, personal contact with study authors (Mann, Hoffmann))	DSM-IV/ICD-10 alcohol dependence	free goal-choice;		31	167	n.a., survival analysis	pharmacotherapy (naltrexone, acamprosate, PLC), MM, abstinence-oriented		unknown/high
Öjehagen et al. 1989[54]	DSM-III alcohol dependence	free goal-choice	within 2 years, 20% of pop. from AB to CD, 24% back and forth, 56% always retained goal	18	32	24	individualized goal-specific (CD or AB) outpatient treatment	subpopulations: unchanged goal vs. final goal after switching	low
Vollmer et al. 1982[55]	alcoholics (according to KFA (Feuerlein et al. 1976)) (dependence or abuse), AUD on average persistent for 6 years, age 19-30 years, average daily consumption 210g ethanol (range 80-430g),	free goal-choice; goal-choice after abstinence phase (halfway during treatment)		42	16	24	individualized goal-specific (CD or AB) CBI, social competence training, outpatient treatment, average treatment duration 5 months		unknown/high

Table 1:
Studies ordered by study type (random or non-random allocation to intervention). AB=abstinence, alc.=alcoholalt=alternative, BSCT=behavioral self control training, Cat.=category, CBI=cognitive behavioral intervention, CBT=cognitive behavioral therapy, CD=controlled drinking, MET=motivational enhancement therapy, MI=motivational interviewing, MM=medical management, n.=number, PT=psychotherapy, RCT=randomized controlled trial, RoB=risk of bias, SBNT=social and behavioral network therapy, SM=self management training, TAU=treatment as usual, WC=worst case analysis,

Table 2: Numerical results – primary outcomes, subgroup and sensitivity analyses

Primary Outcome								
		OR	95%-CI	p	I^2 (%)	In favor of	NNT	N studies
RCT		1.32	0.51-3.39	0.57	0	CD	14	2
Non-RCT		0.60	0.40-0.90	0.013	65.2	AB	8	12
Subgroup and Sensitivity Analyses	CD goal within defined low-risk limits	0.68	0.43-1.08	0.099	60.0	AB	11	10
	goal-specific treatment intervention, CD goal within low-risk limits	0.79	0.40-1.56	0.492	68.0	AB	19	8
	low Risk of bias (Non-RCT)	0.73	0.49-1.09	0.119	57.7	AB	15	7
	goal-specific treatment intervention, low Risk of bias (Non-RCT)	0.98	0.44-2.20	0.967	69.7	AB	212	5
	alcohol-dependent patients only	0.61	0.29-1.27	0.183	68.9	AB	8	5
	follow-up 24-42 months	1.49	0.78-2.85	0.224	0	CD	12	4
Per group Analyses	AB oriented group Success Rate	95%-CI	CD oriented group Success Rate	95%-CI		In favor of	NNT	N studies
Worst case analysis	44.1%	30.3%-58.9%	34.0%	25.7%-43.3%		AB	9	13
CD goal within low-risk limits, goal-specific treatment intervention	39.9%	24.7%-57.2%	36.1%	28.5%-44.4%		AB	16	9
Goal-specific treatment intervention, low Risk of bias (Non-RCT)	37.6%	13.0%-70.9%	39.2%	33.8%-44.9%		CD	63	4

Table 2: Numerical results from primary outcomes, subgroup and sensitivity analyses. AB=abstinence, CD=controlled drinking, CI=confidence interval, NNT=number needed to treat, RCT=randomized controlled trial.