Addiction
RESEARCH REPORT
doi:10.1111/add.12167

# Randomized controlled trial of cognitive behaviour therapy for comorbid post-traumatic stress disorder and alcohol use disorders

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## ABSTRACT

**Aims** This study aimed to test the efficacy of integrated cognitive behaviour therapy (CBT) for coexisting post-traumatic stress disorder (PTSD) and alcohol use disorders (AUD). **Setting** Clinics across Sydney, Australia. **Design** Randomized controlled trial of 12 once-weekly individual sessions of either integrated CBT for PTSD and AUD (integrated therapy, IT; $n = 33$) or CBT for AUD plus supportive counselling (alcohol-support, AS; $n = 29$). Blind assessments were conducted at baseline and post-treatment and at 5 [standard deviation (SD) = 2.25] and 9.16 (SD = 3.45) months post-treatment. **Participants** Sixty-two adults with concurrent PTSD and AUD. **Measurements** Outcomes included changes in alcohol consumption (time-line follow-back), PTSD severity [clinician-administered PTSD scale (CAPS)], alcohol dependence and problems, and depression and anxiety. **Findings** Reductions in PTSD severity were evident in both groups. IT participants who had received one or more sessions of exposure therapy exhibited a twofold greater rate of clinically significant change in CAPS severity at follow-up than AS participants [IT 60%, AS 39%, odds ratio (OR): 2.31, 95% confidence interval (CI): 1.06, 5.01]. AS participants exhibited larger reductions than IT participants in alcohol consumption, dependence and problems within the context of greater treatment from other services during follow-up. Results lend support to a mutually maintaining effect between AUD and PTSD. **Conclusions** Individuals with severe and complex presentations of coexisting post-traumatic stress disorder (PTSD) and alcohol use disorders (AUD) can derive substantial benefit from cognitive behaviour therapy targeting AUD, with greater benefits associated with exposure for PTSD. Among individuals with dual disorders, these therapies can generate significant, well-maintained treatment effects on PTSD, AUD and psychopathology.

**Keywords** Alcohol dependence, cognitive behaviour therapy (CBT), exposure therapy, post-traumatic stress disorder (PTSD), randomized controlled trial (RCT).

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Submitted 25 June 2012; initial review completed 2 August 2012; final version accepted 17 February 2013

## INTRODUCTION

Post-traumatic stress disorder (PTSD) is a debilitating disorder with a life-time population prevalence ranging from 6.8 to 7.2% and 12-month prevalence ranging from 3.5 to 4.4% [1–3]. PTSD is twice as common among women than men and is associated with significant comorbidity with alcohol use disorders (AUD), with a greater association with alcohol dependence than abuse [3,4]. Men with PTSD have a 6.5-fold and women a 4.5-fold increased risk of AUD than individuals without PTSD [5]. Compared with AUD only, comorbid AUD–PTSD is associated with greater physical and social impairment, higher rates of affective, anxiety and personality disorders and increased trauma-related craving [6–8].

The evidence supports a functional association between PTSD and AUD, with alcohol acting to regulate the negative emotion of PTSD [9–12]. It is hypothesized that once both disorders are established, there is a

maintaining and escalating reciprocal effect through alcohol's short-term anxiolytic effect on PTSD symptoms and an exacerbation of PTSD symptoms through repeated alcohol intoxication and withdrawal [13,14].

Research examining the impact of improvement in one disorder on the other has yielded mixed results. For example, in a 12-week randomized controlled trial (RCT) of either sertraline or placebo ($n = 94$) [15], in which both groups received cognitive behaviour therapy (CBT) for alcohol dependence but no psychological treatment for PTSD, Brady and colleagues reported large, significant decreases in alcohol consumption and PTSD symptoms in both groups. Improvements in alcohol dependence occurred either before or in conjunction with improvements in PTSD symptoms [16], but early reductions in PTSD symptoms had a greater impact on improvement in alcohol dependence than the reciprocal relationship. The authors conclude that treatment of PTSD may optimize treatment outcomes [16]. This concurs with preliminary findings among veterans with PTSD and substance use disorders (SUD), that dual-focus treatment is associated with superior outcomes to single-focus treatment [17,18].

Despite developments in efficacious treatment in PTSD [19] and AUD [20], there is little agreement regarding best practice for coexisting PTSD–AUD. Studies of the few PTSD–SUD interventions developed have achieved promising results [9], but have been characterized by small sample sizes [21,22], uncontrolled designs [23,24], drug use [21,23,24], a pre-requirement of SUD treatment [25] or equivalent results to addiction relapse prevention or health education [26–29].

Exposure-based CBT, a recommended treatment for PTSD [30], has received increasing endorsement as a viable treatment for PTSD–SUD [31], with preliminary support emanating from laboratory-based [8,31] and treatment [21,22,24] studies. Among the most relevant to the present study, two [23,24,32] combined exposure with CBT for SUD. The first [32] consisted of 20 sessions of CBT for cocaine abuse, stress inoculation and *in-vivo* exposure for PTSD. It was compared to Twelve-Step facilitation in a controlled trial ($n = 19$). One month post-treatment, both groups had improved in SUD, PTSD and psychiatric severity [21]. The second [23,24] consisted of 16 sessions of exposure for PTSD [33] and CBT for cocaine dependence and was tested in an uncontrolled design ($n = 39$). The authors reported large treatment effect sizes in PTSD and SUD for treatment completers ($n = 15$).

These studies provide preliminary support for the feasibility of exposure-based CBT with PTSD–SUD. However, to date there have been no RCTs of exposure-based CBT for comorbid PTSD–AUD [31]. The purpose of this study was to test whether combining existing therapies for AUD and PTSD would produce better outcomes than treating AUD only. The study aimed to compare the efficacy of integrated exposure-based CBT for PTSD and AUD (integrated therapy; IT) with CBT for AUD plus supportive counselling (alcohol support; AS). We hypothesized that both treatment conditions would produce significant reductions in alcohol consumption and PTSD symptoms and that these improvements would be significantly greater in IT than AS.

## METHOD

### Participants

Participants were recruited from a range of services in metropolitan Sydney, Australia, between October 2007 and October 2009. Participants were eligible if they were aged 18 years and over, consumed alcohol at hazardous levels [34] (men 29 or more and women 15 or more 10-g ethanol drinks per week) and met Diagnostic and Statistical Manual of Mental Disorder (4th edn; DSM-IV) [35] diagnostic criteria for PTSD, determined by the clinician-administered PTSD scale (CAPS) [36]. AUD diagnosis was determined by the Structured Clinical Interview (SCID) DSM-IV [37]. Participants on stable doses (for 2 months or longer) of pharmacotherapy for depression or alcohol dependence were eligible, as were participants who needed and completed alcohol withdrawal [38]. Participants were excluded if they were 17 years or younger, had current psychosis, severe suicide risk, significant cognitive impairment, limited English comprehension and severe substance dependence [39,40].

Of the 154 participants screened by telephone, 90 met study criteria and were offered a full face-to-face assessment. A description of participant characteristics is presented in Table 1. Written informed consent was obtained from all participants as approved by the University of New South Wales Human Ethics Review Committee (HREC 07112) and the ethics committees of the participating hospitals. Participants were informed that they would be allocated randomly to one of two treatment conditions and reimbursed ($30) for each assessment, but not for treatment attendance.

Participant flow is summarized in Fig. 1. Sixty-two participants were randomized equally to either IT ($n = 33$) or AS ($n = 29$). All available participants were re-assessed at follow-up irrespective of treatment attendance. Forty-eight participants (77%) completed two or more follow-ups, 56 (90%) one or more and six (10%) had no follow-up data (three per group).

### Procedure

The study involved participant-level randomization to conditions, which was conducted, according to a random

**Table 1** Participant characteristics by group (IT and AS).

| *Variable* | *IT*[a] *n = 33* | *AS*[a] *n = 29* | *Total N = 62* |
|---|---|---|---|
| Demographics | | | |
| Age (years) | 41.85 (12.62) | 40.41 (11.21) | 41.18 (11.91) |
| Gender, *n* (%) | | | |
| Male | 14 (42) | 15 (52) | 29 (47) |
| Female | 19 (58) | 14 (48) | 33 (53) |
| Employed, *n* (%) | 14 (42) | 14 (48) | 28 (45) |
| Education, years | 11.12 (1.27) | 10.66 (1.31) | 10.90 (1.30) |
| Married/cohabitating, *n* (%) | 10 (30) | 8 (28) | 18 (29) |
| Living alone, *n* (%) | 11 (33) | 10 (35) | 21 (34) |
| Recruited from drug and alcohol treatment services *n* (%) | 17 (52) | 12 (42) | 29 (47) |
| Alcohol and other substances | | | |
| Alcohol-dependent, *n (%)* | 30 (91) | 29 (100) | 59 (95) |
| Age of onset of alcohol dependence | 29.81 (10.64) | 27.98 (8.47) | 28.94 (9.64) |
| SADQ | 32.07 (17.22) | 32.52 (14.45) | 32.28 (15.82) |
| DDD | 13.41 (7.36) | 15.99 (6.86) | 14.62 (7.19) |
| PDA, median (range) | 10.00 (0–76) | 13.00 (0–58) | 12.50 (0–76) |
| SIP | 25.61 (10.43) | 27.92 (11.08) | 26.70 (10.70) |
| SDS: other substance-dependent, *n* (%) | 6 (18) | 3 (10) | 9 (15) |
| Alcohol pharmacotherapy, *n* (%) | 8 (24) | 7 (24) | 15 (24) |
| Antidepressants, *n* (%) | 14 (42) | 12 (41) | 26 (42) |
| Trauma and PTSD | | | |
| TEQ type of trauma, *n* (%) | | | |
| Violent crime (rape, robbery, assault) | 10 (30) | 9 (31) | 19 (31) |
| Child physical/sexual abuse | 5 (15) | 9 (31) | 14 (23) |
| Witnessed injury/killing/mutilation | 6 (18) | 3 (10) | 9 (15) |
| News of someone close | 4 (12) | 3 (10) | 7 (11) |
| Adult abusive relationship | 2 (6) | 2 (7) | 4 (7) |
| Accident/fire/explosion | 2 (6) | 2 (7) | 4 (7) |
| Danger of losing life/other | 4 (12) | 1 (3) | 5 (8) |
| Age of onset of most traumatic event | 23.58 (12.83) | 21.59 (12.67) | 22.65 (12.69) |
| Years since index trauma | 18.27 (14.81) | 18.83 (13.25) | 18.53 (13.99) |
| CAPS full diagnostic criteria, *n* (%) | 30 (91) | 28 (97) | 58 (94) |
| CAPS–severity total | 68.00 (23.63) | 68.07 (21.10) | 68.03 (22.30) |
| PDS–re-experiencing | 8.76 (3.29) | 8.19 (3.62) | 8.49 (3.43) |
| PDS–avoidance | 13.66 (5.14) | 13.15 (4.74) | 13.42 (4.91) |
| PDS–arousal | 10.66 (3.33) | 10.04 (3.19) | 10.36 (3.25) |
| PDS–total | 33.07 (10.43) | 31.38 (10.43) | 32.27 (10.37) |
| PTCI | 12.55 (4.11) | 12.51 (2.62) | 12.53 (3.45) |
| Other psychopathology | | | |
| BDI-II | 30.37 (13.99) | 28.50 (9.15) | 29.49 (11.88) |
| STAI–State | 55.89 (14.78) | 55.96 (10.80) | 55.92 (13.00) |
| STAI–Trait | 59.52 (12.52) | 59.68 (10.61) | 59.60 (11.30) |
| MSI-BPD, *n (%)* | 21 (64) | 20 (68) | 41 (66) |
| SF12–mental | 32.53 (12.29) | 32.61 (11.63) | 32.57 (11.87) |
| SF12–physical | 46.23 (10.57) | 42.75 (9.93) | 44.59 (10.32) |

Data are means (standard deviations) unless otherwise noted. [a]There were no statistical differences between treatment groups on any variable. IT: integrated therapy; AS: alcohol + support; SADQ: Severity of Alcohol Dependence Questionnaire; DDD: drinks per drinking day; PDA: proportion of days abstinent; SIP: Short Inventory of Problems; SDS: Severity of Dependence Scale; TEQ: Traumatic Events Questionnaire [83]; CAPS: clinician-administered PTSD scale; PDS: Post-traumatic Stress Diagnostic Scale; PTCI: Post-traumatic Cognitions Inventory [84]; BDI-II: Beck Depression Inventory; STAI: Spielberger State–Trait Anxiety Inventory; MSI-BPD: McLean Screening Instrument for Borderline Personality Disorder (cut-off score of 7) [85]; SF12: Short-Form Health Survey [86].

numbers system, by a person independent of the study. Treatment allocation was concealed in sequentially numbered, double-lined, opaque, security-sealed envelopes, held centrally. Following diagnostic assessment, therapists phoned the administrator to be told the next participant's treatment allocation. This ensured that randomization was not influenced by participant characteristics.

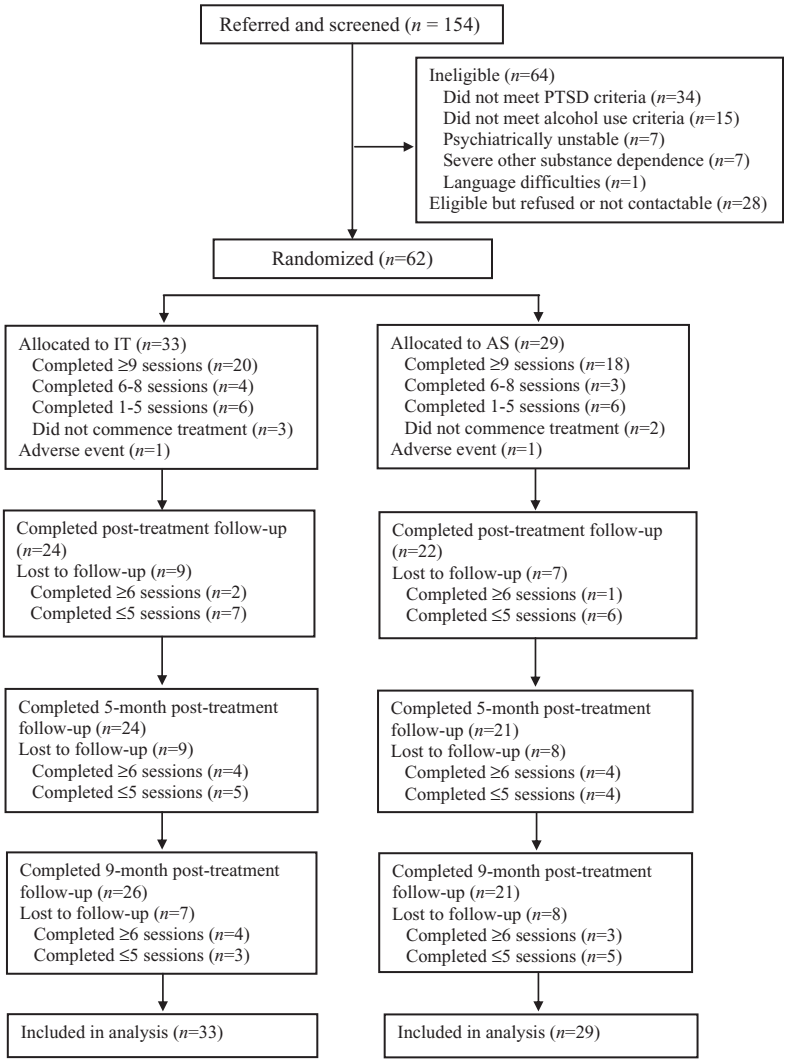


**Figure 1** Participant flow [Consolidated Standards of Reporting Trials (CONSORT)] diagram

Assessment was conducted prior to randomization (baseline), post-treatment and a mean of 5 [standard deviation (SD) = 2.25] and 9.16 (SD = 3.45) months after the last day of attendance, with measures re-administered at each time-point. Follow-up assessments were conducted by independent clinicians who were unaware of the participants' treatment condition and did not have access to participant clinical or supervision notes or treatment allocation.

## Measures

### *Primary outcomes*

Severity of PTSD symptomatology (past month) was determined using the CAPS [36] with the original scoring rules (frequency >1/intensity ≥2) for each symptom [36,41]. Alcohol consumption (drinks per drinking day, DDD; and proportion of days abstinent, PDA) was measured (past 90 days) using the alcohol time-line follow-back method [42], which has high test–re-test reliability (0.79–0.96) and content, construct and criterion validity [42].

### *Secondary outcomes*

Broader treatment response was assessed by the Severity of Alcohol Dependence Questionnaire (SADQ-C) [43]; the Short Inventory of Problems (SIP) [44]; the Beck Depression Inventory (2nd edn; BDI-II) [45]; the State–Trait Anxiety Inventory (STAI) [46]; and the Post-traumatic Disorder Scale (PDS) [47], which was also administered weekly during treatment to monitor symptoms of PTSD.

## Treatment conditions

Two PhD-level and two masters-level clinical psychologists provided therapy in both conditions. Formal training in exposure for PTSD and CBT for AUD and weekly clinical supervision were provided by clinical

psychologists with expertise and extensive experience treating each disorder.

Treatment in both conditions was manual-guided, and consisted of 12, once-weekly 90-minute, individual sessions with structured daily homework tasks. All treatment sessions were recorded. Homework, daily monitoring records and PDS scores were checked at each session in both treatment conditions.

IT and AS treatment components are outlined in Table 2. Participants in both conditions received the same treatment targeting AUD, which was based on the Project MATCH CBT manual [20,48] and the motivationally enhanced Combined Behavioral Intervention Manual (COMBINE) [49], interventions with a strong empirical support for efficacy with AUD [20,50,51]. To equalize time in treatment and therapist attention, AS participants also received supportive counselling, a generic, present-centred, manualized control condition, developed and tested by Bryant and colleagues [52]. Equal time was devoted to AUD treatment and supportive counselling. AS treatment targeted AUD symptoms only, not PTSD symptoms.

IT integrated CBT for AUD with a manualized, exposure-based CBT [52–54], incorporating exposure therapy [54] with cognitive restructuring for PTSD-related cognitions [55,56]. Combined exposure and cognitive restructuring, while not in wide current practice, have been shown to be at least comparable to each alone [57,58] and, in some cases, superior to exposure alone in terms of PTSD and depression [53].

During imaginal exposure, participants were instructed to provide a narrative of their trauma that involved reciting the experience in the first person and present tense, with specific instructions to focus on the full range of sensory and affective responses to the trauma. The narrative was repeated if necessary to ensure that exposure occurred for 45 minutes. Participants were given explicit instructions to rehearse the exercise daily and listen to recordings of their narrative between sessions. In cases with multiple trauma the most currently distressing experience took precedence [59]. Monitoring forms for imaginal exposure were completed during sessions and for daily homework.

### Treatment integrity

Recordings of 116 (21% of 562) therapy sessions were selected randomly and rated by two independent clinical

**Table 2** Integrated therapy (IT) and alcohol-support (AS) therapy components.

| *Sessions*[a] | *Integrated therapy* | *Alcohol support* |
|---|---|---|
| 1–2 | Motivational interviewing to increase readiness for change and realistic alcohol consumption goal-setting; brief description of treatment; rationale for exposure; obtaining a brief account of the trauma; developing an initial case formulation; and introducing monitoring tasks | Motivational interviewing to increase readiness for change and realistic alcohol consumption goal-setting; brief description of treatment and rationale; introducing monitoring tasks; supportive counselling[b] |
| 3–4 | Assessing high-risk situations; coping with cravings and urges; PTSD psychoeducation; rationale for imaginal exposure and *in-vivo* exposure; sharing an individualized PTSD–AUD symptom maintenance model ('vicious cycle') | Assessing high-risk situations; coping with cravings and urges; rationale for treatment of alcohol dependence; supportive counselling |
| 5–6 | Identifying trauma-related cognitive distortions and thoughts about alcohol and drinking; prolonged imaginal exposure imaginal exposure narrative (recounting the traumatic memory in the present tense for a minimum of 45 minutes); introduction to daily imaginal exposure practice; introduction to *in-vivo* exposure and developing a hierarchy of feared situations and homework | Identifying thoughts about alcohol and drinking; coping with cravings and urges; an individualized coping plan and 'lapses'; supportive counselling |
| 7–9 | Managing negative moods; pleasant events scheduling; dealing with lapses; cognitive restructuring for PTSD; in-session imaginal exposure and daily practice; *in-vivo* exposure hierarchy and daily practice | Managing negative moods; pleasant events scheduling; coping with cravings and urges; dealing with lapses; supportive counselling |
| 10–12 | Managing thoughts about alcohol; cognitive restructuring for PTSD; in-session imaginal exposure; *in-vivo* exposure practice; a personal lapse plan; relapse prevention for AUD and PTSD; review and consolidation of progress; and termination | Managing thoughts about alcohol; a personal lapse plan; relapse prevention for AUD; review and consolidation of progress; supportive counselling; and termination |

[a]Each session commenced with a review of the previous week, a risk assessment (suicide, harm), a discussion of alcohol consumption, urges and coping, administration of Post-traumatic Stress Diagnostic Scale (PDS), and review of post-traumatic stress disorder (PTSD)-related imaginal exposure and *in-vivo* exposure tasks. [b]Supportive counselling consisted of empathic, generic, present-centred counselling and problem solving. Equal time was devoted to alcohol use disorder (AUD) treatment and supportive counselling.

psychologists experienced in CBT. These clinicians noted the time spent on each component and rated its presence or absence, without regard to treatment condition or session. They also indicated the quality of therapy provided on a seven-point scale (1 = unacceptable, 7 = very good). There was high inter-rater consistency on treatment components on eight sessions rated by both clinicians (Spearmen's rho = 0.72, $P < 0.001$). The mean quality ratings for treatment components across conditions was 6.2 (SD = 1.18).

### Data analysis

All analyses were based on intent-to-treat, including all participants who entered the trial. Baseline characteristics were analysed using analysis of variance for continuous, $\chi^2$ tests for categorical data, Mann–Whitney *U*-test for non-parametric data and logistic regression for dichotomous data. Jacobson & Truax's [60] third operational definition of clinically significant change was calculated for CAPS–severity which yielded a cut-off of <37 at follow-up. Generalized estimating equations (GEE) with autoregressive correlation matrices were conducted to determine differences on outcomes by treatment over time. GEE is designed to analyse correlated data arising from repeated measurements, requires no parametric distribution and provides robust inference with respect to mis-specification of the within-subjects correlation. GEE also allows for examination of data which may be missing for some participants either because of a missed session or dropout; thus, complete information for all participants is not needed. All inferences from incomplete or missing data are presumed valid, provided the data are missing at random [61,62]. As IT and AS did not differ in treatment attendance, study retention or follow-up completion, these inferences were valid. Statistical analyses were conducted using PASW statistics version 20.

An initial power analysis estimated that a sample of 175 would be required to identify an effect size of 0.5 between treatment groups, 6 months post-treatment, in a regression model, with power = 0.8, alpha = 0.05. As the final sample size was 62, due to a slower-than-expected recruitment rate, the power of the study was re-calculated, using the actual sample size and longitudinal design with four time-points. A sample size of 62 had 80% power to detect a difference in change in CAPS–severity over time by treatment [63] under the assumptions of a large effect size in trauma-focused compared to non-trauma-focused treatment [52] and a two-sided alpha = 0.05. The sample size had 39% power to detect a difference in change in alcohol consumption over time by treatment, under the assumption of a small-to-moderate effect size for alcohol consumption [64] and a two-sided alpha = 0.05.

## RESULTS

### Baseline characteristics

There were no significant differences in baseline demographic and clinical characteristics by randomized treatment allocation. Comparisons of 45 participants who completed 50% or more therapy sessions with 17 participants who completed 0–5 sessions revealed that the latter had higher DDD (mean = 17.76, SD = 8.94 versus mean = 13.43, SD = 6.11, $P < 0.05$) and PDS–total score (mean = 39.20, SD = 10.23 versus mean = 30.73, SD = 9.86, $P < 0.05$) than the former group.

### Treatment and study retention

Group differences in treatment attendance, completion and follow-up were not significant. A median of 10.50 (range 0–16) sessions (15.75 hours) of therapy (IT, 11.00; AS, 10.00, $P = 0.420$) were attended, within a mean of 19.87 (SD = 11.97) weeks (IT, 21.21, AS, 18.34, $P = 0.351$), with similar proportions attending 0–5 sessions (IT, 27%; AS, 28%, $P = 0.600$), and similar proportions completing each follow-up assessment (post-treatment: IT, 72%, AS, 75%, $P = 0.505$; 5-month: IT, 73%, AS, 73%, $P = 0.600$; and 9-month: IT, 78%, AS, 72%, $P = 0.386$).

Differences (minutes) in session length (IT: mean = 79.28, SD = 24.23; AS: mean = 83.45, SD = 18.85, $P = 0.343$) and time spent on CBT for AUD (IT: mean = 45.71, SD = 29.81; AS: mean = 55.33, SD = 22.89, $P = 0.061$) were not significant. Eighteen of 33 IT participants (55%) had exposure (imaginal exposure: mean = 4.00, SD = 2.13 sessions; in-*vivo* exposure: median = 4, range 1–6 sessions), during a median of 13.00 (range 6–16) sessions (19.5 hours) of therapy, over a mean of 24.22 (SD = 9.17) weeks. Of the 15 who had trauma-focused CBT without exposure, 11 (67%) discontinued before exposure; two (13%) refused exposure; and two were deemed to be a serious suicide risk and were referred to appropriate services.

### Treatment from other services

Prior to the 5-month follow-up, significantly more AS than IT participants [60 versus 29% respectively; odds ratio (OR): 3.64, 95% confidence interval (CI): 1.04, 12.78] had additional alcohol-related treatment (defined as one or more admission and/or three or more visits). Post-treatment, those with greater additional treatment had higher DDD (mean = 10.23, SD = 7.60 versus mean = 6.47, SD = 3.94, $P < 0.05$), PDS–total (mean = 29.26, SD = 13.60 versus mean = 15.83, SD = 12.29, $P < 0.01$) and BDI-II (mean = 32.84, SD = 15.74 versus mean = 19.88, SD = 13.88, $P < 0.01$) scores. Final GEE models were adjusted for additional treatment to control for differences.

### Between-treatment differences

Descriptive statistics for outcomes over time are presented in Table 3. Final GEE models are presented in Table 4.

#### *Alcohol consumption*

There was a significant time × treatment interaction for DDD at the 5-month follow-up with lower consumption among AS (mean = 6.91, SD = 6.22) than IT participants (mean = 8.81, SD = 5.89). Differences by group in PDA were not significant. Figures 2 and 3 show DDD and PDA by group over time.

There was a significant time × treatment interaction for SADQ at the 5-month follow-up, with lower dependence reported by AS (mean = 19.10, SD = 17.04) than IT (mean = 25.92, SD = 20.08) participants. There was a significant treatment × time interaction for SIP scores, whereby at the 5- and 9-month follow-ups there were fewer problems reported by AS than IT participants (Table 3). Between-group differences in the percentage of participants with an AUD diagnosis were not significant.

#### *PTSD, depression and anxiety*

Between-group differences in CAPS–severity over time, as shown in Fig. 4, were not significant. Logistic regression, predicting reductions (of 30 points or greater [65]) in CAPS–severity, identified higher rates of improvement among IT than AS participants (IT 55%, AS 32%, OR:

**Table 3** Descriptive statistics[a] by group (IT, AS) for the primary and secondary outcomes post-treatment and at the 5-month and 9-month post-treatment follow-up.

| *Outcomes* | *Group* | *Baseline n = 62* | *Post-treatment n = 46* | *5 months n = 45* | *9 months n = 47* |
|---|---|---|---|---|---|
| Alcohol | | | | | |
| DDD | IT | 13.41 (7.36) | 7.47 (5.22) | 8.81 (5.89) | 6.97 (4.16) |
| | AS | 15.99 (6.89) | 8.74 (9.51) | 6.91 (6.22) | 7.90 (6.24) |
| | Tot | 14.62 (7.19) | 8.03 (7.52) | 7.95 (6.05) | 7.38 (5.11) |
| PDA, median (range) | IT | 10 (0–76) | 28.00 (0–90) | 35.50 (0–89) | 27.50 (0–90) |
| | AS | 13.00 (0–58) | 61.00 (11–90) | 32.00 (0–90) | 48.50 (0–90) |
| | Tot | 12.50 (0–76) | 44.50 (0–90) | 33.50 (0–90) | 39.00 (0–90) |
| SADQ | IT | 32.07 (17.22) | 23.38 (16.03) | 25.92 (20.08) | 22.65 (16.15) |
| | AS | 32.52 (14.45) | 21.77 (15.11) | 19.10 (17.04) | 21.95 (16.61) |
| | Tot | 32.28 (15.82) | 22.61 (15.44) | 22.73 (18.83) | 22.34 (16.18) |
| SIP | IT | 25.61 (10.43) | 18.46 (12.9) | 20.46 (13.25) | 20.38 (13.61) |
| | AS | 27.92 (11.08) | 17.86 (13.22) | 14.95 (13.90) | 15.33 (13.58) |
| | Tot | 26.70 (10.70) | 18.17 (12.91) | 17.89 (13.67) | 18.13 (13.69) |
| AUD diagnosis, *n* (%) | IT | 33 (100) | 16 (64) | 10 (44) | 14 (52) |
| | AS | 29 (100) | 12 (50) | 7 (33) | 9 (43) |
| | Tot | 62 (100) | 28 (57) | 17 (37) | 23 (48) |
| PTSD | | | | | |
| CAPS–severity | IT | 68.00 (23.63) | 42.80 (26.45) | 40.39 (23.49) | 43.30 (28.25) |
| | AS | 68.07 (21.10) | 46.71 (26.27) | 49.71 (22.90) | 41.19 (34.17) |
| | Tot | 68.03 (22.30) | 44.71 (26.16) | 44.84 (23.42) | 42.38 (30.65) |
| PTSD diagnosis, *n* (%) | IT | 30 (91) | 10 (40) | 8 (36) | 9 (33) |
| | AS | 28 (97) | 9 (38) | 10 (46) | 9 (43) |
| | Tot | 58 (94) | 19 (39) | 18 (41) | 18 (38) |
| PDS–total | IT | 33.07 (10.43) | 21.88 (14.66) | 20.88 (13.37) | 22.88 (16.68) |
| | AS | 31.38 (10.43) | 24.18 (14.05) | 24.48 (16.00) | 20.81 (17.00) |
| | Tot | 32.27 (10.37) | 22.98 (14.26) | 22.56 (14.60) | 21.96 (16.67) |
| Depression and anxiety | | | | | |
| BDI-II | IT | 30.37 (13.99) | 25.13 (17.96) | 26.79 (18.35) | 23.38 (15.14) |
| | AS | 28.50 (9.15) | 25.45 (12.52) | 25.33 (12.56) | 22.24 (14.82) |
| | Tot | 29.49 (11.88) | 25.28 (15.43) | 26.11 (15.76) | 22.87 (14.85) |
| STAI–S | IT | 55.89 (14.78) | 48.83 (15.90) | 53.17 (14.41) | 52.00 (14.74) |
| | AS | 55.96 (10.80) | 53.64 (10.47) | 54.71 (14.30) | 49.81 (14.76) |
| | Tot | 55.92 (13.00) | 51.13 (13.65) | 54.24 (14.20) | 51.02 (14.63) |

[a]Data are means (standard deviations) unless otherwise noted. IT: integrated therapy; AS: alcohol + support; DDD: drinks per drinking day; PDA: proportion of days abstinent; SADQ: Severity of Dependence Questionnaire; SIP: Short Inventory of Problems; AUD: alcohol use disorder; CAPS–severity: clinician-administered PTSD scale severity; PTSD: post-traumatic stress disorder; PDS–total: Post-traumatic Stress Diagnostic Scale total score; BDI-II: Beck Depression Inventory; STAI-S: Spielberger State–Trait Anxiety Inventory—State.

**Table 4** Between-group intent-to-treat final generalized estimating equations (GEE) models for primary and secondary outcomes over time (baseline, post-treatment and 5-month and 9-month follow-up).[a]

| *Outcomes* | *β* | *SE* | *P* |
|---|---|---|---|
| Alcohol | | | |
| DDD | | | |
| Treatment × post-treatment | −0.08 | 0.24 | 0.735 |
| Treatment × 5 months | 0.40 | 0.20 | 0.048 |
| Treatmen × 9 months | 0.15 | 0.19 | 0.431 |
| PDA | | | |
| Treatment[b] | −0.35 | 0.18 | 0.053 |
| Time[c] | | | |
| Post-treatment | 0.98 | 0.13 | 0.001 |
| 5 months | 0.90 | 0.16 | 0.001 |
| 9 months | 0.95 | 0.14 | 0.001 |
| SADQ[bc] | | | |
| Treatment × post-treatment | 3.42 | 3.90 | 0.381 |
| Treatment × 5 months | 10.74 | 4.03 | 0.008 |
| Treatment × 9 months | 1.48 | 4.58 | 0.746 |
| SIP[bc] | | | |
| Treatment × post-treatment | 4.58 | 3.29 | 0.164 |
| Treatment × 5 months | 10.19 | 3.26 | 0.002 |
| Treatment × 9 months | 8.09 | 3.16 | 0.010 |
| AUD diagnosis[e] | | | |
| Treatment[b] | 0.42 | 0.41 | 0.306 |
| Time[d] | | | |
| 5 months | −0.78 | 0.40 | 0.053 |
| 9 months | −0.46 | 0.40 | 0.248 |
| PTSD | | | |
| CAPS–severity | | | |
| Treatment[b] | 0.16 | 5.76 | 0.977 |
| Time[c] | | | |
| Post-treatment | −21.98 | 3.54 | 0.001 |
| 5 months | −22.08 | 2.68 | 0.001 |
| 9 months | −23.97 | 3.48 | 0.001 |
| PTSD diagnosis[e] | | | |
| Treatment[b] | −0.30 | 0.51 | 0.554 |
| Time[d] | | | |
| Post-treatment | 0.15 | 0.29 | 0.607 |
| 5 months | −0.25 | 0.24 | 0.307 |
| PDS-Total | | | |
| Treatment[b] | 1.30 | 3.09 | 0.675 |
| Time[c] | | | |
| Post-treatment | −8.31 | 1.52 | 0.000 |
| 5 months | −9.60 | 1.31 | 0.000 |
| 9 months | −9.77 | 1.75 | 0.000 |
| Depression and anxiety | | | |
| BDI-II | | | |
| Treatment[b] | 1.64 | 3.02 | 0.586 |
| Time[c] | | | |
| Post-treatment | −3.21 | 1.76 | 0.069 |
| 5 months | −3.28 | 2.12 | 0.121 |
| 9 months | −6.07 | 1.78 | 0.001 |
| STAI-S | | | |
| Treatment[b] | 0.28 | 2.80 | 0.923 |
| Time[c] | | | |
| Post-treatment | −3.87 | 2.00 | 0.053 |
| 5 months | −1.01 | 2.28 | 0.658 |
| 9 months | −4.96 | 2.30 | 0.031 |

[a]Models are adjusted for additional treatment. [b]Reference category is AS. [c]Reference category is baseline. [d]Reference category is post-treatment. Baseline diagnostic data could not be included in the model because of total separation which created a singular hessian matrix and impeded convergence. [e]Reference category is 0 ('no diagnosis'). DDD: drinks per drinking day; PDA: proportion of days abstinent; SADQ: Severity of Dependence Questionnaire; SIP: Short Inventory of Problems; AUD diagnosis: alcohol use disorder diagnosis; CAPS–severity: clinician-administered PTSD scale severity; PTSD diagnosis: post-traumatic stress disorder diagnosis; PDS–total: Post-traumatic Stress Diagnostic Scale total score; BDI-II: Beck Depression Inventory; STAI–S: Spielberger State–Trait Anxiety Inventory—State; SE: standard error.

2.53, 95% CI: 1.27, 5.04), largely reflecting differences at the 5-month follow-up (IT 57%, AS 18%, OR: 5.85, 95% CI: 1.44, 22.83). However, a clinical significance test of CAPS–severity at follow-up was only marginally significant (IT 54%, AS 39%, $\chi^2$ 3.28, d.f. 1, $P = 0.050$). Between-group differences in the percentage of participants with a PTSD diagnosis, PDS–total score, BDI-II and STAI–State were not significant.

### Exposure therapy

The impact of exposure on outcomes was tested by including a three-way variable ('exposure': IT no exposure; IT exposure, defined as one or more therapy session; and AS) in final GEE models. There were no significant differences by exposure on any outcomes. Exposure was then used to predict a CAPS–severity reduction (30 points or greater) in a logistic regression. A reduction in CAPS–severity was significantly more likely among IT exposure than AS participants (62 versus 18%, respectively; OR: 4.05, 95% CI: 1.78, 9.20) but not IT no exposure participants (50%) (OR: 1.45, 95% CI: 0.57, 3.74). IT exposure only (60%), but not IT no exposure (47%), remained significant relative to AS (39%) when tested in a logistic regression predicting clinical significant change in CAPS–severity at follow-up (OR: 2.31, 95% CI: 1.06, 5.01).

### During treatment differences

Data collected during treatment were analysed, using GEE, to determine early between-group differences in response. Significantly more drinks per week were consumed by IT than AS participants (median = 27.00, range 0–150; median = 18.00, range 0–40, respectively; Wald $\chi^2 = 4.48$, d.f. 1, $P < 0.05$), especially during exposure, with greater PDS–re-experiencing (time × group interaction, Wald $\chi^2 = 24.97$, d.f. 11, $P < 0.01$). Median drinks per week and mean PDS–re-experiencing are shown in Figs 5 and 6.

## DISCUSSION

The results support the hypothesized improvement for both treatment conditions. From baseline to 9 months post-treatment, significant improvements were evident in both groups on measures of PTSD, AUD, depression and anxiety. There was marginal support for the hypothesized superior outcomes of IT over AS, despite large differences in symptom reduction (30 points or greater [65]), especially 5 months post-treatment. Clinically significant differences were, however, evident by exposure therapy. Compared to AS participants, only IT participants who had received one or more session of exposure therapy had a twofold greater likelihood of a clinically significant reduction in CAPS–severity at follow-up.

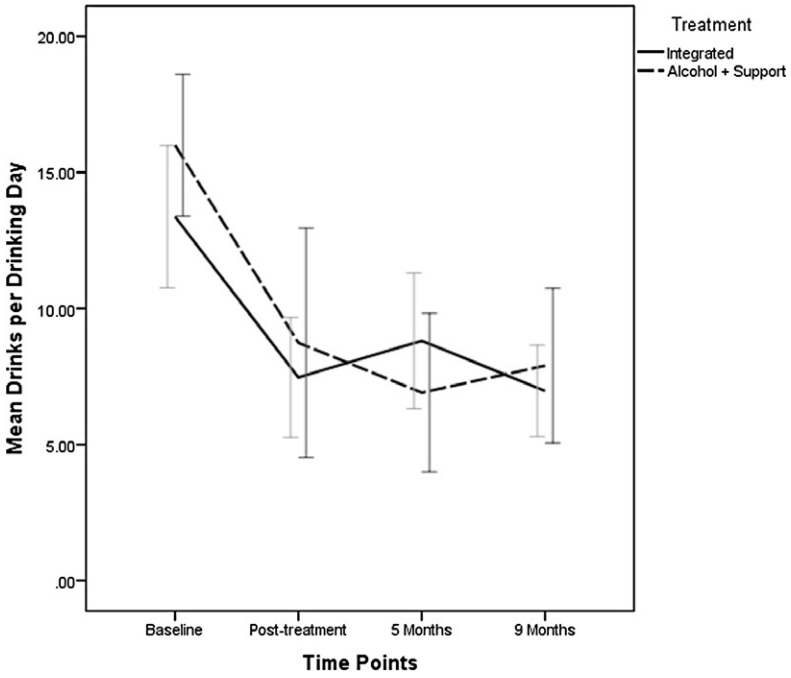


**Figure 2** Mean (with 95% confidence intervals) drinks per drinking day (DDD) at baseline, post-treatment and 5 and 9 months post-treatment follow-up by treatment condition [integrated therapy (IT) and alcohol + support (AS)]

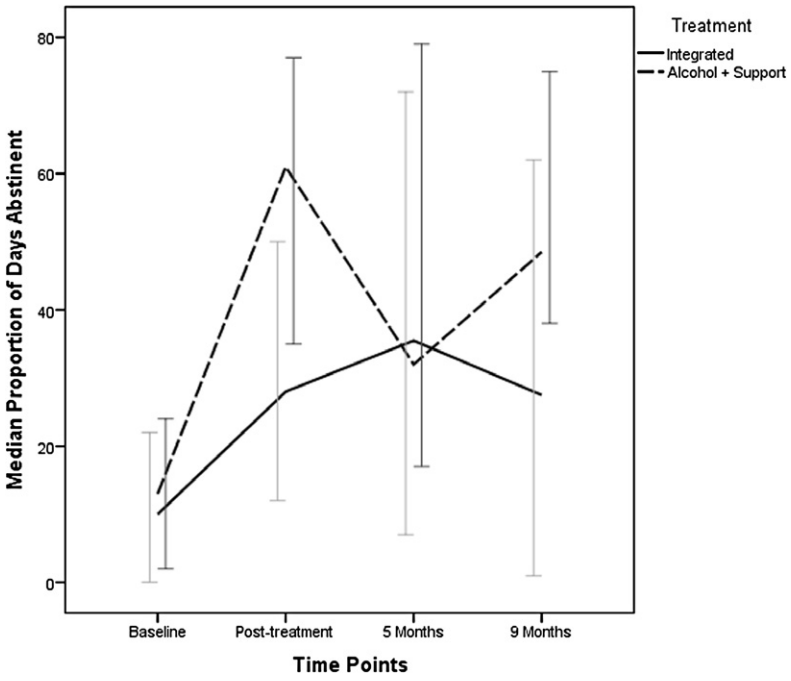


**Figure 3** Median (with 95% confidence intervals) proportion of days abstinent at baseline, post-treatment and 5 and 9 months post-treatment follow-up by treatment condition [integrated therapy (IT) and alcohol + support (AS)]

AUD outcomes were more mixed. Although AS participants during follow-up reported lower alcohol consumption, dependence and problems than IT participants, they were also three times more likely than their counterparts to receive treatment from other services. Extra treatment was associated with higher post-treatment PTSD, alcohol consumption and depression. Therefore, it may be argued that without extra treatment their impairment would have escalated.

There are several possible explanations for the limited advantage of IT over AS in PTSD treatment outcomes; the most likely is an insufficient PTSD treatment 'dose', with only 55% of IT participants receiving exposure therapy (a mean of four sessions of each imaginal and *in-vivo* exposure). This interpretation is underscored by the finding of a significant association between IT exposure and reduced PTSD–severity. An insufficient treatment dose may also explain the attenuated alcohol-related outcomes achieved by IT, and raises

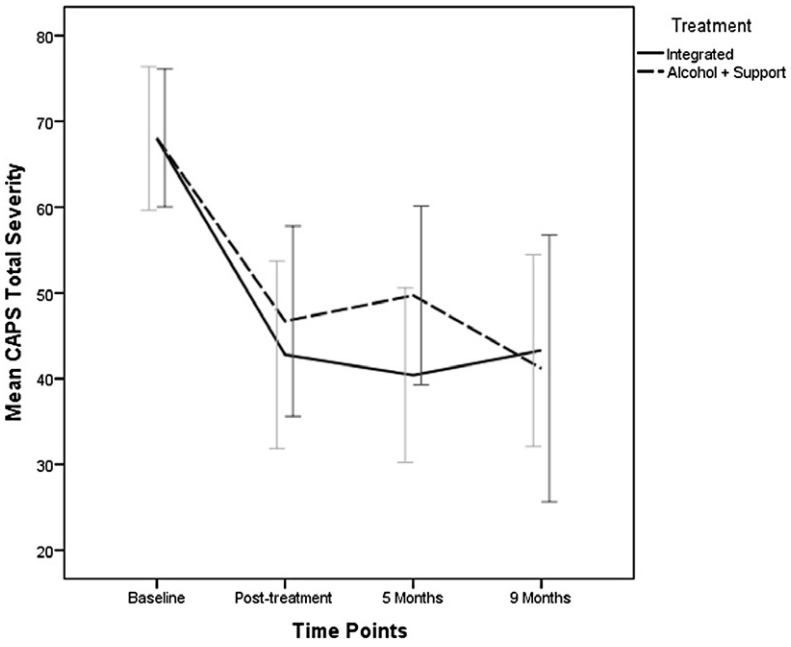


**Figure 4** Mean (with 95% confidence intervals) clinician-administered post-traumatic stress disorder (PTSD) scale (CAPS) severity at baseline, post-treatment and 5 and 9 months post-treatment follow-up by treatment condition [integrated therapy (IT) and alcohol + support (AS)]

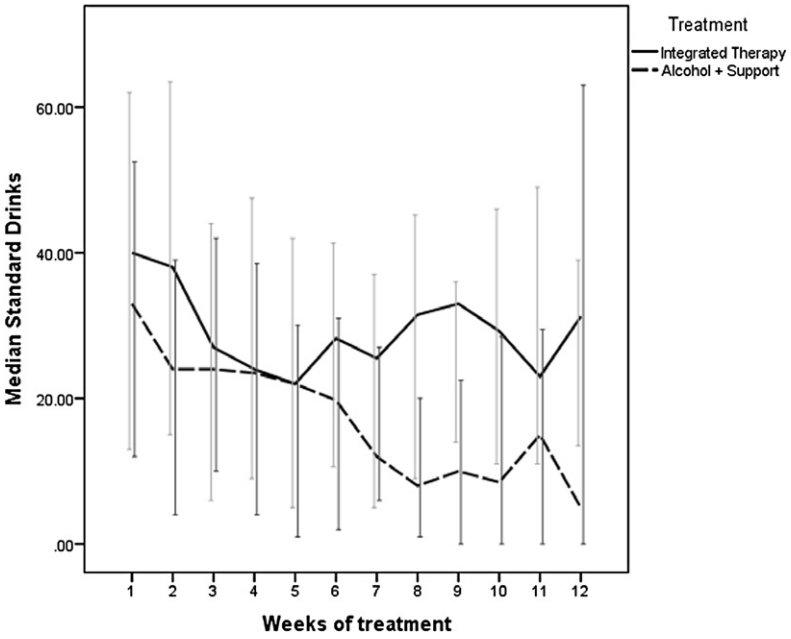


**Figure 5** Median (with 95% confidence intervals) number of drinks per week by group during treatment

the possibility that combining therapies may reduce the impact of each [66–68].

The finding of comparable between-group improvements in PTSD and AUD is consistent with previous research. For example, significant improvement in PTSD in the absence of specific PTSD treatment was reported following sertraline and CBT for AUD [15], SUD treatment [69], relapse prevention and health education [28,29], Twelve-Step facilitation [21], substance withdrawal [70] and pharmacotherapy for cocaine [71]. Comparable outcomes between dual treatment and single-focus AUD treatment have been reported in RCTs of comorbid panic disorder [72], social phobia [68] and depression [73], and are thought to be mediated by a reduction in general psychopathology following reduced alcohol consumption [74–76].

Comparable between-treatment improvement in PTSD may also result from generalization of learning, from CBT for AUD to trauma, among AS participants. Amelioration of untargeted comorbid disorders has been reported in RCTs of CBT for panic [67] and generalized anxiety disorders [67], and has been attributed to increased self-efficacy and coping and reduced negative affectivity [67]. Furthermore, improvement in PTSD

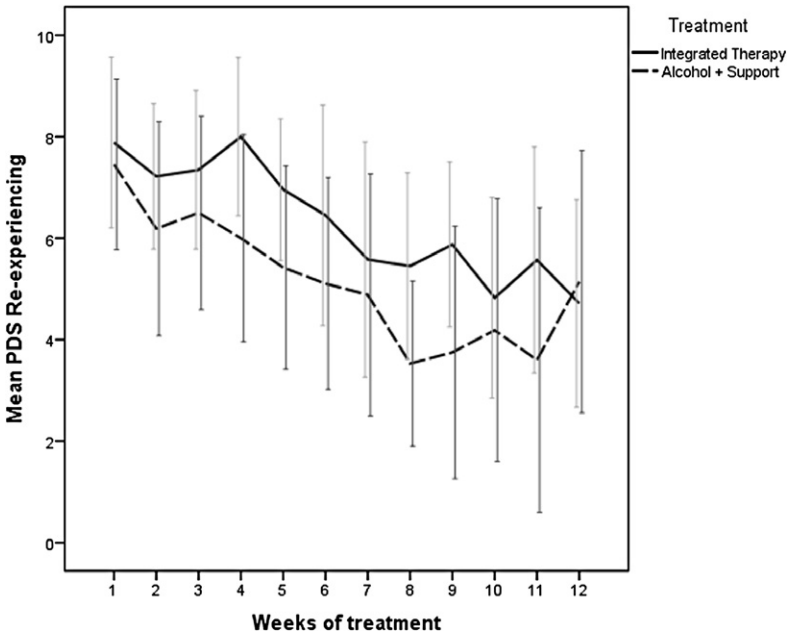


**Figure 6** Mean (with 95% confidence intervals) weekly post-traumatic diagnostic scale re-experiencing scores by group during treatment

symptomatology can occur in the absence of systematic confrontation of trauma memories [77,78].

Improvement in the absence of specific trauma treatment is consistent with the view that alcohol and PTSD may be related causally, with alcohol exerting a maintaining effect on PTSD and psychopathology more generally [10,13,79]. If treating AUD ameliorates PTSD, then targeting AUD first may avoid diluting the impact of AUD treatment. However, these results also suggest that treating PTSD immediately after AUD would prevent the deterioration in function observed among AS participants. Treatment of PTSD following SUD treatment has been associated with significant, sustained improvements in PTSD and SUD [25] and SUD remission status 5 years post-treatment [18]. Staged SUD–PTSD treatment has been recommended as a means of reducing treatment attrition and optimizing gains [80].

Study results are tempered by several limitations. Only half the IT participants received exposure, which limits extrapolations about the efficacy of exposure therapy in this population. The absence of a trauma-focused therapy alone condition precluded inferences concerning the impact of reducing PTSD symptoms on AUD. Although within the acceptable range for detecting differences [81], our sample size was small, especially in the context of considerable study attrition, which limited power. Alcohol consumption measures, despite their reliability and validity [82], were based on self-report data and lacked biological corroboration. Finally, IT combined several interventions to address PTSD–AUD which, together, have not been trialled previously and may not reflect current clinical practice.

Study strengths include random assignment, blind follow-up, manualized treatment, therapy-adherence assessment, psychological control and multiple measures. Notable and sustained pre- to post-treatment reductions on alcohol-related measures, PTSD, depression and anxiety were achieved with a sample characterized by considerable psychiatric comorbidity. By 9 months post-treatment, 13 months from baseline, the rates of diagnosis of PTSD and AUD among participants were 38 and 48%, respectively, noteworthy improvements in a sample which excluded only the most severely impaired individuals.

In conclusion, the present study, one of the first RCTs of coexisting PTSD–AUD, has demonstrated that individuals with these problems can benefit from existing empirically supported treatment for PTSD and AUD. Future clinical research combining exposure and other trauma-focused therapy with AUD treatment merits further exploration.

### Clinical trial registration

This RCT was registered with the Australian New Zealand Clinical Trials Registry (number ACTRN1260800050 6392).

### Declaration of interests

None.

### Acknowledgements

This research was supported by National Health and Medical Research Council (ID 455221). We acknowledge the contribution of our colleagues Ms Leanne Humphreys, Dr Katherine Mills, Dr Kim Felmingham, Dr Tim Slade, Ms Barbara Toson, Dr Paul Haber, Dr Glenys Dore

and Ms Robyn Murray. We extend our appreciation to the collaborating hospitals and clinics and to the men and women who participated in this study.

## References


1. Kessler R. C., Berglund P., Demler O., Jin R., Merikangas K. R., Walters E. E. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62**: 593–602.
2. McEvoy P. M., Grove R., Slade T. Epidemiology of anxiety disorders in the Australian general population: findings of the 2007 Australian National Survey of Mental Health and Wellbeing. *Aust NZ J Psychiatry* 2011; **45**: 957–67.
3. Kessler R. C., Chiu W. T., Demler O., Merikangas K. R., Walters E. E. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62**: 617–27.
4. Slade T., Johnston A., Oakley Browne M. A., Andrews G., Whiteford H. 2007 National Survey of Mental Health and Wellbeing: methods and key findings. *Aust NZ J Psychiatry* 2009; **43**: 594–605.
5. Creamer M., Burgess P., McFarlane A. C. Post-traumatic stress disorder: findings from the Australian Survey of Mental Health and Well-being. *Psychol Med* 2001; **31**: 1237–47.
6. Riggs D. S., Ruckstalis M., Volpicelli J. R., Kalmanson D., Foa E. B. Demographic and social adjustment characteristics of patients with comorbid posttraumatic stress disorder and alcohol dependence: potential pitfalls to PTSD treatment. *Addict Behav* 2003; **28**: 1717–30.
7. Mills K. L., Teesson M., Ross J., Peters L. Trauma, PTSD, and substance use disorders: findings from the Australian National Survey of Mental Health and Well-Being. *Am J Psychiatry* 2006; **163**: 651–8.
8. Coffey S. F., Stasiewicz P. R., Hughes P. M., Brimo M. L. Trauma-focused imaginal exposure for individuals with comorbid posttraumatic stress disorder and alcohol dependence: revealing mechanisms of alcohol craving in a cue reactivity paradigm. *Psychol Addict Behav* 2006; **20**: 425–35.
9. Brady K. T., Back S. E., Coffey S. Substance abuse and posttraumatic stress disorder. *Curr Dir Psychol Sci* 2004; **13**: 206–9.
10. Jacobsen L. K., Southwick S. M., Kosten T. R. Substance use disorders in patients with Posttraumatic Stress Disorder: a review of the literature. *Am J Psychiatry* 2001; **158**: 1184–90.
11. Stewart S. H., Conrod P. J. Psychosocial models of functional associations between posttraumatic stress disorder and substance use disorder. In: Ouimette P. C., Brown P. J., editors. *Trauma and Substance Abuse: Causes, Consequences and Treatment of Comorbid Disorders*. Washington, DC: American Psychological Association; 2003, p. 29–55.
12. Khantzian E. J. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am J Psychiatry* 1985; **142**: 1259–64.
13. Stewart S. H. Alcohol abuse in individuals exposed to trauma: a critical review. *Psychol Bull* 1996; **120**: 83–112.
14. McFarlane A. C. Epidemiological evidence about the relationship between PTSD and alcohol abuse: the nature of the association. *Addict Behav* 1998; **23**: 813–25.
15. Brady K. T., Sonne S., Anton R. F., Randall C. L., Back S. E., Simpson K. Sertraline in the treatment of co-occurring alcohol dependence and posttraumatic stress disorder. *Alcohol Clin Exp Res* 2005; **29**: 395–401.
16. Back S. E., Brady K. T., Sonne S. C., Verduin M. L. Symptom improvement in co-occurring PTSD and alcohol dependence. *J Nerv Ment Dis* 2006; **194**: 690–6.
17. Abueg F. R., Fairbank J. A. Behavioral treatment of the PTSD-substance abuser: a multidimensional stage model. In: Saigh P., editor. *Posttraumatic Stress Disorder: A Behavioral Approach to Assessment and Treatment*. New York: Pergamon Press; 1991, p. 111–46.
18. Ouimette P. C., Moos R. H., Finney J. PTSD treatment and 5-year remission among patients with substance use and posttraumatic stress disorder. *J Consult Clin Psychol* 2003; **71**: 410–4.
19. Powers M. B., Halpern J. M., Ferenschak M. P., Gillihan S. J., Foa E. B. A meta-analytic review of prolonged exposure for posttraumatic stress disorder. *Clin Psychol Rev* 2010; **30**: 635–41.
20. Project Match Research Group. Matching alcoholism treatments to client heterogeneity: project MATCH post-treatment drinking outcomes. *J Stud Alcohol* 1997; **58**: 7–29.
21. Triffleman E. Gender differences in a controlled pilot study of psychosocial treatments in substance dependent patients with post-traumatic stress disorder: design considerations and outcomes. *Alcohol Treat Q* 2000; **18**: 113–26.
22. Najavits L. M., Schmitz M., Gotthardt S., Weiss R. D. Seeking safety plus exposure therapy: an outcome study on dual diagnosis men. *J Psychoact Drugs* 2005; **27**: 425–35.
23. Back S. E., Dansky B. S., Carroll K. M., Foa E. B., Brady K. T. Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: description of procedures. *J Subst Abuse Treat* 2001; **21**: 35–45.
24. Brady K. T., Dansky B., Back S. E., Foa E. B., Carroll K. Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: preliminary findings. *J Subst Abuse Treat* 2001; **21**: 47–54.
25. Donovan B., Padin-Rivera E., Kowaliw S. 'Transcend': initial outcomes from a posttraumatic stress disorder/substance abuse treatment program. *J Trauma Stress* 2001; **14**: 757–72.
26. Najavits L. M. *Seeking Safety: A Treatment Manual for PTSD and Substance Abuse*. New York: Guilford Press; 2002.
27. Najavits L. M., Weiss R. D., Shaw S. R., Muenz L. R. 'Seeking safety': outcome of a new cognitive–behavioral psychotherapy for women with posttraumatic stress disorder and substance dependence. *J Trauma Stress* 1998; **11**: 437–56.
28. Hien D. A., Cohen L. R., Miele G. M., Litt L. C., Capstick C. Promising treatments for women with comorbid PTSD and substance use disorders. *Am J Psychiatry* 2004; **161**: 1426–32.
29. Hien D. A., Wells E. A., Jiang H., Suarez-Morales L., Campbell A. N. C., Cohen L. R. *et al*. Multisite randomized trial of behavioral interventions for women with co-occurring PTSD and substance use disorders. *J Consult Clin Psychol* 2009; **77**: 607–19.
30. Foa E. B., Keane T. M., Friedman J. M., Cohen J. A. E. *Effective Treatments for PTSD: Practice Guidelines from the International Society for Traumatic Stress Studies*, 2nd edn. New York: Guilford Press; 2009.
31. Coffey S. F., Schumacher J. A., Brimo M. L., Brady K. T. Exposure therapy for substance abusers with PTSD. *Behav Modif* 2005; **29**: 10–38.


 

32. Triffleman E., Carroll K., Kellogg S. Substance dependence posttraumatic stress disorder therapy: an integrated cognitive-behavioral approach. *J Subst Abuse Treat* 1999; **17**: 3–14.
33. Foa E. B., Rothbaum B. O. *Treating the Trauma of Rape*. New York: Guilford Press; 1998.
34. National Health and Medical Research Council (NHMRC). *Australian Alcohol Guidelines: Health Risks and Benefits*. Canberra: NHMRC; 2001.
35. American Psychiatric Association. *Diagnostic and Statistical Manual of the Mental Disorders*. Washington DC: American Psychiatric Association; 1994.
36. Blake D., Weathers F., Nagy L., Kaloupek D., Gusman F., Charney D. *et al*. The development of a clinician administered PTSD scale. *J Trauma Stress* 1995; **8**: 75–90.
37. First M. B., Gibbon M., Spitzer R. L., Williams J. B. W. *User's Guide for the Structured Interview for DSM–IV Axis I Disorders – Research Version (SCID-I, Version 2.0, February 1996 Final Version)*. New York: Biometrics Research; 1996.
38. Sullivan J., Sykora K., Schneiderman J., Naranjo C. A., Sellers E. M. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989; **84**: 1353–7.
39. Darke S., Ward J., Hall W., Heather N., Wodak A. *The Opiate Treatment Index (OTI) Researcher's Manual*. Technical Report no. 11. Sydney: National Drug and Alcohol Research Centre; 1991.
40. Gossop M., Darke S., Griffiths P., Hando J., Powis B., Hall W. *et al*. The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction* 1995; **90**: 607–14.
41. Weathers F. W., Ruscio A. M., Keane T. M. Psychometric properties of nine scoring rules for the Clinician-Administered Posttraumatic Stress Disorder Scale. *Psychol Assess* 1999; **11**: 124–33.
42. Sobell L. C., Sobell M. B. *Alcohol Timeline Followback Users' Manual*. Toronto, Canada: Addiction Research Foundation; 1995.
43. Stockwell T., Sitharthan T., McGrath D., Lang E. The measurement of alcohol dependence and impaired control in community samples. *Addiction* 1994; **89**: 167–74.
44. Forcehimes A. A., Tonigan S. J., Miller W. R., Kenna G. A., Baer J. S. Psychometrics of the Drinker Inventory of Consequences (DRIncC). *Addict Behav* 2007; **32**: 1699–704.
45. Beck A. T., Steer R. A., Brown G. K. *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation; 1996.
46. Spielberger C. D., Gorsuch R. L., Lushene R., Vagg P. R., Jacobs G. A. *Manual for the State–Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press; 1983.
47. Foa E. B. *Posttraumatic Stress Diagnostic Scale: Manual*. Minneapolis, MN: National Computer Systems; 1995.
48. Kadden R., Carroll K. M., Donovan D., Cooney N., Monti P., Abrams D. *et al*. *Cognitive–Behavioral Coping Skills Therapy Manual: A Clinical Research Guide for Treating Individuals with Alcohol Abuse and Dependence*, Project Match Monograph series, vol. **3**. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 1995.
49. Miller W. R. *Combined Behavioral Intervention Manual: A Clinical Research Guide for Therapists Treating People with Alcohol Abuse and Dependence*, COMBINE Monograph Series, vol. **1**. DHHS Publication no. (NIH) 04-5288. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2004.
50. Project Match Research Group. Matching alcoholism treatments to client heterogeneity: project MATCH three-year drinking outcomes. *Alcohol Clin Exp Res* 1998; **22**: 1300–11.
51. Anton R. F., O'Malley S. S., Ciraulo D. A., Cisler R. A., Couper D., Donovan D. M. *et al*. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA* 2006; **295**: 2003–17.
52. Bryant R. A., Moulds M. L., Guthrie R. M., Dang S. T., Nixon R. D. V. Imaginal exposure alone and imaginal exposure with cognitive restructuring in treatment of posttraumatic stress disorder. *J Consult Clin Psychol* 2003; **71**: 706–12.
53. Bryant R. A., Moulds M. L., Guthrie R. M., Dang S. T., Mastrodomenico J., Nixon R. D. V. *et al*. A randomized controlled trial of exposure therapy and cognitive restructuring for posttraumatic stress disorder. *J Consult Clin Psychol* 2008; **76**: 695–703.
54. Foa E. B., Dancu C. V., Hembree E. A., Jaycox L. H., Meadows E. A., Streets G. P. A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorders in female assault victims. *J Consult Clin Psychol* 1999; **67**: 194–200.
55. Bryant R. A., Harvey A. G. *Acute Stress Disorder: A Handbook of Theory, Assessment, and Treatment*. Washington, DC: American Psychological Association; 2000.
56. Beck A. T., Emry G., Greenberg R. *Anxiety Disorder and Phobias: A Cognitive Perspective*. New York: Basic Books; 1985.
57. Marks I., Lovell K., Noshirvani H., Livanou M., Thrasher S. Treatment of posttraumatic stress disorder by exposure and/or cognitive restructuring: a controlled study. *Arch Gen Psychiatry* 1998; **55**: 317–25.
58. Resick P. A., Nishith P., Weaver T. L., Astin M. C., Feuer C. A. A comparison of cognitive processing therapy, prolonged exposure, and a waiting condition for the treatment of posttraumatic stress disorder in female rape victims. *J Consult Clin Psychol* 2002; **70**: 867–79.
59. McDonagh A., Firedman M., McHugo G., Ford J., Sengupta A., Mueser K. *et al*. Randomized trial of cognitive–behavioral therapy for chronic posttraumatic stress disorder in adult female survivors of childhood sexual abuse. *J Consult Clin Psychol* 2005; **73**: 515–24.
60. Jacobson N. S., Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol* 1991; **59**: 12–9.
61. Gibbons R. D., Hedeker D., Dutoit S. Advances in analysis of longitudinal data. *Annu Rev Clin Psychol* 2010; **6**: 79–107.
62. Zeger S. L., Liang K. Y. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986; **42**: 121–30.
63. Diggle P. J., Heagerty P. J., Liang K. Y., Zeger S. L. *Analysis of Longitudinal Data*. New York: Oxford University Press; 2002.
64. Berglund M., Thelander S., Salaspuro M., Franck J., Andréasson S., Öjehagen A. Treatment of alcohol abuse: an evidence based review. *Alcohol Clin Exp Res* 2003; **27**: 1645–56.
65. Weathers F. W., Keane T. M., Davidson J. R. Clinician administered PTSD scale: a review of the first 10 years of research. *Depress Anxiety* 2001; **13**: 132–56.
66. Resick P. A., Galovski T. E., O'Brien Uhlmansiek M., Scher C. D., Clum G. A., Young-Xu Y. A randomized clinical trial to dismantle components of cognitive processing therapy for

Posttraumatic Stress Disorder in female victims of interpersonal violence. *J Consult Clin Psychol* 2008; **76**: 243–58.
67. Tsao J. C. I., Mystkowski J. L., Zucker B. G., Craske M. G. Effects of cognitive–behavioral therapy for panic disorder on comorbid conditions: replication and extension. *Behav Ther* 2002; **33**: 493–509.
68. Randall C. L., Thomas S., Thevos A. K. Concurrent alcoholism and social anxiety disorder: a first step toward developing effective treatments. *Alcohol Clin Exp Res* 2001; **25**: 210–20.
69. Read J. P., Brown P. J., Kahler C. W. Substance use and posttraumatic stress disorders: symptom interplay and effects on outcome. *Addict Behav* 2004; **29**: 1665–72.
70. Coffey S. F., Schumacher J. A., Brady K. T., Dansky Cotton B. Changes in PTSD symptomatology during acute and protracted alcohol and cocaine abstinence. *Drug Alcohol Depend* 2007; **87**: 241–8.
71. Dansky B. S., Brady K. T., Saladin M. E. Untreated symptoms of PTSD among cocaine-dependent individuals: changes over time. *J Subst Abuse Treat* 1998; **15**: 499–504.
72. Bowen R. C., D'Arcy C., Keegan D., Senthilselvan A. A controlled trial of cognitive behavioral treatment of panic in alcoholic inpatients with comorbid panic disorder. *Addict Behav* 2000; **25**: 593–7.
73. McGrath P. J., Nunes E. V., Stewart J. W., Goldman D., Agosti V., Ocepek-Welikson K. *et al*. Imipramine treatment of alcoholics with primary depression. *Arch Gen Psychiatry* 1996; **55**: 232–40.
74. Grant B. F., Stinson F. S., Dawson D. A., Chou P., Dufour M. C., Compton W. *et al*. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on alcohol and related conditions. *Arch Gen Psychiatry* 2004; **61**: 807–16.
75. Brown S. A., Irwin M., Schuckit M. Changes in anxiety among abstinent male alcoholics. *J Stud Alcohol* 1991; **52**: 55–61.
76. Brown S. A., Inaba R. K., Gillin J. C., Schuckit M. A., Stewart M. A., Irwin M. R. Alcoholism and affective disorder: clinical course of depressive symptoms. *Am J Psychiatry* 1995; **152**: 45–52.
77. Ehlers A., Bisson J., Clark D. M., Creamer M., Pilling S., Richards D. *et al*. Do all psychological treatments really work the same in posttraumatic stress disorder? *Clin Psychol Rev* 2010; **30**: 269–76.
78. Cloitre M. Effective psychotherapies for posttraumatic stress disorder: a review and critique. *CNS Spectr* 2009; **14**: 32–43.
79. Kushner M. G., Abrams K., Borchardt C. The relationship between anxiety disorders and alcohol use disorders: a review of major perspectives and findings. *Clin Psychol Rev* 2000; **20**: 149–71.
80. Conrod P. C., Stewart S. H. A critical look at dual-focused cognitive-behavioural treatments for comorbid substance use and psychiatric disorders: strengths, limitations, and future directions. *J Cogn Psychother* 2005; **19**: 261–84.
81. Chambless D. L., Hollon S. D. Defining empirically supported therapies. *J Consult Clin Psychol* 1998; **66**: 7–18.
82. Del Boca F. K., Darkes J. The validity of self-reports of alcohol consumption: state of the science and challenges for research. *Addiction* 2003; **98**: 1–12.
83. Vrana S. R., Lauterbach D. Prevalence of traumatic events and post-traumatic psychological symptoms in a nonclinical sample of college students. *J Trauma Stress* 1994; **7**: 289–301.
84. Foa E. B., Ehlers A., Clark D. M., Tolin D. F., Orsillo S. M. The Posttraumatic Cognitions Inventory (PTCI): development and validation. *Psychol Assess* 1999; **11**: 303–14.
85. Zanarini M. C., Vujanovic A. A., Parachini E. A., Boulanger J. L., Frankenburg F. R., Hennen J. A screening measure for BPD: the McLean Screening Instrument for Borderline Personality Disorder (MSI-BPD). *J Personal Disord* 2003; **17**: 568–73.
86. Ware J. E. J., Kosinski M., Keller S. D. A 12-item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34**: 220–33.