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Is Specialized Integrated Treatment for Comorbid Anxiety, Depression and Alcohol Dependence Better than Treatment as Usual in a Public Hospital Setting?

K.C. Morley[1,*], A. Baillie[2], S. Leung[3], C. Sannibale[4], M. Teesson[5], and P.S. Haber[1,4]

[1]NHMRC Centre of Research Excellence in Mental Health and Substance Use, Discipline of Addiction Medicine, University of Sydney, Sydney, NSW, Australia, [2]NHMRC Centre of Research Excellence in Mental Health and Substance Use, Department of Psychology, Macquarie University, Sydney, NSW, Australia, [3]Central Clinical School, University of Sydney, Sydney, NSW, Australia, [4]Drug Health Services, Royal Prince Alfred Hospital, Camperdown, NSW, Australia, and [5]NHMRC Centre of Research Excellence in Mental Health and Substance Use, National Drug and Alcohol Research Centre, University of New South Wales, Randwick, Australia

*Corresponding author: Tel.:+61295153636; Fax: +61295158970, E-mail: kirsten.morley@sydney.edu.au

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Abstract

Aim: To assess the effectiveness of a 12 week specialized, integrated intervention for alcohol dependence with comorbid anxiety and/or mood disorder using a randomized design in an outpatient hospital setting.

Methods: Out of 86 patients meeting the inclusion criteria for alcohol dependence with suspicion of comorbid anxiety and/or depressive disorder, 57 completed a 3-week stabilization period (abstinence or significantly reduced consumption). Of these patients, 37 (65%) met a formal diagnostic assessment of an anxiety and/or depressive disorder and were randomized to either (a) integrated intervention (cognitive behavioural therapy) for alcohol, anxiety and/or depression, or (b) usual counselling care for alcohol problems.

Results: Intention-to-treat analyses revealed a beneficial treatment effect of integrated treatment relative to usual counselling care for the number of days to relapse ($\chi^2 = 6.42$, $P < 0.05$) and lapse ($\chi^2 = 10.73$, $P < 0.01$). In addition, there was a significant interaction effect of treatment and time for percentage days of abstinence ($P < 0.05$). For heavy drinking days, the treatment effect was mediated by changes in DASS anxiety ($P < 0.05$). There were no significant treatment interaction effects for DASS depression or anxiety symptoms.

Conclusions: These results provide support for integrated care in improving drinking outcomes for patients with alcohol dependence and comorbid depression/anxiety disorder.

Trial Registration: ClinicalTrials.gov Identifier: NCT01941693.

INTRODUCTION

A strong association between alcohol use disorders (AUDs), mood and anxiety disorders has been recognized worldwide. A meta-analysis of epidemiological surveys from 1990 to 2014 reported an odds ratio of 2.42 for co-occurring AUD and major depression and an odds ratio of 2.11 for co-occurring AUD and any anxiety disorder (Lai *et al.*, 2015). These sub-populations are significantly more debilitated with higher health service utilization than those with alcohol use disorders and

no comorbid mental disorder (Teesson *et al*., 2009). Results from the large alcohol treatment trial, Project MATCH, highlight psychiatric co-morbidity as a significant factor influencing treatment response for alcohol dependence (AD) (Project Match Research Group, 1998). Similarly, our previous work has demonstrated that clinically significant levels of depression among AD patients predicted poor response to alcohol treatment (Morley *et al*., 2006, 2010).

In many clinical services, including our own, the treatment of AD and psychological disorders is the responsibility of different outpatient services. One potential pathway for alcohol outpatient units to improve how they deal with mental health comorbidity could be to offer an integrated psychosocial intervention delivered in the same treatment setting. An integrated intervention may be the most effective and accessible form of treatment for dual diagnosis and this approach is now receiving increased attention (for review see Kelly and Daley, 2013; Riper *et al*., 2014).

There are a growing number of studies investigating psychosocial treatment for comorbid AD and comorbid depression targeting outpatient individuals (e.g. Riper *et al*., 2014). Brown and colleagues observed differences in the benefit of cognitive behavioural therapy for depression (CBT-D) depending on the treatment setting (Brown *et al*., 1997, 2011). In a small inpatient sample, adding CBT-D to alcohol treatment was more effective than alcohol treatment alone in reducing depressive symptoms and some drinking outcomes (Brown *et al*., 1997), yet this effect was not replicated in a larger outpatient sample (Brown *et al*., 2011). The largest outpatient trial to date demonstrated that individual integrated CBT treatment was more effective for AD and comorbid depression than a single-focused treatment (Baker *et al*., 2010). However, this superiority of integrated CBT versus a single-focused intervention was not subsequently observed in a pooled meta-analysis of community and clinic samples (Riper *et al*., 2014).

With regards to comorbid anxiety disorders, while reductions in alcohol consumption have been observed to mediate PTSD responsiveness (Brady *et al*., 2005), early improvements in PTSD symptoms appear to have a greater impact on recovery in alcohol dependence than the reciprocal relationship, thus prompting recommendations for integrated treatment (Back *et al*., 2006). Sannibale *et al*. (2013) investigated the extent to which combining existing cognitive behavioural therapies for alcohol use disorder and PTSD (integrated therapy with exposure) would produce better outcomes than treating alcohol use disorder only (alcohol-support). A 2-fold greater clinically significant change in PTSD severity was revealed for integrated therapy participants that attended one or more exposure sessions relative to alcohol-support participants.

There have been two randomized studies evaluating the efficacy of psychosocial interventions for patients with AD and comorbid social phobia and panic (Randall *et al*., 2001; Schadé *et al*., 2005). Firstly, Randall *et al*. (2001) explored the efficacy of concurrent CBT for comorbid AD and social anxiety disorder but demonstrated worse outcomes for the group treated for both anxiety and alcohol problems relative to CBT for alcohol only. This could have been due to diagnostic problems such as the inability to differentiate baseline alcohol-related anxiety from non-alcohol-related anxiety symptoms in patients with severe alcoholism. In addition, the treatment was provided in parallel rather than integrated. Secondly, Schadé *et al*. (2005), observed that additional therapy for anxiety in AD patients significantly reduced anxiety symptoms and also reported a trend for reduced relapse to alcohol. However, the treatment was poorly integrated with the alcohol and anxiety interventions delivered at separate clinics by different clinicians.

We aimed to assess the effectiveness of an integrated CBT intervention for alcohol dependent patients with co-morbid anxiety and/or depression in an outpatient clinic setting (Morley *et al*., 2013). Alcohol dependent outpatients underwent a stabilization period from alcohol and then received a formal diagnosis of comorbid anxiety and/or depression before random allocation to receive either usual or integrated care.

METHODS

Design

The study design borrowed from the stepped care approach to interventions for alcohol dependence (Sobell and Sobell, 1999, 2000) by providing the additional care for a second comorbid diagnosis when that diagnosis becomes evident. The rationale for the design is outlined in Sannibale and Baillie (2007). Briefly, differentiating alcohol-related anxiety from non-alcohol-related symptoms at baseline assessment is important given that patients in withdrawal may exhibit anxiety symptoms resulting from alcohol withdrawal. In addition, symptoms of depression and anxiety may resolve with abstinence so that further treatment is not required. However, in other cases where abstinence is achieved, these symptoms persist or worsen. Thus, alcohol dependent outpatients underwent a stabilization period from alcohol after which patients with a formal diagnosis of comorbid anxiety and/or depression were randomly allocated to receive either usual or integrated care.

The first phase of the study was to establish a stabilization period from alcohol for 3 weeks before entering the randomization step of the study. During the stabilization period, participants had the option of pharmacotherapy using naltrexone (50 mg, 1 tablet daily), acamprosate (333 mg, 2 tablets 3 times daily, reduced to 4/day for women <65 kg), or a combination of the two as medically prescribed based on physician judgment and participant preference. After a 3–4 week stabilization period, patients completed formal assessment for anxiety and depression and those with a positive diagnosis were offered the next step of care. Patients continued to receive further alcohol pharmacotherapy as medically prescribed but were randomized to one of two treatment groups: (a) integrated intervention for comorbid alcohol, anxiety and/or depression, (b) usual counselling care (alcohol support). The trial was conducted over a period of 24 months at the outpatient clinic of Drug Health Services, Royal Prince Alfred Hospital, NSW, Australia. The study was approved by The Sydney Local Health District Ethics Review Committee (X05-0275). The trial was registered with the ClinicalTrials.gov registry: NCT01941693.

Participants

Potential male and female participants were identified by treating clinicians at the outpatient drug and alcohol unit, advertisements at local GPs, print and online media. Inclusion for study enrolment (step 1) were the following: (a) alcohol dependence according to DSM-IV criteria, with alcohol as the subject's drug of choice, (b) age 18–65, (c) adequate cognition and English language skills to give valid consent and complete research interviews, (d) willingness to give written consent, (e) abstinence from alcohol for between 3 and 21 days (standard clinical criteria for use of acamprosate or naltrexone), (f) resolution of any clinically evident alcohol withdrawal as measured by Clinical Institute Withdrawal Assessment for Alcohol-revised (CIWA-Ar) (Reoux and Miller, 2000), and a positive score on the initial comorbidity suspicion checklist which was a brief assessment undertaken at the first appointment comprising of a one page checklist filled in by one of the assessing clinicians including one of either (a) anxiety/

depressive symptoms, (b) previous diagnoses of comorbid conditions (anxiety disorder or depression), (c) previous history of treatment for comorbid conditions (anxiety disorder or depression), (d) a score above screening cut-offs on either the Mini Social Phobia Inventory (Mini-SPIN) screen for social anxiety (Connor *et al*., 2001) or the K10 measure of psychological distress (Kessler *et al*., 2002) as a screen for anxiety and depression. Exclusion criteria were: (a) active major psychiatric disorder associated with significant suicide risk, (b) pregnancy or lactation, (c) advanced liver disease, (d) other serious medical illness that would interfere with adherence to the study protocol.

Inclusion criteria for randomization (step 2) were the following: (a) abstinence and/or clinically significant reduction in alcohol use as per clinician judgement, (b) resolution of any clinically evident alcohol withdrawal (CIWA-Ar), (c) diagnosis of anxiety or depression. Exclusion criteria were: (a) alcohol consumption at baseline levels. These patients were offered further treatment as appropriate within the service.

Procedure

The consort diagram for the flow of participants is shown in Fig. 1. The treatment procedure and frequency of assessments were explained to all eligible individuals and a study information sheet was provided. Prior to enrolment at step 1, individuals read and signed the informed consent. At step 2 of the study design, eligible participants were allocated to usual or integrated care (1:1) by referring to the consecutively assigned subject identification number to a matched numbered envelope containing a random assignment card. Randomization was stratified according to concomitant selective serotonin reuptake inhibitors (SSRI) use. Assessors were blind to treatment allocation for the follow-up diagnostic interviews and the same assessor did not assess the participant they assessed at baseline. Participants were asked not to mention their therapist or details of their therapy during their follow-up assessment. A paper wall was implemented whereby the researchers that obtained follow-up data had no knowledge of treatment group allocation.

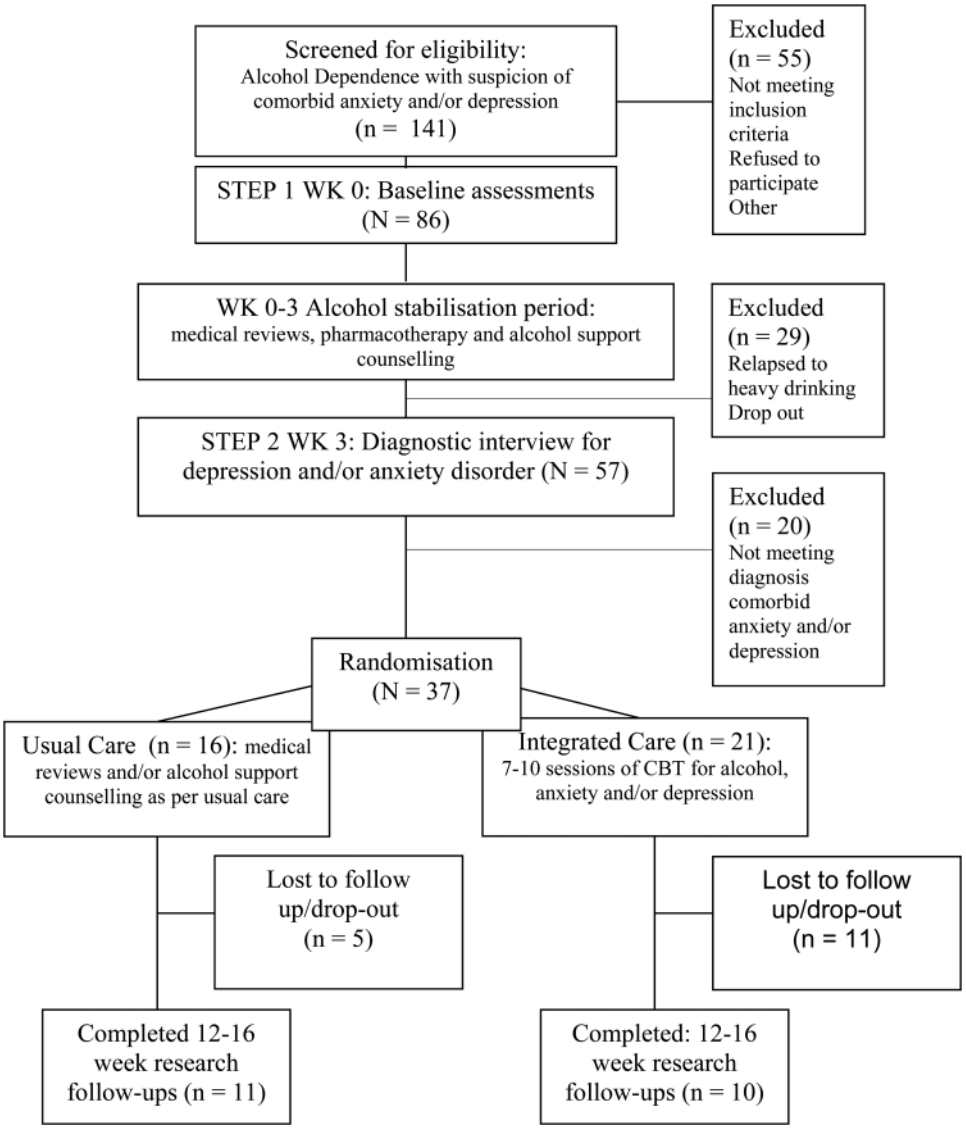

Fig. 1. Flow of participants through the trial.

Intervention

Usual care: Counselling for the treatment of alcohol dependence was according to standard practice at the participating treatment site. This entailed alcohol support in the form of brief individualized motivation enhancement therapy (feedback of assessment findings, reinforcement, empathy, enhancing client's own motivation) (Jarvis *et al*., 1995). Usual care alcohol support counselling was also available to all participants on the trial during the initial 3 week alcohol stabilization period. Quality control measures: counsellors were supervised by senior staff and engaged in weekly meetings; treatment was delivered according to the evidence-based treatment manual of Jarvis *et al.* (1995).

Integrated care for alcohol and comorbid anxiety and/or mood disorder: As outlined in Morley *et al.* (2013), trained therapists delivered specific cognitive behavioural therapy based upon evidence-based treatment manuals for alcohol use, anxiety and depressive disorders (Rapee, 1998; Rapee and Sanderson, 1998; Foa and Rothbaum, 2001; Najavits, 2001; Persons *et al*., 2001; Andrews *et al*., 2003a, b). Cognitive restructuring and behavioural experiments or graded exposure are approaches that are common to CBT for most of these disorders. Cognitive restructuring entails assisting patients to recognize the major beliefs they hold about themselves, the external world, others and the future that maintain their drinking, anxiety or depression and facilitating the patient to challenge and develop more helpful alternative beliefs. Graded exposure and behavioural experiments involve the gradual and scheduled confronting of feared situations and is thought to be the single most successful technique for overcoming phobias. Cognitive-behavioural coping skills and motivational enhancement strategies for alcohol consumption were used where appropriate (Miller *et al*., 1995; Monti *et al*., 2002). The interventions were delivered in 7–10 sessions. To ensure therapists adopted and maintained the principles of the therapy as described in the manual, sessions with consenting participants were randomly audiotaped for discussion with the therapist. Supervision was provided by A.B. and C.S. on a regular basis.

Assessments

Baseline: Demographics, long-term alcohol consumption, medical history of alcohol- and non-alcohol-related illness, drug abuse, age of onset and family history of alcohol problems were collected. Recent (last 30 days) alcohol consumption was assessed by the time line (TLFB) method (Skinner and Sheu, 1982). Severity of dependence was assessed by the obsessive-compulsive drinking scale (OCDS) (Anton *et al*., 1996) and by the Alcohol Dependence Scale (ADS) (Skinner and Allen, 1982). Depression, anxiety and stress levels were measured by the Depression, Anxiety, Stress Scale (DASS) (Lovibond and Lovibond, 1995). History of other drug use was determined by the Opiate Treatment Index (OTI) interviewer-conducted questionnaire [57] (Darke *et al*., 1991).

Formal diagnosis for comorbid anxiety or depression (stepped-care assessment): Diagnoses of anxiety and affective disorders were established by the Anxiety Disorders Interview Schedule (ADIS-IV) for DSM-IV (Brown *et al*., 1994). The structured interview for the Hamilton Depression Rating Scale (HDRS) was used to measure the severity of depressive disorders (Williams, 1988). The International Personality Disorders Examination Screening questionnaire (Loranger and Sartorius, 1994) was used to screen for personality disorders.

Follow-up schedule: Brief reviews were scheduled with clinic medical staff at Weeks 1, 3, 6, 12, 16 and 24 and clinical and psychosocial events related to alcohol were recorded. Research instruments were administered at Weeks 3, 12, 16 and 24 as described above: TLFB, DASS, ADS, OCDS. At Week 16, sections of diagnostic interviews relevant to diagnoses established at randomization (entry to Step 2) were re-administered by a blind assessor. Recent alcohol consumption was also assessed with a daily diary. Participants provided information concerning at least two contacts and received three attempts at telephone or mail reminders of forthcoming appointments.

Outcome measures

Primary outcomes: (a) Time to consumption of any alcohol (lapse); (b) Time to relapse as ≥4 drinks for women, ≥5 drinks for men; (c) amount of alcohol consumed (percentage days abstinent, percentage heavy drinking days as defined above and standard drinks per drinking day). Secondary outcomes: (d) improvement in depressive, anxiety or stress symptoms (DASS-21), alcohol dependence severity (ADS), craving (OCDS); (e) change in severity of primary ADIS diagnosis; (f) moderation of drinking outcomes by diagnostic group (presence of depression, presence of phobia); (g) mediation of drinking outcomes by change in severity of primary ADIS diagnosis, DASS Depression and Anxiety scores.

Statistical analysis

Data were analysed using the intention-to-treat principle such that all participants who attended the first intervention session were included (Lehert, 1993). The success of randomization was tested by comparing baseline characteristics of the treatment groups, with potentially confounding variables included as covariates. Analysis of variance (ANOVA) was used to compare continuous variables and categorical variables were compared using a chi-square test. The effect of treatment on time-related outcome measures such as relapse and lapse were analysed by Kaplan–Meier survival analysis. Patients that were lost to follow-up were taken to have relapsed to baseline drinking levels. Mixed models were employed to determine differences between integrated care and usual care groups on primary and secondary outcomes (baseline-follow-up). The treatment by time interaction examines whether treatment leads to a difference in the rate of change in the dependent variable and was the main effect of interest in the analyses. One previous study (Brown *et al*., 1997) with a similar design demonstrated combined CBT treatment of alcohol dependence and comorbid depression to significantly improved alcohol use outcomes with a moderate effect size ($N = 35$). Thus, power analysis was performed such that a sample of $N = 37$ subjects has 80% power of detecting a moderate difference between the two arms of care at alpha = 0.05. All analyses were conducted with significance level at $P < 0.05$.

RESULTS

Sample characteristics

Over the 24 month-year period 141 individuals were referred for participation in the study and 86 subjects were enrolled in the trial for Step 1. Of these, 29 were lost to follow-up or relapsed during the 3 weeks alcohol stabilization period. The remaining 57 underwent a structured diagnostic interview for anxiety and depression and 37 (65%) were diagnosed with a depressive and/or anxiety disorder and entered Step 2 to be randomized to receive IC ($n = 21$) or UC ($n = 16$).

For those randomized to UC and IC, the average age was 41 ± 12.86 years, 46% were male. There were no significant differences between the treatment groups at baseline except for scores on the ADS ($F_{1,35} = 4.16$, $P < 0.05$), DASS Anxiety ($F_{1,35} = 5.80$, $P < 0.05$) and

Table 1. Baseline characteristics

Measure	Usual care ($N = 16$)	Integrated care ($N = 21$)
Gender (%F)	38	52
Age	43.13 ± 12.86	40.05 ± 8.05
Drinks per drinking day+	12.43 ± 8.03	13.99 ± 10.10
Years of problem drinking	13.19 ± 7.82	14.06 ± 6.75
Previous alcohol treatment (Y), %	69	76
Alcohol Dependence Scale (ADS)*	17.87 ± 8.27	24.19 ± 9.75
DASS-21 Depression	22.53 ± 10.24	26.00 ± 10.26
DASS-21 Anxiety*	10.80 ± 6.18	17.67 + 9.70
DASS-21 Stress*	17.07 ± 7.17	23.43 ± 8.27
OCDS total	22.75 ± 6.06	21.43 ± 9.05
OCDS obsessive	7.69 ± 2.80	7.62 ± 4.01
OCDS compulsive	15.06 ± 5.04	13.81 ± 5.61

Data represent raw mean ± SD unless otherwise stated. * indicates significant differences between Integrated Care and Usual Care, $P < 0.05$. + during the 30 days prior to enrolment. Baseline characteristics at Step 1 = Week 0 preceding 21 day alcohol stabilization phase and randomization to Step 2 (Integrated Care versus Usual Care).

DASS Stress ($F_{1,35} = 5.77$, $P < 0.05$) (Table 1). These variables were treated as covariates in further analyses. There were no differences between the treatment groups on severity of ADIS diagnosis ($F = 0.38$, $P = 0.54$). Primary diagnoses included: alcohol dependence or abuse (45%), major depressive disorder (24%), social phobia (9%), dysthymia (6%), generalized anxiety disorder (6%), obsessive compulsive disorder (3%), panic disorder (3%), PTSD (3%). Secondary diagnoses included: alcohol dependence or abuse (34%), major depressive disorder (31%), social phobia (16%), generalized anxiety disorder (9%), bipolar (3%), dysthymia (3%), panic disorder (3%). One quarter of patients also had a tertiary diagnosis clustered evenly across each of the above disorders.

Subject retention and treatment compliance

Of the 37 randomized patients formally diagnosed with a depressive and/or anxiety disorder, 21 (57%) completed the study in full (attended the week 12 follow-up research appointment), with 11 randomized to receive usual care and 10 randomized to integrated care. The overall dropout rate for the protocol was 69% for the IC group and 48% for the UC but this difference was not significant ($\chi^2 = 1.27$, $P = 0.26$). There were no significant differences on baseline characteristics between those participants who retained in the study versus those that dropped out (P's > 0.11).

During the treatment period, the average number of service contacts for the usual care and integrated intervention was 4.75 and 9.57 respectively, which was significantly different ($F_{1,35} = 8.41$, $P < 0.001$). For those randomized to the UC group, the mean and median amount of alcohol support counselling sessions attended was 3.8 and 3.5 respectively (range: 0–12). For those randomized to the IC group, the mean and median number of CBT treatment sessions attended was 6.3 and 7 respectively (range: 0–12), with 76% of patients attending more than 80% of the minimum 7 treatment sessions (treatment compliant). This was in addition to an average of two alcohol support counselling sessions during the initial alcohol stabilization period.

The rate of SSRI use was 50% for the usual care group and 61% for the integrated care group ($\chi^2 = 0.52$, $P = 0.47$). The rate of alcohol pharmacotherapy (naltrexone/acamprosate) initiated at the baseline alcohol stabilization period was 69% for the usual care group and 52% for the integrated care group ($\chi^2 = 1.01$, $P = 0.31$) with the average number of 30 day scripts being 1.0 and 1.23 respectively ($F_{1,35} = 0.32$, $P = 0.57$).

Main efficacy outcomes: drinking

Primary outcomes are listed in Table 2. Survival analysis revealed a significant difference between treatment groups in the number of days to relapse and lapse following the 21 day alcohol stabilization period ($\chi^2 = 6.42$, $P < 0.05$; $\chi^2 = 10.73$, $P < 0.01$ respectively).

For percentage days abstinent, mixed models (−2loglikelihood = 442.13) revealed a significant effect time ($F_{1,35} = 6.84$, $P < 0.05$), a non-significant effect of treatment ($F_{1,35} = 1.06$, $P = 0.31$) and significant treatment × time interaction effect ($F_{1,35} = 5.44$, $P < 0.05$) from baseline to follow-up (see Fig. 2). Thus, the percentage days abstinent from alcohol significantly increased over the duration of the treatment period and the rate of change was significantly different between the treatment groups. For the percentage of heavy drinking days (−2loglikelihood = 480.08), there was a significant effect of time ($F_{1,35} = 27.42$, $P < 0.001$) but no effect of treatment ($F_{1,35} = 0.03$, $P = 0.86$) nor any treatment × time effect ($F_{1,35} = 1.30$, $P = 0.26$).

For drinks per drinking day (−2loglikelihood = 368.24), there was a significant effect of time ($F_{1,35} = 11.49$, $P < 0.01$) but no effect of treatment ($F_{1,35} = 0.02$, $P = 0.89$) nor any treatment × time effect ($F_{1,35} = 0.41$, $P = 0.53$).

Secondary outcomes

Secondary outcomes are listed in Table 2. For DASS anxiety scores, mixed models (2loglikelihood = 380.91) revealed a significant effect of time ($F_{1,35,} = 10.17$, $P < 0.01$), a trend for a significant effect for treatment ($F_{1,\ 35} = 3.17$, $P = 0.08$) but no significant effect of treatment × time ($F_{1,35} = 1.83$, $P = 0.18$) (see Fig. 2). For DASS Depression and Stress scores there was a significant effect of time ($F_{1,35} = 4.86$, $P < 0.05$; $F_{1,35} = 6.82$, $P < 0.05$ respectively) and no significant effect of treatment ($F_{1,35} = 0.00$, $P = 0.99$; $F_{1,35} = 1.45$, $P = 0.23$ respectively) or treatment × time interaction ($F_{1,35} = 0.30$, $P = 0.59$; $F_{1,35} = 0.91$, $P = 0.35$ respectively). For ADS scores there was a significant effect of time ($F_{1,35} = 11.48$, $P < 0.01$) and no significant effect of treatment ($F_{1,35} = 1.25$, $P = 0.27$) or treatment × time interaction ($F_{1,35} = 1.57$, $P = 0.22$). For OCD obsessive and compulsive scores there were no significant effects for time (P's > 0.19 res), treatment (P's > 0.97) or treatment × time interaction (P's > 0.71). For change in severity of the primary ADIS diagnosis there was a significant effect of treatment ($F_{1,35} = 4.99$, $P < 0.05$) and no significant effect of time ($F_{1,35} = 2.49$, $P = 0.13$) or treatment × time interaction ($F_{1,35} = 1.26$, $P = 0.28$).

Moderators of drinking outcomes by diagnostic specificity

The moderating effect of diagnostic specificity on the effect of treatment on outcome was determined by placing the dummy variables into the mixed models for drinking outcomes: the presence of major depression (65%) or presence of a phobia (50%). None of the variables were significant factors in the model for heavy drinking or percentage days abstinent (P's > 0.88) and there was no interaction effect with time and/or treatment (P's > 0.93).

Mediators of drinking outcomes

Change in DASS Anxiety and Depression scores over the treatment period were added as predictors to the mixed model for alcohol consumption outcomes. DASS Anxiety scores significantly influenced heavy drinking ($F_{1,35} = 63.91$, $P < 0.01$), with a significant treatment × change

Table 2. Outcome measures

Measure	Usual care ($N = 16$)	Integrated care ($N = 21$)
Primary outcomes		
Percent days abstinent*	49.97 ± 11.00	80.69 ± 10.78
Drinks per drinking day	7.12 ± 1.58	6.17 ± 1.58
Percent heavy drinking days	22.10 ± 8.50	12.39 ± 7.24
Days until lapse post 21 day stabilization period**	7.80 ± 2.16	42.75 ± 10.06
Days until relapse post 21 day stabilization period*	14.20 ± 8.38	46.50 ± 10.88
Secondary outcomes		
Alcohol Dependence Scale (ADS)	12.28 ± 3.07	11.82 ± 3.07
DASS-21 Depression	18.63 ± 4.17	16.83 ± 4.0
DASS-21 Anxiety	8.00 ± 1.89	8.83 ± 1.81
DASS-21 Stress	14.36 ± 2.86	15.00 ± 2.76
OCDS obsessive	5.40 ± 1.52	6.45 ± 1.45
OCDS compulsive	11.10 ± 2.20	11.91 ± 2.10

Unless otherwise stated, data represent means (±SD) at week 12 follow-up. Baseline DASS Stress, DASS anxiety and ADS values were placed as covariates in Mixed Model analyses. * indicates significant differences between Integrated Care and Usual Care, $P < 0.05$; **$P < 0.01$.

in DASS anxiety effect ($F_{1,35} = 11.79$, $P < 0.05$). There was no significant meditating effect of DASS Anxiety on percentage days abstinent ($F_{1,35} = 2.59$, $P = 0.06$) or drinks per drinking day ($F_{1,35} = 1.07$, $P = 0.45$). DASS Depression scores did not significantly influence percentage days abstinent ($F_{1,35} = 1.39$, $P = 0.29$), heavy drinking ($F_{1,35} = 3.35$, $P = 0.09$) or drinks per drinking day ($F_{1,35} = 3.88$, $P = 0.06$).

DISCUSSION

The main aim of the current study was to assess the effectiveness of a CBT integrated intervention for alcohol dependent patients with comorbid anxiety and/or depression. We compared integrated CBT with usual counselling care (alcohol support) in reducing alcohol consumption and symptoms of anxiety and depression in an outpatient hospital setting.

There was support for the hypotheses across some primary outcomes. For the main efficacy drinking outcomes, there was support for integrated care to be more effective than usual care for most measures of alcohol consumption. Integrated care resulted in a significantly longer time to lapse, longer time to relapse and higher percentage of days abstinent. However, the beneficial treatment effect was not apparent for the variable drinks per drinking day.

We did not detect any differences between treatment groups in the change of severity in the primary ADIS diagnosis over the treatment period. There was little support for the hypothesis that integrated care would result in significantly greater improvements in anxiety and depression levels relative to usual care. In a large study of CBT for coexisting depression and alcohol problems, Baker *et al.* (2010), demonstrated that integrated treatment yielded greater reductions in depression levels compared to single-focused interventions at 15 weeks post-baseline. It is thus possible that we did not have adequate power to detect a similar effect on depression or that our follow-up assessment length was not sufficient. However, a meta-analysis of integrated treatment for comorbid depression and alcohol dependence reported that the therapeutic impact on depression may be achieved earlier than for alcohol use (Riper *et al.*, 2014). A 'sleeper effect' of CBT for reducing alcohol use has been documented whereby the skills learnt during treatment are applied after the follow-up period, thus

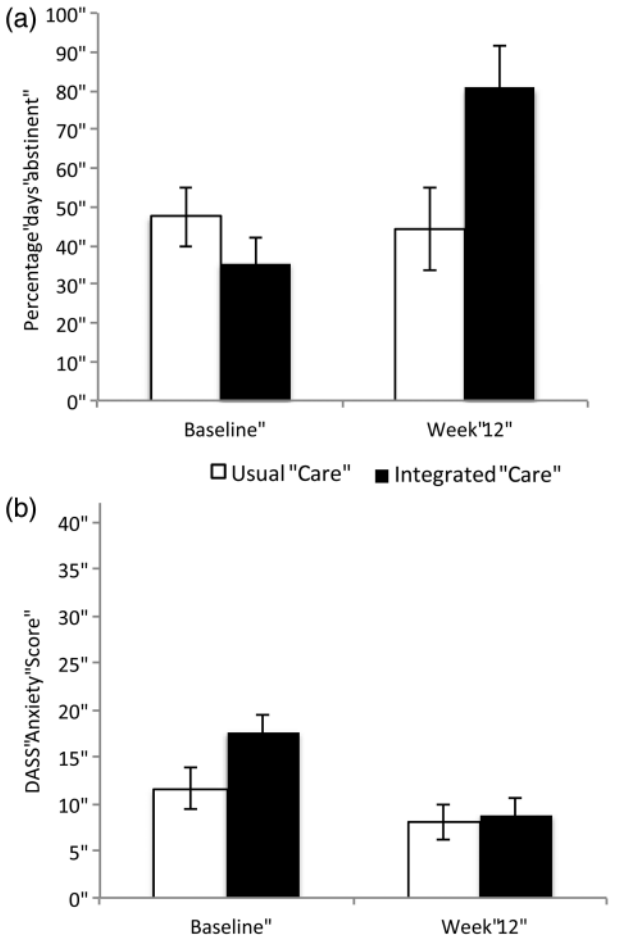

Fig. 2. Mean (**a**) percentage days abstinent from alcohol (within the previous 30 days) and (**b**) DASS Anxiety scores at different observation times (baseline and follow-up) ± SEM. There was a significant time × treatment (Integrated Care vs Usual Care) for percentage days abstinent, $P < 0.05$.

delaying and sustaining the effect of CBT on alcohol (Rawson *et al.*, 2006; Dutra *et al.*, 2008). According to this hypothesis, any treatment effect on depression would be observable before an effect on alcohol consumption. The current results are not consistent with this given the substantial reduction of alcohol consumption in patients receiving integrated care while demonstrating little effect on depression levels.

For DASS anxiety levels, there was a trend for patients randomized to integrated care to demonstrate a greater improvement relative to usual care, however this was not statistically significant. It is possible that the research follow-up point was not sufficiently long enough to elucidate a greater reduction in mental health symptoms in the integrated care group. However, Baillie *et al.* (2013) have reported preliminary results from the CASP study of integrated CBT for comorbid alcohol and social phobia indicating a therapeutic effect of integrated treatment for drinking outcomes but not social phobia outcomes. The current results are consistent with this preliminary data. Some previous work delivering CBT concurrently for both anxiety and dependence (Randall *et al.*, 2001) has demonstrated poor outcomes, possibly due to the research design precluding the capacity to differentiate alcohol-related anxiety from non-alcohol-related symptoms.

One of the strengths of the current study is the unique stepped-design that potentially facilitates a clear distinction between alcohol-related mental health symptoms and those that remain once heaving drinking

has resolved. In many studies initial diagnoses are confounded by the inability to distinguish between these. Patients may exhibit anxiety symptoms resulting from alcohol withdrawal for example. In addition, symptoms of depression and anxiety may resolve with abstinence so that further treatment is not required while in other cases where abstinence is achieved, these symptoms persist or worsen. From our current results, we can tentatively suggest that integrated treatment leads to better drinking outcomes, a trend for a reduction in anxiety symptoms and does not worsen anxiety nor depressive symptoms.

We were able to identify some factors that mediate the relationship between treatment, drinking and mood outcomes. While we did not observe that the presence of a depression or phobia diagnosis moderated the effect of treatment on drinking outcomes, we did find a significant mediating effect of DASS anxiety levels over time on treatment. This suggests that changes in anxiety influenced the relationship between treatment condition and heavy drinking. That is, the beneficial treatment effect of integrated CBT care on heavy drinking relative to usual care was observed in the context of changes in anxiety symptoms. One of the limitations of the current study is the lack of sufficient power to more thoroughly elucidate the differential effect of each primary and secondary diagnosis on treatment and also to examine factors relating to the maintenance of alcohol-related psychiatric comorbidity.

The current study investigated a potential pathway for which Drug and Alcohol units can address psychiatric comorbidity. Some possibilities include training existing counselling staff, utilizing a psychiatric consultation model or the introduction of experienced specialist clinical psychologists to deliver integrated interventions. Our results suggest that there is some value in applying a specialized service with experienced staff using an integrated treatment for comorbid anxiety and/or depression in an alcohol outpatient service to improve drinking outcomes.

AUTHORS' CONTRIBUTIONS

A.B. made contributions to the design of the study, developed, delivered and supervised the delivery of the CBT intervention. K.C.M. made contributions to the design of the study, wrote the manuscript and contributed to analysis. S.L. coordinated the study, collated the data and contributed to analysis. C.S. made contributions to the design of the study and delivered the integrated CBT interventions. M.T. contributed to the design of the study. P.S.H. made contributions to the design of the study and delivered medical treatment and supervised the implementation of the study. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

None declared.

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