Addiction

REVIEW

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Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: a meta-analysis

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ABSTRACT

Background and Aims To review published studies on the effectiveness of combining cognitive-behavioural therapy (CBT) and motivational interviewing (MI) to treat comorbid clinical and subclinical alcohol use disorder (AUD) and major depression (MDD) and estimate the effect of this compared with usual care. **Methods** We conducted systematic literature searches in PubMed, PsycINFO and Embase up to June 2013 and identified additional studies through cross-references in included studies and systematic reviews. Twelve studies comprising 1721 patients met our inclusion criteria. The studies had sufficient statistical power to detect small effect sizes. **Results** CBT/MI proved effective for treating subclinical and clinical AUD and MDD compared with controls, with small overall effect sizes at post-treatment [$g = 0.17$, confidence interval (CI) = 0.07–0.28, $P < 0.001$ for decrease of alcohol consumption and $g = 0.27$, CI: 0.13–0.41, $P < 0.001$ for decrease of symptoms of depression, respectively]. Subgroup analyses revealed no significant differences for both AUD and MDD. However, digital interventions showed a higher effect size for depression than face-to-face interventions ($g = 0.73$ and $g = 0.23$, respectively, $P = 0.030$). **Conclusions** Combined cognitive-behavioural therapy and motivational interviewing for clinical or subclinical depressive and alcohol use disorders has a small but clinically significant effect in treatment outcomes compared with treatment as usual.

Keywords Alcohol use disorders, cognitive-behavioural therapy, comorbidity, major depression, meta-analysis, motivational interviewing, randomized controlled trials, treatment effect.

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INTRODUCTION

Alcohol use disorders (AUD) often co-occur with major depressive disorder (MDD), both in treatment and in general populations [1,2]. Among AUD treatment populations, comorbid depression can mount to 50% [3]. Similarly, MDD treatment populations have up to 40% lifetime probability of developing AUD [4,5]. Co-occurrence of AUD and MDD results in even greater disease burdens than the separate disorders [6]. Some of the burdens experienced by people with comorbid AUD and MDD are high morbidity and mortality levels, functional impairment and increased suicide risk [7]. Not surprisingly, the costs to society are substantial, owing to high levels of health-care consumption, inadequate treatment outcomes, high work absenteeism and lost productivity [8,9].

Combined treatment of comorbid AUD and MDD could hence be vitally important from a clinical and a public health viewpoint [10]. Combined treatment has never been common clinical practice [11]. The comorbid disorder was either not recognized or was not treated, under the assumption that it would resolve once the primary disorder was treated [12]. Today, a growing number of combined treatments for comorbid AUD and MDD are available; these include psychotherapeutic

treatments either as an adjunct to treatment as usual (TAU) or as an alternative to it [7,13,14].

Studies that have evaluated the impact of various psychotherapies—including cognitive-behavioural therapy (CBT [15]), Twelve-Step facilitation (TSF [16]) and motivational interviewing (MI [17])—on MDD or on AUD alone have found them effective. These therapies have also proved effective for subclinically depressed populations [18] and for populations that do not fulfil the DSM-IV criteria [19] for AUD but still experience problems with alcohol, such as those drinking beyond guidelines for low-risk drinking [20–22]. Integrated treatment approaches are often based on components of these CBT and/or MI interventions [23], mainly with a focus on both depression and alcohol, and with or without pharmacological intervention [14]. Brown and colleagues [24], for example, evaluated the effectiveness of a treatment intervention made up of components of the evidence-based CBT course Coping with Depression [25] and the cognitive-behavioural alcohol skills training components identified by Project Match [16].

Studies on the effectiveness of psychotherapy for people with comorbid AUD and MDD have shown promising results. A first indication of effectiveness came indirectly from the seminal meta-analysis by Nunes & Levin [26]. Their review of 14 studies assessed the impact of antidepressant medication in the treatment of comorbid MDD and substance use disorders (SUD) compared to placebo controls, with or without adjunct psychotherapies (some of which were manual-guided CBT). Antidepressant medication appeared effective for depression [$d = 0.38$; confidence interval (CI) = 18–58] and for alcohol reduction ($d = 0.25$; CI = 0.08–0.42). Subgroup analyses revealed that studies adding psychotherapeutic interventions in both experimental and control groups, such as the study by Roy-Byrne and colleagues in 2000 [27], showed a higher placebo response in the control groups than the set of studies without added psychotherapies, such as the study by Altamura and colleagues in 1990 [28]. The higher placebo response in the study by Roy-Byrne *et al.* and thus a lower between-group effect size was hence potentially explained by the psychotherapeutic interventions. Hides and colleagues [29] included 12 studies in their review, eight of which focused on comorbid alcohol and depression and four on depression and SUD. They found positive results for the effectiveness of psychotherapies, including CBT (either alone [30] or in combination with antidepressant medication [31]). They concluded, however, that the evidence was not yet strong enough, due to the small numbers of studies they had for their review, the diversity among them and the low methodological qualities of some. Such diversity was also seen in the systematic review by Baker and colleagues [32]. The Randall *et al.* study [33], for instance, evaluated the effectiveness of a CBT procedure focused on alcohol only in comparison with a combined CBT alcohol and social phobia treatment. Markowitz *et al.* [34] focused on the effectiveness of interpersonal psychotherapy for populations with comorbid AUD and dysthymia.

The results of these reviews suggest some preliminary evidence that psychological interventions (in particular CBT/MI) may be effective for treating co-occurring clinical or subclinical MDD and AUD. As no meta-analysis was yet available, we performed a review to gain evidence on the effectiveness of CBT/MI for treating such comorbid conditions. On the basis of the existing literature, we also expected that depression improvement would mediate an effect of CBT on alcohol improvement and vice versa [14,26]. We therefore also examined associations between depression and alcohol effect sizes.

To the best of our knowledge, this is the first meta-analysis of the impact of CBT/MI on the treatment of comorbid depression and AUD.

METHOD

Identification and selection of studies

We used a database of 1344 studies on the psychological treatment of depression. Details of this database have been described elsewhere [35]. It has been used in more than 30 published meta-analyses (see also http://www.evidencebasedpsychotherapies.org). It is updated continuously through comprehensive literature searches (from 1966 to January 2013). We examined a total of 13 407 abstracts in Pubmed (3320 abstracts), PsycInfo (2710), Embase (4389) and the Cochrane Central Register of Controlled Trials (2988). The abstracts were identified by combining terms indicative of psychological treatment and depression (both MeSH terms and text words). Primary studies from 42 meta-analyses of psychological treatment for depression were also examined for our database to ensure that no published studies were missed. From the 13 407 abstracts (9860 after removal of duplicates), 1344 full-text papers were retrieved for possible inclusion in the database. From these [which included 351 randomized controlled trials (RCTs)], we selected those papers that were suitable for our meta-analysis (see Fig. 1). We also identified studies on the basis of cross-references in these studies and references found in additional systematic reviews. We included studies that examined effects of CBT/MI on alcohol use (AUD, abuse or dependence) as assessed by diagnostic interviewing or by screening for scores above a cut-off point on a self-report alcohol measure (such as those based on guidelines for low-risk drinking; see Table 1). We followed a similar procedure for the assessment of depression. We did not apply any age or language

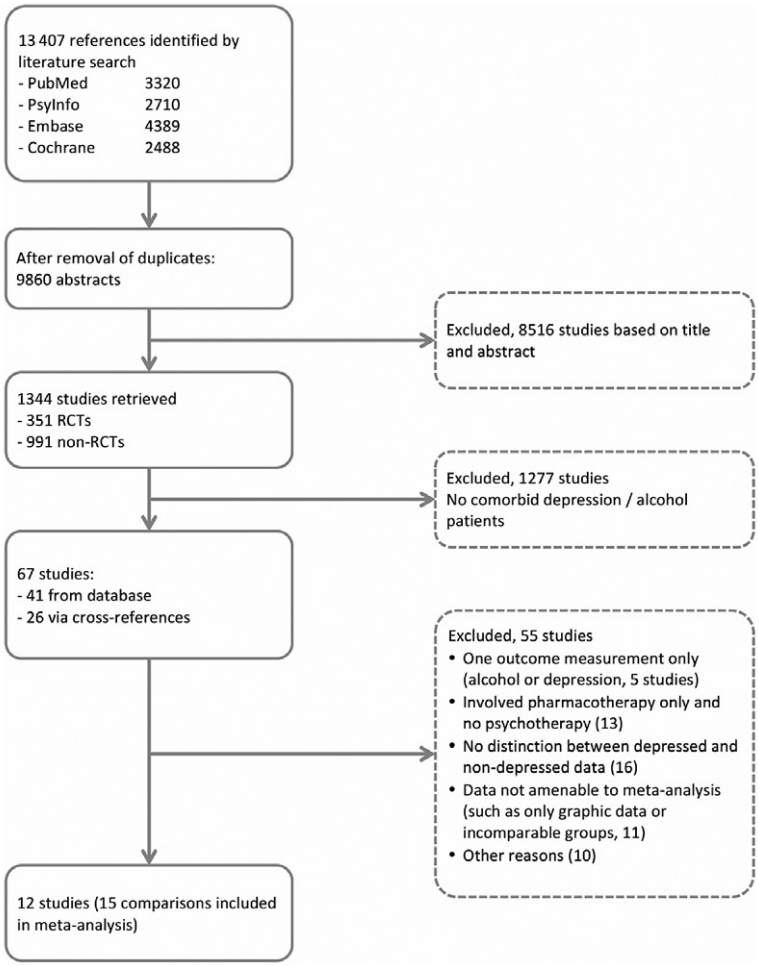

Figure 1 Flow-chart of study inclusion

restrictions. Our original search concentrated on randomized controlled trials focused on comorbid alcohol and depression. However, in due course it emerged that the number of RCTs in that domain was still limited and that a number of high-quality non-randomized studies were available. We therefore decided to include the latter in the meta-analysis. We included only randomized and non-randomized controlled studies in which (i) CBT/MI was compared with TAU or (ii) CBT/MI was compared with another psychological treatment. Comparative controlled studies were included only if allocation was not influenced by individual patients, therapists or researchers.

For studies with more than one post-treatment assessment, we used the earliest to ensure maximum consistency in follow-up durations. Our initial selection from the first search was based on information derived from titles, abstracts and keywords; if these yielded insufficient information to assess inclusion criteria, the full paper was retrieved. All papers were assessed independently on inclusion and exclusion criteria and quality by two independent raters (H.R. and J.d.W.). Any disagreement was resolved by discussion and consensus. Authors were approached ([8], H.R.) when relevant data were missing.

Quality assessment

We assessed the validity of the included studies using four criteria from the Risk of Bias Assessment tool, developed by the Cochrane Collaboration [36]. The tool (which can be applied to both randomized and non-randomized studies) verifies study attributes that are possible sources of bias, including adequate generation of the allocation sequence, concealment of the allocation to the different conditions, preclusion of knowledge of the allocated interventions (blinding of assessors) and handling of incomplete outcome data. We rated incomplete data handling as positive if intention-to-treat analyses were conducted (see Table 1).

Study characteristics

We coded characteristics of the analysed studies as described in Table 1.

Meta-analyses

We calculated mean effect sizes (Hedges's *g*) for each comparison, using the computer program Comprehensive

Table 1 Characteristics of included studies comparing cognitive-behavioural therapy/motivational interviewing (CBT/MI) plus treatment as usual (TAU) with TAU alone, or brief other psychological treatments.

Author, year, country	*Target group*	*Recruitment source*	*Inclusion criteria*	*Conditions*	*Intensity of treatment*	*n (% male)*	*Symptoms of depression outcome measures*	*Alcohol consumption outcome measures*	*Post-treatment (pt) and follow-up (fu) assessments*	*Study attrition (%)*	*Methodological qualities*
Agyapong 2012, 2013 [57,76] Ireland	Adults 18+ who completed in-patient double diagnosis programme	Clinic	1. DSM-IV MDD 2. DSM-IV AUD 3. MMSE ≥ 24	1. ICBT/MI mobile text messages + TAU 2. Placebo mobile text messages + TAU	1. 2 per day, 3 months 2. 2 per month, 3 months	1. 26 2. 28 (46%)	BDI-II	1. No. of days abstinent 2. No. of days to first drink 3. No. of drinks per drinking day 4. No. of patients abstinent	pt: 3 m fu: 6 m	pt: 7.4% fu:11%	1. Yes 2. Yes 3. Yes 4. Yes
Baker 2010 [30] Australia	Young adults ≥16	Media and referrals by health professionals	• BDI-II ≥ 17 • m ≥ 4/f ≥ 2 drinks per day in past month	1. CBT/MI-D 2. CBT/MI-A 3. iCBT/MI 4. Brief (control)	1. 9 × 1 hour 2. 9 × 1 hour 3. 9 × 1 hour 4. 1.5 hours	1. 71 2. 68 3. 75 4. 70 (53%)	BDI-II	1. Mean drinks p.w. 2. Mean drinking days p.w. 3. Max. no. of drinks per day 4. Mean drinks per day	pt: 4.5 m	pt: 16	1. Yes 2. Yes 3. Yes 4. Yes
Battersby 2013 [77] Australia	Adults 18+, out-patients (Vietnam veterans)	Referrals by health-care settings and media	• AUDIT ≥ 8 • Chronic condition (mental or physical)	1 CBT/MI + TAU TAU	6 × 2.5 hour –gr self-care manual	1. 46 2. 31 (100%)	HADS	1. AUDIT	pt: 9 m	pt: 6%	1. Yes 2. Yes 3. Yes 4. Yes
Brown 1997 [31] USA	Out-patients in substance use hospital programme (age range 27–58 years)	Clinic	• DSM-III-R alcohol dependence • BDI ≥ 10	1. CBT-D + TAU 2. Placebo control + TAU	1. 8 × 45 m 2. 8 × 45 m	1. 19 2. 16 (71%)	BDI MHAM-D POMS	1. % of days abstinent 2. Drinks per drinking day 3. % totally abstinent 4. % drinking heavily	pt: 3 m fu: 6 m	pt: 3 fu: 8.6	1. No 2. n.i. 3. No 4. No
Brown 2006 [24] USA	Out-patient veterans in double diagnosis programme (age range 31–68)	Clinic	• DSM-IV alcohol, cannabis and/or stimulant dependence • DSM-IV MDD	1. iCBT/MI (gr) + TAU 2. TSF (gr) + TAU	1. 36 × 1 hour 2. 36 × 1 hour	1. 48 2. 42 (92%)	HAM-D-21	1. % of days abstinent	pt: 6 m fu: 9, 12 m	pt: 26.7	1. Yes 2. No 3. No 4. No
Brown 2011 [78] USA	Out-patients aged 18–65 years in substance use programme	Clinic	• DSM-IV alcohol dependence • BDI ≥ 15	1. CBT-D + TAU 2. Placebo control + TAU	1. 8 × 45 m 2. 8 × 45 m	1. 83 2. 83 (67%)	BDI HAM-D	1. % of days abstinent 2. Drinks per drinking day	pt: 1.5 m fu: 3, 6, 12 m	pt: 14 fu 3: 7 fu 6: 5 fu 12: 7	1. Yes 2. Yes 3. Yes 4. Yes
Hides 2011 [58] Australia	Out-patients aged 16–25 in substance use service	Clinic	• K10 ≥ 17 • Weekly AOD use above recommended level in past month	1. ICBT/MI + TAU 2. TAU	1. 12 sessions	1. 60 2. 28 (63%)	CES-D HAM-D-17 K 10	1. Days of use per month 2. Mean drinks p.m. 3. Mean drinks per drinking day	pt: 3 m fu: 6 m	pt: 24 fu: 24	1. No 2. No 3. Yes 4. No

Table 1 *Cont.*

Author, year, country	*Target group*	*Recruitment source*	*Inclusion criteria*	*Conditions*	*Intensity of treatment*	*n (% male)*	*Symptoms of depression outcome measures*	*Alcohol consumption outcome measures*	*Post-treatment (pt) and follow-up (fu) assessments*	*Study attrition (%)*	*Methodological qualities*
Hunter 2012 [59] USA	Out-patients aged 18+ in substance use programme	Clinic	• BDI >13 • One or more substance use disorders (AUDIT-C or DAST)	1. ICBT/MI (gr) + TAU 2. TAU	1. 18 × 2 hours	1. 47 2. 26 (52%)	BDI-II	1. Drinks per drinking day	pt: 3 m fu: 6 m	pt: 12.3 fu: 5.5	1. Yes 2. Yes 3. Yes 4. Yes
Kay-Lambkin 2009 [56] Australia	Adults ≥17	Referrals alcohol/other health-care settings; TV and print media	• BDI-II ≥ 17 • DSM-IV life-time MDD • Current problematic AOD use above recommended level	1. ICBT/MI + BI 2. ICBT/MI-c + BI 3. BI	1. 10 × 1 hour 2. 10 × 1 hour 3. 1 session	1. 21 2. 22 3. 24 (46%)	BDI-II	1. Mean no. of alcohol use occasions	pt: 3 m fu: 6, 12 m	pt: 15.5 fu 6: 18.6 fu 12: 15.5	1. Yes 2. Yes 3. Yes 4. Yes
Kay-Lambkin 2011 [79] Australia	Adults ≥16	Referrals alcohol/other health-care settings; TV and print media	• BDI-II ≥ 17 • Alcohol or cannabis use at harmful levels last month	1. ICBT/MI (face-to-face)[a] 2. ICBT/MI-c[a] 3. PCT	1. 10 × 1 hour 2. 10 × 1 hour 3. 10 × 1 hour	1. 185[a] 2. 89 (57%)	BDI-II	1. Mean drinks per day 2. % abstinent 3. % with ≥50% reduction 4. % drinking above harmful threshold	pt: 3 m	pt: 40.5	1.Yes 2. n.i. 3. Yes 4. Yes
Lydecker 2010 [60] USA	Out-patient veterans in double diagnosis programme	Clinic	• DSM-IV alcohol, cannabis/stimulant dependence • DSM-IV life-time MDD • Recent substance use • HDRS >20	1. ICBT/MI (gr) + pharma. 2. TSF (gr) + pharma.	1. 36 × 1 hour 2. 36 × 1 hour	1. 107 2. 99 (92%)	HAM-D-21	1. % of days substance-use–abstinent	pt: 6 m fu:15 m	pt:19.4 fu: 34.5	1. Yes 2. n.i. 3. No 4. Yes
Watkins 2011 [61] USA	In-patients aged +18 in substance use programme	Clinic	• PHQ-8 ≥ 5 • PHQ-8 ≥ 5 • BDI-II ≥ 17	1. ICBT/MI (gr) + TAU 2. TAU	1. 16 × 2 hours	1. 140 2. 159 (52%)	BDI-II	1. Alcohol use days as % of days available for use	pt: 3 m fu: 6 m	pt:13 fu:14.4	1. No 2. No 3. No 4. Yes

Methodological qualities: 1, adequate sequence generation; 2, allocation to conditions by an independent party; 3, blinding of outcome assessors or use of self-report outcomes only; 4, intention-to-treat analyses. [a]In the meta-analysis the CBT/MI face-to-face and computerized experimental conditions are combined and compared to the PCT control condition, as this was the way the data were presented and amenable. Adverts = advertisements; alc = alcohol; alcpo = alcohol population; AOD = alcohol and other drugs; AUDIT = Alcohol Use Disorder Identification Test; BDI = Beck Depression Inventory; BI = brief intervention; BSP = brief supportive psychotherapy; C = control condition; CBT = cognitive-behavioural therapy; CBT-D = cognitive-behavioural treatment for depression; CES-D = Center for Epidemiologic Studies Depression Scale; CO = completers-only analysis; DAST = Drugs Abuse Screening Test; DSM = Diagnostic Statistical Manual of Mental Disorders; depr = depression; f = female; fu = follow-up; GAF = Global Assessment of Functioning; gr = group sessions; HADS = Hamilton Anxiety and Depression Scale; HAM-D = Hamilton Rating Scale for Depression; ICBT = integrated cognitive–behavioural therapy; ICBT/MI-c = integrated cognitive–behavioural therapy-computerized 'integrated', focusing on both alcohol and depression; IPT-DD = interpersonal psychotherapy adapted for dysthymic disorder; ITT = intention-to-treat analysis; K10 = Kessler Psychological Distress Scale; m = male; max. = maximum; MCMI = Millon Clinical Multiaxial Inventory; MDD = major depressive disorder; MHAM-D = Modified Hamilton Depression Rating Scale; MI = motivational interviewing; MMPI = Minnesota Multiphasic Personality Inventory; n.i. = no information; no. = number; PHQ = Patient Health Questionnaire; pharma. = pharmacotherapy; PCT = person-centred therapy; POMS = Profile of Mood States; pt = post-treatment; p.w. = per week; SCL-90 = Symptom Checklist; SET = self-examination therapy; s-r = self-reports; TAU = treatment as usual; TSF = 12-Step Facilitation Therapy.

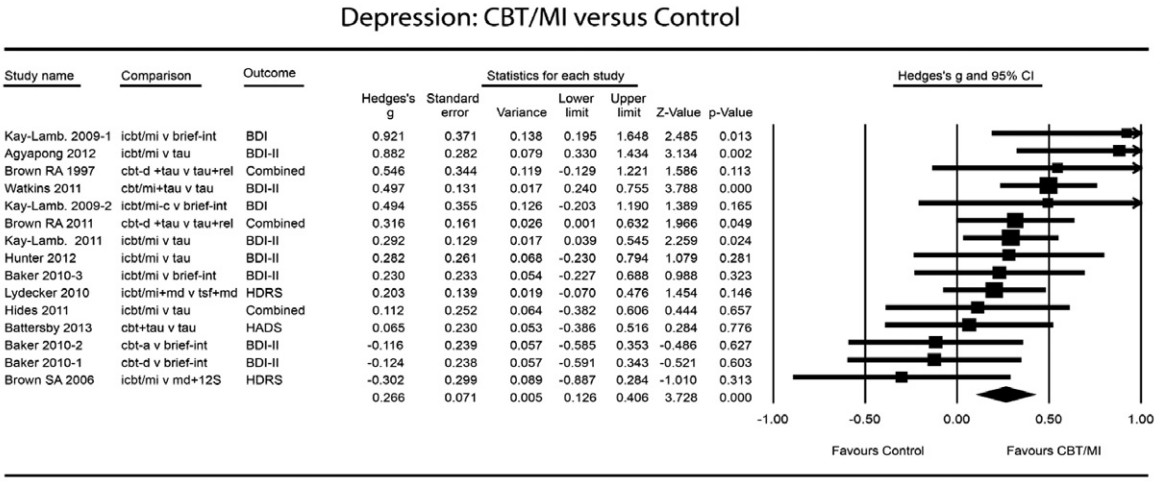

Figure 2 Depression: cognitive-behavioural therapy/motivational interviewing (CBT/MI) versus control

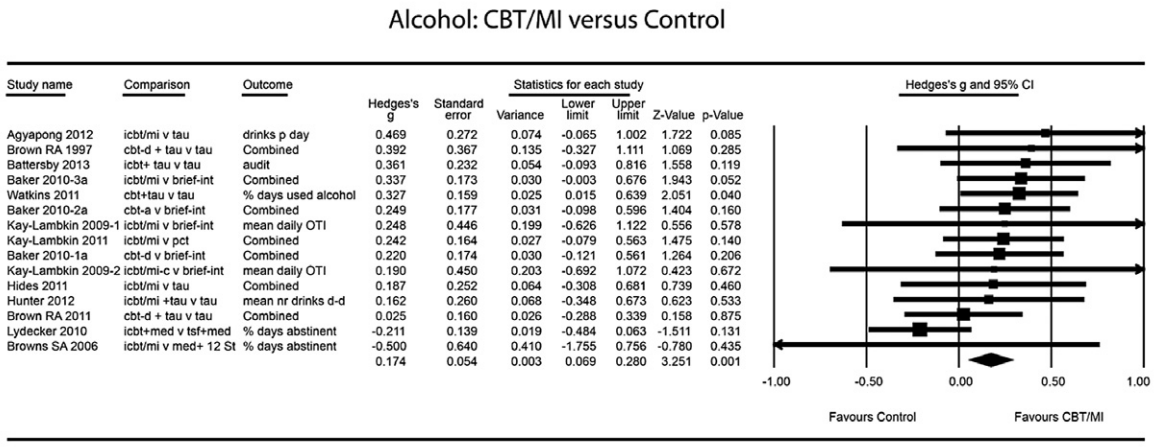

Figure 3 Alcohol: cognitive-behavioural therapy/motivational interviewing (CBT/MI) versus control

Meta-Analysis (CMA, version 2.2.021 [37]). Cohen's *d* is the standardized difference between the two means divided by the pooled standard deviation at post-test. Hedges's *g* is a variation of Cohen's *d* that corrects for potential bias due to small sample sizes [38]. Effect sizes of approximately 0.8 can be considered large, 0.5 moderate and 0.2 small [39]. Because several studies had small samples, we corrected the effect sizes for bias using the procedures suggested by Hedges & Olkin [38].

We calculated separate effect sizes for depression and for alcohol consumption (the primary outcome measures in the analysed studies). If means and standard deviations were not reported, we contacted the study authors to obtain these and/or used other statistics to calculate the effect sizes according to the procedures implemented in our meta-analysis software. Where possible, data from intention-to-treat analyses were used; completers-only data were used if the former were unavailable. If more than one depression or alcohol outcome measure was reported in a single study, we averaged the effect sizes from those measures to produce a single summary effect size for use in the meta-analysis, adjusting those calculations statistically to account for variance introduced by the multiple measures [40]. Figures 2 and 3 show the studies for which this was the case; outcome was then indicated with 'combined'.

As we expected considerable heterogeneity among the studies, we calculated the mean effect sizes using a random-effects model. This assumes that the included studies were drawn from 'populations' of studies that differ systematically from one another (heterogeneity). It thus assumes that the effect sizes resulting from included studies differ not only because of the random error within studies (as in the fixed-effects model), but also because of true variation in effect size from one study to the next. We calculated the Q-statistic, which assesses the presence

versus the absence of heterogeneity, but report only whether or not it was significant. As a test of homogeneity of effect sizes, we also calculated the I^2-statistic, which quantifies the heterogeneity in percentages. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity, with 25% as low, 50% as moderate and 75% as high [41].

We also calculated numbers needed to treat (NNTs), using the formulae provided by Kraemer & Kupfer [42]. NNT estimates the number of patients that need to be treated in order to have a beneficial impact on one person.

Subgroup analyses were conducted according to the mixed-effects model, whereby studies within subgroups are pooled with the random-effects model and tests for significant differences between subgroups are conducted with the fixed-effects model. We also used meta-regression analyses to identify any associations between the effects on depression and those on alcohol outcomes.

To detect possible publication bias, we examined the funnel plots visually for the primary outcome measures for symmetry. A funnel plot is a scatterplot of treatment effect against a measure of study size. A symmetrical inverted funnel shape indicates low publication bias, whereas an asymmetrical funnel indicates potential publication bias which may jeopardize the results and conclusion of the meta-analysis conducted. We conducted Egger's linear regression test [43] of the intercept to quantify the bias captured by the funnel plot and test whether or not it was significant. The Duval & Tweedie [44] trim-and-fill analysis was performed to further verify an unbiased estimate of the pooled effect size. This method enables an estimation of the number of missing studies that might exist in a meta-analysis and the effect that these studies might have had on its outcome.

Power calculations

We calculated beforehand how many would be needed to ensure sufficient statistical power to identify relevant effects. This was important because we sought studies based on treatment-to-treatment comparisons, so that small effect sizes were to be expected. The power calculation was conducted according to the procedures described by Borenstein and colleagues [40]. We hoped to find enough studies to enable identification of a small effect size of $d = 0.30$ based on the random-effects model. The power calculations indicated that this would require at least 15 studies with a mean sample size of 40 (20 participants per condition). Conservatively, that assumes a medium level of between-study variance (τ^2), a statistical power of 0.80 and a significance level of $\alpha < 0.05$. Alternatively, we would need 10 studies with 60 participants each to detect an effect size of $d = 0.30$.

RESULTS

Selection and inclusion of studies

Figure 1 shows a flow-chart describing the study selection procedure. Twelve studies (15 comparisons) were included in the meta-analysis. In reporting the results we followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist [45].

Characteristics of included studies: CBT/MI plus TAU versus control conditions

Table 1 summarizes selected study characteristics. They assessed a total of 1721 patients (1026 in experimental and 695 in control conditions) and thus provided sufficient statistical power (see Power calculations section). Three studies assessed the presence of depression and alcohol use disorders with diagnostic interviews. In the remaining studies, patients scored above a cut-off point on a self-report depression or alcohol scale. Nine studies applied a randomized controlled study design, three a controlled design only. Ten of the 15 CBT/MI conditions consisted of combined treatment strategies focusing on both alcohol and depression, four applied depression-focused CBT only and one applied CBT for alcohol only. Most CBT/MI procedures were added to TAU. TAU included psychosocial counselling and/or medication treatment. All the studies used validated outcome assessment instruments (for assessment of symptoms of depression: Beck Depression Inventory (BDI) and BDI-II [46], Hospital Anxiety and Depression Scale (HADS) [47], Hamilton Rating Scale for Depression (HAM-D) [48], Center for Epidemiologic Studies—Depression (CES-D) [49], Symptom Checklist-90 Revised, Depression (SCL-90-R-D) [50], Profile of Mood States (POMS) [51,52], Kessler Psychological Distress Scale (K10) [51] or Children's Depression Rating Scale (CDRS) [53]). Alcohol use was measured by various consumption outcomes such as quantity and abstinence measures, as assessed using the alcohol time-line follow-back (TLFB [54] and Alcohol Use Disorders Identification Test (AUDIT) questionnaires [55]).

Quality of included studies

The quality of the studies varied (see Table 1). Nine reported adequate sequence generation; three were non-randomized. Seven reported allocation to conditions by an independent party. Eight reported blinding of outcome assessors or used only self-report outcomes. Eight conducted intention-to-treat analyses. Dropout rates varied from 3 to 40%. Six studies met all four pre-defined quality criteria.

Effects of CBT/MI versus control groups: depression

Figure 2 and Table 2 show that the effects of CBT/MI on decrease of depression symptoms over controls were small but significant at post-test ($g = 0.27$, 95% CI = 0.13–0.41, $P < 0.001$, random-effects model; NNT = 6.58). Heterogeneity was low and non-significant ($I^2 = 37.51$). Between-study variance (τ^2) was small (0.005), resulting in considerable statistical power. A post-hoc power calculation showed that our set of studies had sufficient statistical power (1.00) on the basis of the random-effects model (based on the low level of between-study variance, $\tau^2 = 0.003$, and a significance level of 0.05).

Two studies [30,56] compared groups receiving different types of CBT/MI with a single control group, so that multiple comparisons from these studies were included in the same analysis. The fact that these were not independent of one another could have reduced artificially the heterogeneity of the analysed studies, thereby affecting the pooled effect size. We therefore conducted sensitivity analyses that included only one effect size per study: one meta-analysis incorporating the largest effect size only and a second incorporating the smallest only. As Table 2 shows, these had little influence on the pooled effect size, nor did they produce differences in heterogeneity.

Effects of CBT/MI versus control groups: alcohol

The overall mean effect size indicating the post-test difference between CBT/MI and control groups concerning a decrease in alcohol consumption was small ($g = 0.17$, 95% CI = 0.07–0.28, $P < 0.001$; random-effects model; NNT = 10.42). Results are shown in Fig. 3 and Table 3. Heterogeneity was very low ($I^2 = 0.15$). A post-hoc power calculation showed that our set of studies had sufficient statistical power (0.87) on the basis of the random-effects model (based on the low level of between-study variance, $\tau^2 = 0.003$, and a significance level of 0.05). There were two studies that compared groups receiving different types of CBT/MI with a single control group [30,56].

Table 2 Effects of adjunct cognitive-behavioural therapy/motivational interviewing (CBT/MI) on decrease in symptoms of depression in comparison with treatment-as-usual control groups, and subgroup analyses of associations between effect sizes and study characteristics (Hedges's g[a]).

CBT/MI versus TAU	*Subgroup*	*n comp*	*g*	*95% CI*	I^{2b}	P^c	*NNT*
All studies		15	0.27	0.13 to 0.41***	37.51		6.58
One effect size per study (lowest excluded)		13	0.27	0.14 to 0.41***	27.42		6.58
One effect size per study (highest excluded)		13	0.26	0.09 to 0.44**	46.31		6.85
Subgroup analyses							
Type of control	TAU	9	0.30	0.11 to 0.47***	39.34	0.624	5.95
	Brief treatment	6	0.22	–0.03 to 0.47	41.48		8.06
Randomization	Yes	12	0.23	0.07 to 0.39**	38.80	0.197	7.69
	No	3	0.43	0.21 to 0.64***	0		4.20
Analyses	ITT	12	0.26	0.09 to 0.43**	48.36	0.803	6.85
	CO	3	0.30	0.05 to 0.54*	0		5.95
Recruitment	Community	6	0.22	–0.01 to .47	41.48	0.624	8.06
	Clinic	9	0.30	0.12 to 0.47***	39.34		5.95
Population	Alcohol	7	0.23	–0.01 to 0.47*	46.91	0.640	7.69
	Substance use (incl. alcohol)	8	0.30	0.13 to 0.47***	33.08		5.95
Age	(Young) adults ≥16 years	7	0.20	–0.01 to 0.41	31.07	0.446	8.93
	Adult ≥18 years	8	0.31	0.12 to 0.56***	44.14		5.75
Diagnosis of both conditions	Yes	3	0.26	–0.29 to 0.81	76.65	0.965	6.85
	No	12	0.27	0.14 to 0.41***	19.82		6.58
Focus of treatment	Integrated	10	0.27	0.10 to 0.45**	32.56	0.828	6.58
	Single (depression or alcohol)	5	0.24	–0.03 to 0.51	55.43		7.46
Patient status	In-patient	1	0.50	0.24 to 0.75***	0	0.082	3.62
	Out-patient	14	0.23	0.09 to 0.38***	31.69		7.69
Individual/group	Individual	10	0.30	0.11 to 0.49**	38.75	0.597	5.95
	Group	5	0.22	–0.02 to 0.45	47.97		8.06
Digital versus face-to-face	Internet	2	0.73	0.30 to 1.16***	0	0.030	2.54
	Face-to-face	13	0.23	0.09 to 0.36***	30		7.69

CI = confidence interval; n comp = number of comparisons; NNT = number needed to treat; CO = completers-only analysis; ITT = intention-to-treat analysis; TAU = treatment as usual. [a]According to the random-effects model. [b]The P-values in this column indicate whether the Q-statistic is significant (I^2-statistics do not include a test of significance). [c]The P-values in this column indicate whether the difference between the effect sizes in the subgroups is significant. *$P \leq 0.05$; **$P < 0.01$; ***$P \leq 0.001$.

Table 3 Effects of adjunct cognitive-behavioural therapy/motivational interviewing (CBT/MI) on decrease in alcohol consumption in comparison with treatment-as-usual control groups, and subgroup analyses of associations between effect sizes and study characteristics (Hedges's g[a]).

CBT/MI versus TAU	*Subgroup*	*n comp*	*g*	*95% CI*	I^{2b}	P^c	*NNT*
All studies		15	0.17	0.07 to 0.28**	0.15		10.42
One effect size per study (lowest excluded)		13	0.18	0.05 to 0.31**	13.94		9.80
One effect size per study (highest excluded)		13	0.16	0.04 to 0.28**	7.75		11.11
Subgroup analyses							
Type of control	TAU	9	0.11	–0.04 to 0.32	33.13	0.354	16.13
	Other treatment	6	0.26	0.10 to 0.42**	0		6.85
Randomization	Yes	12	0.15	0.03 to 0.28*	12.59	0.310	11.90
	No	3	0.30	0.05 to 0.55*	0		5.95
Analyses	ITT	12	0.20	0.07 to 0.32**	13.65	0.546	8.93
	CO	3	0.11	–0.04 to 0.36	0		16.13
Recruitment	Community	6	0.26	0.10 to 0.42**	0	0.354	6.85
	Clinic	9	0.14	–0.04 to 0.32	33.13		12.82
Population	Alcohol	7	0.24	0.10 to 0.39***	0	0.270	7.46
	Substance use	8	0.11	–0.07 to 0.29	21.73		16.13
Diagnoses of both conditions	Yes	3	0.00	–0.54 to 0.54	62.75	0.394	
	No	12	0.24	0.12 to 0.35***	0		7.46
Age	(young)-adult i ≥16 years	7	0.25	0.10 to 0.40***	0	0.411	7.14
	Adult	8	0.14	–0.06 to 0.35	41.05		12.82
Focus of treatment	Integrated	10	0.15	0.00 to 0.33	21.57	0.699	11.90
	Single (depression or alcohol)	5	0.21	0.05 to 0.37**	0		8.47
Patient status	In-patient	1	0.33	0.01 to 0.64*	0	0.310	5.43
	Out-patient	14	0.15	0.04 to 0.27**	0		11.90
Individual/group	Individual	10	0.23	0.10 to 0.39***	0	0.454	7.69
	Group	5	0.11	–0.19 to 0.40	56.23		16.13
Digital versus face-to-face	Internet	2	0.39	–0.06 to 0.85	0	0.346	4.59
	Face-to-face	13	0.16	0.05 to 0.28**	6.26		11.11

CI = confidence interval; *n* comp = number of comparisons; NNT = number needed to treat; CO = completers-only analysis; ITT = intention-to-treat analysis; TAU = treatment as usual. [a]According to the random-effects model. [b]The *P*-values in this column indicate whether the Q-statistic is significant (I^2-statistics do not include a test of significance).[c]The *P*-values in this column indicate whether the difference between the effect sizes in the subgroups is significant. *$P \leq 0.05$; **$P < 0.01$; ***$P \leq 0.001$.

Sensitivity analyses showed little influence of these on the pooled effect size or differences in heterogeneity (Table 3).

Subgroup analyses

No significant differences emerged for decrease of depression symptoms or alcohol consumption in association with any of the subgroup analyses we conducted (see Tables 2 and 3). The comparison between digital and face-to-face CBT/MI for depression was, however, significant ($P = 0.030$) in favour of digital CBT/MI ($g = 0.73$, CI = 0.30–1.16 and $g = 0.23$, CI = 0.09–0.36, respectively).

Meta-regression

A higher number of sessions was associated negatively and significantly with the effect size for alcohol outcome ($\beta = -0.016$, 95% CI = –0.027 to –0.005, $P = 0.004$); for depression, the association was non-significant. A higher effect size for alcohol outcome was associated significantly with a higher effect size for depression ($\beta = 0.511$, 95% CI = –0.04 to 0.99, $P = 0.003$); the reverse relationship was not significant.

Follow-up assessments

For seven studies (eight comparisons [24,56–61]), we could assess the impact of CBT/MI on depressive symptoms at a follow-up measurement 6–12 months post-treatment. A similar small effect size ($g = 0.26$, 95% CI = –0.01 to 0.54; random-effects model) was found, but with only a trend towards significance and with a high level of heterogeneity ($P = 0.063$, $I^2 = 65.433$). For the impact of CBT/MI on decrease of alcohol consumption [61], a significant effect was maintained and increased at follow-up ($g = 0.31$, 95% CI = 0.16–0.47, $P < 0.001$; random-effects model; nil heterogeneity; eight studies, nine comparisons [24,29,31,56,57,59,60]).

Publication bias

Inspection of the funnel plot and performance of the trim-and-fill procedure indicated no publication bias for the studies in terms of depression effect sizes; bias for alcohol was low. After adjustment for missing studies, the effect size for alcohol outcome diminished from $g = 0.17$ to $g = 0.14$ (95% CI = 0.04–0.25; trimmed studies = 3), and Egger's test did not indicate an asymmetrical funnel plot ($P > 0.10$).

DISCUSSION

CBT/MI as an adjunct to treatment as usual (or as an alternative to it) appears effective for treating (young) adult patients with comorbid MDD and AUD (clinical or subclinical). Effect sizes were small but significant and comparable to those found by Hobbs and colleagues [14] (a review that included only two studies on alcohol, depression and psychotherapy). We had expected small effect sizes, given that our meta-analysis involved treatment-to-treatment comparisons. These effect sizes and corresponding NNTs are lower than those found in the meta-analysis of Nunes & Levin [26] for the antidepressant treatment of comorbid MDD and substance use dependency. This meta-analysis showed NNTs of 4.72 (depression) and 7.14 (alcohol), while our study found NNTs of 6.58 (depression) and 10.42 (alcohol).

Follow-up assessments up to 12 months post-treatment showed that the effect size for depression was maintained, with a trend towards significance ($P = 0.063$). A similar enduring CBT effect for patients with depression only has been found in a recent meta-analysis [62]. The beneficial effect of CBT/MI on alcohol outcomes in our study even strengthened over time (from $g = 0.18$ to $g = 0.32$, $P < 0.001$). This apparent delayed impact of CBT in reducing alcohol use has been labelled by Carroll and colleagues as a 'sleeper effect' [63]. It may be explained by the cognitive and relapse skills that patients learn during treatment and can still apply afterwards [64,65].

In our study, the impact on depression appears to have been achieved earlier than the effect on alcohol use. At least two points may arise from that finding. First, the alcohol outcome may result from good CBT/MI depression response *per se*. Secondly, reduced alcohol consumption during treatment may have also been a factor, in view of the positive association between reduced alcohol consumption and improved mood found in our analysis. In our study, however, a higher effect size for depression outcome did not correspond significantly with a higher effect size for alcohol outcome, as was the case in Nunes & Levin's meta-analysis of antidepressant medication. This may also suggest an alcohol sleeper effect in our study. Such results must be interpreted with caution, however, as assessing moderators from study-level data is subject to various difficulties, such as limited power for moderator analyses [66]. Meta-analysis using individual patient-level data may overcome some of these problems (see e.g. [21]).

Another possible explanation for our lack of association between depression and alcohol outcomes is that there may not have been enough variation in effect sizes to detect such associations (see Limitations). That could also be one reason for the lack of significant differences between any of the subgroups we evaluated (in combination with the small numbers of studies in some subgroup comparisons). The comparison between digital and face-to-face treatments was, however, significant. Digitally delivered treatments such as those over the internet have been proved clinically and are cost-effective for clinical and subclinical AUD [20,67,68] and depression [69,70]. Given that most comorbid patients receive out-patient treatment [71], easily accessible treatment facilities such as those delivered partly via the internet or smartphone are worth exploring in more detail.

We did not find a significant difference between integrated and single-focus CBT/MI. Hence, we cannot argue the superiority of the former over the latter, as carried out by some studies that recommend integrated psychotherapeutic treatment for MDD and AUD [13,32].

Interestingly, we found that a higher number of CBT/MI sessions was associated significantly and negatively with alcohol outcome ($P < 0.001$) and non-significantly with depression outcome. This may suggest a lack of superior effect of intensive CBT/MI over briefer alcohol treatments. A similar lack of superiority was reported in the meta-analysis by Moyer and colleagues for problem drinkers and in the Project March results [22,72]. This suggests that brief alcohol interventions could be explored as first-step treatments for comorbid alcohol problems, to be followed by more intensive components for patients who do not respond adequately. Another question yet to be answered within this context relates to the minimal required number of brief treatment sessions in order to obtain treatment effectiveness.

Study limitations

We assessed overall outcomes in terms of depressive symptoms and alcohol consumption. The effect sizes for alcohol use were based on varying measures, and there were not enough studies to look separately at distinctions such as abstinence or percentage of heavy drinking days. Such diversity of measures is a common problem in alcohol studies, as noted by Sobell and colleagues [73]; and, as Hobbs and colleagues [14] have pointed out, that

may have resulted in less variability in outcome than would have been found in studies with fewer or single measures. To minimize this potential bias, we followed guidelines in meta-analytical strategy manuals [40].

We included both randomized and non-randomized controlled studies in our analyses, but found no difference between those two designs in terms of effect sizes for alcohol or depression. Such a difference might have been expected, as randomization often yields lower clinical outcomes [74].

Generalization of our study results requires caution, as all but one of the included studies involved outpatients only.

Clinical considerations

Combined CBT/MI treatment of comorbid clinical and subclinical MDD and AUD, both for clinical and community samples, shows promising results. The observed effects were small, but they could still imply a major health impact in view of the high prevalence of comorbidity of these disorders, the related high burden of disease and the preference by many patients of CBT/MI over antidepressants [75].

CONCLUSION

Further research is needed in terms of large-scale randomized controlled trials that could strengthen the findings of this meta-analysis. Future studies should focus on the feasibility of brief and digital interventions, single-focus versus integrated CBT/MI, clear descriptions of what treatment-as-usual involves, possible predefined moderators and mediators of treatment outcomes, long-term follow-ups, alcohol outcome measures such as reliable clinical change and cost-effectiveness. Our meta-analysis may provide a basis for such efforts.

Declaration of interests

None.

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