Feasibility and acceptability of integrated psychological therapy versus treatment as usual for people with bipolar disorder and co-morbid alcohol use: a single blind randomised controlled trial

Steven Jones[1*], Lisa Riste[2] , Heather Robinson[1], Fiona Holland[3] , Sarah Peters[4] , Rosalyn Hartwell[5] , Katherine Berry[4] , Mike Fitzsimmons[6] , Ian Wilson[5] , Claire Hilton[1] , Rita Long[1], Lucy Bateman[4] , Emma Weymouth[4], Rebecca Owen[4] , Chris Roberts[3], Christine Barrowclough[4]

[*]Professor Steven Jones, Spectrum Centre for Mental Health Research, Faculty of Health and Medicine, Lancaster University, Lancaster, Lancashire UK, s.jones7@lancaster.ac.uk, +44 1524 593382.

[1] Spectrum Centre for Mental Health Research, Faculty of Health and Medicine, Lancaster University, Lancaster, Lancashire UK.

[2] Centre for Primary Care, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, Greater Manchester, UK

[3] Institute of Population Health, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, Greater Manchester, UK. [4]Division of Psychology and Mental Health, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, Greater Manchester, UK. [5]Greater Manchester Mental Health NHS Foundation Trust, Manchester, Greater Manchester, UK. [6] Lancashire Care NHS Foundation Trust, Preston, Lancashire, UK

Abstract

Background Alcohol use is a common problem in bipolar disorder (BD) and evidence indicates more promising outcomes for alcohol use than other substances. No trials have evaluated individual integrated motivational interviewing and cognitive behaviour therapy (MI-CBT) for problematic alcohol use in BD. We therefore assessed the feasibility and acceptability of a novel MI-CBT intervention for alcohol use in BD.

Methods A single blind RCT was conducted to compare MI-CBT plus treatment as usual (TAU) with TAU only. MI-CBT was delivered over 20 sessions with participants followed at 3, 6, 9 and 12 months post-randomisation. Primary outcomes were the feasibility and acceptability of MI-CBT (recruitment to target, retention to follow-up, absence of untoward incidents). We also conducted preliminary analyses of alcohol and mood outcomes (frequency and severity of alcohol use and time to mood relapse).

Results 44 participants were recruited with 75% retention to 6 and 12 months follow-up. Therapy participants attended a mean of 17.6 (SD 4.5) sessions. Therapy alliance and treatment fidelity were acceptable. Qualitative interviews indicated the intervention was experienced as collaborative, and helpful, in addressing mood and alcohol issues, although risk of overconfidence following therapy was also identified. Clinical outcomes did not differ between arms at 12 months follow-up.

Limitations As a feasibility and acceptability trial any secondary results should be treated with caution.

Conclusions Integrated MI-CBT intervention is feasible and acceptable, but lack of clinical impact, albeit in a feasibility study, suggests need for further development. Potential adaptations are discussed.

Keywords Bipolar disorder – Alcohol – Substance - Motivational interviewing – Randomised controlled trial – Feasibility study

List of abbreviations

AUDIT – Alcohol Users Disorders Identification Test

BD – Bipolar disorder

CBT – Cognitive behavioural therapy

CTU – Clinical trials unit

HAM-D - Hamilton Depression Rating Scale

ISS - Internal States Scale

MAS - Bech-Rafaelsen Mania Scale

MEDAD - Stephenson Medication Adherence Interview

MI – Motivational interviewing

MI-CBT - motivational interviewing and cognitive behaviour therapy for alcohol use in BD

PHQ-9 - Patient Health Questionnaire–9

PSP - Personal and Social Performance Scale

SCID DSM-IV - Structured Clinical Interview for Diagnostic and Statistical Manual IV

TAU – treatment as usual

TLFB – Time Line Follow Back Interview

WAI-S - Working Alliance Inventory

Background

Substance use in bipolar disorder (BD) has a lifetime prevalence rate ranging from 50-60% for bipolar 1 and 37-40% for bipolar II disorder (Merikangas et al., 2007; 2011), and is associated with worse outcome including poorer functioning (Cardoso et al., 2008; Marshall et al., 2012; Mazza et al., 2009), clinical course (Gaudiano et al., 2008; Rakofsky & Dunlop, 2013) and treatment response (Frye & Salloum, 2006; van Zaane et al., 2010) in both groups.. Alcohol is the most commonly abused substance in BD (Merikangas et al., 2011), and is associated with worse clinical course and outcomes, including more severe mood disturbance (Goldstein et al., 2006), impulsivity (Alloy et al., 2009; Etain et al., 2013; Henna et al., 2013; Swann et al., 2007), suicide (Cardoso, et al., 2008; Bellivier et al., 2011; Oquendo et al., 2010), violence and relapse (Elbogen & Johnson, 2009).

Most psychological interventions research in bipolar has focused on evaluating the effectiveness of cognitive behaviour therapy or psychoeducation interventions intended to reduce relapse of mood episodes (Lam et al.,2003; Scott et al., 2006). However these approaches do not address substance use issues and there have been few developments in integrated therapy to tackle substance use problems in BD. Schmitz et al. (2002) observed no differences between 12 weeks of individual cognitive behavioural therapy (CBT) vs medication monitoring on substance use outcomes but some improvement in mood. Weiss and colleagues (2007; 2009) conducted two randomised controlled trials (RCTs) evaluations of integrated group therapy (IGT) compared with group counselling. . IGT consists of 12 weekly sessions based on CBT principles to address bipolar and substance use issues. IGT led to improvements in substance abuse outcomes, particularly alcohol use. However, mood outcomes were more mixed; one trial indicated worsening of mood symptoms, the other improved overall clinical outcomes (Weiss etal., 2007; 2009). Gold and colleagues (2018) identified a further 4 trials of which one was an RCT targeting substance use in BD (interventions included family focused therapy, acceptance and commitment therapy, CBT and Treatment adherence therapy). None had a specific effect on substance use outcomes although two pilot/open trials indicated possible benefits of CBT/Acceptance and Commitment therapy in addressing smoking cessation in BD (Heffner et al., 2013; 2015)

Given the very mixed outcomes from the limited literature to date, for the current study we have integrated motivational interviewing (MI) with CBT approaches for BD. The addition of MI is important omission, as ambivalence to treatment is common in BD (Liebert, 2013; Weiss et al., 1999) and there is evidence for MI addressing both treatment ambivalence (Miller & Rollnick, 2002) and alcohol and drug issues (Burke et al., 2003; Match, 1997). We have shown previously that integrating MI with CBT for substance use in BD was feasible in a case series of treatment ambivalent individuals with problems with alcohol or cannabis use (Jones et al., 2011). The current report describes the application and evaluation of a therapy approach for addressing alcohol use in BD that integrated MI approaches to engage clients and achieve commitment to change with CBT approaches to provide tools for change and relapse prevention (MI-CBT). We report the valuation through a RCT feasibility and acceptability trial. The primary outcomes for this study were the feasibility and acceptability of MI-CBT for alcohol use in BD with respect to recruitment, retention and feedback from participants. Secondary outcomes were frequency and severity of alcohol use, time to next

bipolar episode, mood symptoms, quality of life, social functioning and medication adherence.

Methods

Study Design

A pragmatic rater-blind RCT comparing up to 20 sessions of integrated MI-CBT for alcohol use in BD compared with treatment as usual (TAU; determined by each participant's responsible clinician, primarily medication and community mental health team support) was conducted across nine NHS Trusts in the North West of England. Randomisation was carried out by an independent Clinical Trials Unit (Manchester Academic Health Science Centre; CTU 9) using a computer generated stochastic allocation with randomly sized permuted blocks. Minimisation (an adaptive stratified sampling approach to minise imbalance between arms; Taves, 1974) was used with respect to gender, number of previous bipolar episodes (<12, 12 or more episodes; mania (including mixed episode), hypomania or depression), and Alcohol Use Disorders Identification Test score. . Clinical outcomes from psychological therapy are typically better for females (Burt & Rasgon, 2004), whilst better outcomes in BD have been linked to fewer previous episodes (Scott et al., 2007), and baseline AUDIT score predicts alcohol relapse (Farren et al., 2013). The trial is reported in accordance with the CONSORT guidelines for non-pharmacological trials (Schulz et al., 2010). The study was reviewed and approved by the UK NHS Ethics Committee process (REC ref: 10/H1014/75) and was pre-registered on the ISRCTN registry (ISRCTN14774583) with a published protocol (Jones et al., 2018). To maintain masking of allocation, research assistants (RAs) provided participant details to the trial coordinator at a separate site, who shared this with the clinical trials unit. The outcome of each allocation was then shared with the participant and, where appropriate, a trial clinician. RAs collecting outcome data were housed separately from clinicians and trial coordinator.

Participants

Recruitment took place from July 2011-June 2013 from NHS adult mental health services and advertised through voluntary organisations, local media, posters and leaflets distributed to both NHS and non-NHS sites to maximise participant access. Potential participants indicated their interest in the study either through their service providers or contacting the research team directly to arrange a screening appointment. Inclusion criteria were: Age 18

years or over; Structured Clinical Interview for Diagnostic and Statistical Manual IV diagnosis of BD I or II (SCID DSM-IV: First et al., 1997); alcohol use exceeding 21 units for males/14 units for females on at least half of the weeks of the previous three months, or at least one alcohol 'binge' (exceeding UK Government recommended number of units of alcohol in a day; six units daily for men, four units daily for women (NICE, 2012)) per fortnight in each of the previous three months; Score of eight or more on the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993); ability to provide informed consent and having a fixed abode.

Procedures

Following written informed consent obtained at a face-to-face visit by an RA at the participants' preferred location (usually their home), diagnostic and alcohol use eligibility were confirmed using the SCID-IV and AUDIT respectively. Eligible participants completed baseline assessment measures prior to randomisation to MI- CBT plus TAU, or TAU only.

Intervention

The MI-CBT is a manualised intervention consisting of MI and CBT elements and was adapted from a treatment programme originally developed for people with substance abuse and psychosis (Barrowclough et al., 2001; adapted manual available from authors). Participants in the therapy arm were offered up to 20 individual; therapy sessions over six months. Sessions were typically 45 to 60 minutes long. Therapy was delivered at participants' preferred location, usually their home consistent with the original protocol developed by Barrowclough et al (2001). This was consistent with the intention to offer a flexible and assertive approach to engagement of participants with potentially low motivation to change at recruitment. NHS services in the region in which the trial took place also offer home visits to engage complex hard to reach clients in care, Sessions were conducted individually without other family members present (where family members were in the house at the time they agreed to give the participant privacy for the session). . All therapists met the British Association of Behavioural and Cognitive Psychotherapies accreditation criteria and to further ensure therapist fidelity and competence were provided with a comprehensive three-month training period and additional weekly supervision sessions with supervisors experienced in both MI and CBT.

MI-CBT was informed by a prior successful case series (Jones et al., 2011) and refined based on feedback from focus groups held with service users with lived experience of BD and

alcohol use and healthcare professionals. Initial sessions focused on engagement, employing MI to develop a shared understanding of the client's key life goals and concerns, to elicit and selectively reinforce the client's own self-motivational statements, and to monitor the client's readiness to reduce their drinking. Therapist and client then worked to develop a shared understanding of how goals and concerns, and particularly how bipolar-relevant symptoms and relapses (depression, hypomania, anger, irritability, impulsiveness and disrupted social rhythms), were related to alcohol use. The formulation was used to identify individual determinants and consequences of the client's key problems. Where motivation for change was achieved, the next stage of therapy involved developing an alcohol reduction/abstinence plan guided by the individual formulation and by the needs of the client drawing on evidence based cognitive behavioural strategies. This phase also included CBT to facilitate alternative approaches to dealing with mood symptoms associated with alcohol use where appropriate. The intervention also included development of a relapse prevention plan that summarised learning from therapy and provided a reference for the client following completion of treatment. For those not ready to change alcohol use, the therapist worked on other client-led problems to maintain engagement whilst continuing to link alcohol use to their concerns through MI techniques. TAU for both groups typically consisted of routine medication (mood stabilisers, antipsychotics and antidepressants) and maintenances predominantly from secondary care services (community mental health team and psychiatrist appointments).

Training and monitoring of trial therapists

Four therapists (RH, KB, MF, IW) were employed and trained to deliver the MI-CBT intervention by CB and SJ. Therapists received group supervision fortnightly, including peer supervision and supervision led by CB. Therapists also had access to attend monthly joint sessions with SJ to discuss CBT-related issues.

Screening measure

The Alcohol Use Disorders Identification Test *(AUDIT; Saunders* et al., 1993) was used as a screening tool to ensure all participants were experiencing problematic drinking at inception. Medium alcohol problems were reflected in a score of *8-15,* whilst High to severe alcohol problems were indicated by AUDIT score of >= 16.

Assessment of outcomes

RAs (EW, LB, HR), blind to treatment allocation, conducted outcome assessments for all available participants at baseline, 3-, 6- (end of therapy), 9- and 12-month follow-up (see

Table 1). All assessments were administered in person, at participants' preferred location (usually their home), and recorded with consent from the participant. Any unblindings were recorded and an alternative, blind RA carried out further assessments.

Primary Feasibility and Acceptability Outcomes

Feasibility and acceptability were evaluated in terms of levels of recruitment into the trial, retention of participants in both arms of the study, and treatment fidelity assessed by the MI-CBT Fidelity Scale (Haddock et al., 2012) adapted for the current study. Scores were recorded for Section A (adherence with procedure) and Section B (appropriate and strategic use of core skills). Therapeutic alliance (Work Alliance Inventory, WAI-S; Tracey & Kokotovic, 1989 client and therapist) and therapy attendance and client evaluation were also recorded.

A nested qualitative study was conducted with 15 participants purposively sampled on number of sessions attended, age, sex, number of relapses, level of alcohol use and outcomes to explore participants' experiences of the MI-CBT intervention. Participants were asked about their prior experience of therapy, their expectations of the current intervention and its timing, their views on therapy sessions and any homework, whether the intervention seemed to address mood and alcohol issues, relevance to their health issues, how they would describe the intervention, how it compared to prior therapy experiences in terms of session location and duration.

Clinical outcomes

Primary clinical outcomes were frequency and severity of alcohol use (Time Line Follow Back Interview (TLFB; Sobell & Sobell, 1992)) and time to next bipolar episode (SCID Life; Keller et al., 1987).

Additional outcomes were:

- Observer-rated mood symptoms (Hamilton Depression Rating Scale; HAM-D; Hamilton, 1960 and Bech-Rafaelsen Mania Scale;MAS; Bech et al., 1978)
- Self-reported mood symptoms(Patient Health Questionnaire–9; PHQ-9; Kroenke et al., 2001 and Internal States Scale;ISS; Bauer et al., 1991)
- Quality of life and social functioning (Personal and Social Performance Scale; PSP; Morosini et al., 2000)

- Medication adherence (Stephenson Medication Adherence Interview; MEDAD; Stephenson et al., 1993).

The Readiness for Change Questionnaire (Rollnick et al., 1992) was employed to evaluate the extent to which progression through stages of change (Prochaska & DiClemente, 1986) (pre-contemplation, contemplation, preparation and action) was associated with clinical outcomes.

Data Analysis

As the primary purpose of the study was to evaluate the feasibility and acceptability of delivering the integrated MI-CBT intervention, a formal power calculation was not appropriate. It was estimated that 24 participants per group would be sufficient to be able to reliably determine primary feasibility outcome allowing a 50% recruitment rate to be estimated with precision +/- 15% (95% confidence intervals) and a 70% rate of study retention estimated with precision +/-20% (95% confidence intervals) consistent with guidance to clearly articulate feasibility study requirements (Lancaster et al., 2004).

Primary outcomes were percentage of participants randomised relative to those referred, percentage of participants completing outcome data, percentage retention to both arms, mean session attendance, therapist adherence to therapy protocol (percentage per session), mean therapeutic alliance, and percentage readiness for change at baseline and end of intervention The study was not powered to evaluate the effectiveness of clinical outcomes but may help inform estimates of the potential treatment effect sizes (secondary objective).

For the time to relapse analysis, a Cox model was fitted with treatment arm, gender, number of previous bipolar episodes (<12 vs 12 or more) and AUDIT score at randomisation (8 to 15 versus 16 or more) as covariates.

Repeated measures models with discrete time were fitted to the TLFB data. In Model 1 (M1) a discrete time by treatment interaction was fitted to estimate the treatment effect and the 95% confidence interval at each follow-up time point. If there was no evidence of an interaction at the 5% level then the interaction term was omitted and the overall treatment effect was estimated (model M2). The same covariates as described above were used for these models, except that the AUDIT score was replaced with the baseline value of the outcome. Summary means and standard deviations by group and assessment point are provided for other clinical and process measures. Additional outcomes are summarised by descriptive statistics by treatment arm and assessment point

Qualitative interviews were audio-recorded, transcribed verbatim and thematically analysed from a realist perspective to explore participants' experiences of MI-CBT (Braun & Clarke, 2006). Themes were compared against the data using a constant comparative approach by a multidisciplinary panel (CH, SP, LR, SJ, CB, RL). Interviews were conducted until thematic saturation was achieved

Results

Participant Characteristics

Participants were on average over 40 years old (MI-CBT = 41.3, SD = 13.1; TAU = 42.1, SD = 10.4) and most were male (52%) with a chronic relapsing course of BD and harmful alcohol use (Audit 16 or more; Table 2). The large majority were white British (>90%) and divorced or never married (>80%), with just under half having no children (48%). Although over 60% of participants had at least begun further or higher education, 75% were currently unemployed and only 8% were in full-time employment. SCID interviews indicated that participants predominantly had bipolar 1 disorder (91%), with high rates of lifetime alcohol abuse (73%) and dependence (62%). Consistent with the focus of the MI-CBT trial, lifetime rates of other substance use were lower (18% abuse; 27% dependence)

Baseline level of mean daily alcohol consumption was in the high-risk range for the MI-CBT arm and on the threshold for high risk in the TAU arm, with frequency of use and frequency of binge days also elevated in comparison to the general UK and EU population in both arms (Rehm et al., 2012) (see Table 3). This pattern suggests that the selection criterion based on AUDIT has appropriately identified participants with problematic patterns of drinking. Depressed mood was at normal levels on HAM-D and mania scores were low on MAS (Online Table 1). In terms of readiness for change, the sample were predominantly at the pre-contemplation or contemplation stages indicating that we recruited participants who were potentially ambivalent about change in their alcohol use, whilst levels of impulsivity were similar at baseline to those observed in previous research with individuals with BD and comorbid substance use (Swann et al., 2004) (Online Tables 2-3). MEDAD scores indicated high medication adherence overall. Three participants were not taking any medication at baseline, the remainder were receiving a variety of medication (antidepressant, mood stabilising, benzodiazepine, antipsychotic) with different numbers of participants receiving each medication type. Across medication types very few days' medication were missed, with mean higher adherence (fewer days missed) in TAU (Online Table 4).

Primary Feasibility Outcomes

Figure 1 presents recruitment and retention rates for participants in the MI CBT and TAU arms respectively, consistent with CONSORT criteria. Seventy-six potentially eligible participants were referred to the study over a period of 23 months. Two people could not be contacted for further assessment and 30 were excluded as they did not meet eligibility criteria at pre-screen (n = 22) or declined to participate (n = 8). Thus, only 10.5% of those offered the opportunity to participate in the trial declined.

Forty-four participants were randomised, 58% of those originally referred (92% of the target figure of 48). Primary clinical outcome data (SCID DSM-IV: SCID Life and TLFB) was collected for 39 (89%) participants at 3 months, 33 (75%) at 6 months, 32 (73%) at 9 months and 33 (75%) at 12 months. Retention for treatment arm was 79% to 12 months and 70% for TAU respectively. There was no evidence for differential retention at any of the follow-up points by arm ($p > 0.25$ for all X^2 comparisons).

Unblindings

Single unblindings were reported for 8 MI-CBT and 2 TAU participants. One unrelated adverse event was recorded, in which an MI-CBT participant took an overdose of medication, sought and received primary care help and was resolved without hospitalisation.

Treatment delivered and treatment fidelity

All of the 24 participants allocated to therapy arm attend at least one therapy session. Mean session attendance was 17.6 (SD = 4.5) with 21/24 attending at least 15 of 20 possible sessions. Proportions of participants attending sessions from 0-20 are as follows: 1-5 = 1 (4.2%), 6-10 = 1 (4.2%), 11-15 = 1 (4.2%), 16-20 = 21(87.5%).

Adherence to MI-CBT approach was independently assessed on the MI-CBT Fidelity Scale for 9 sessions elected across early to late stages of therapy (sessions 4-16). Adherence and fidelity were at least adequate for 8/9 (88.9%) of recordings.

Therapeutic alliance was assessed after session 3 and session 16. At session 3, there were 19 client WAI ratings (mean 63.74, SD 9.12) at session 16 and 17 ratings (mean 65.05, SD 6.50). For therapist rated WAIs there were 22 ratings (mean 59.09, SD 9.76) at session 3 and 19 ratings (mean 62.31, SD 10.54) at session 16.

Readiness to change score indicated increases in proportion of participants in MI-CBT moving to action phase (n=2, 8.7% baseline; n=10, 58.8% 12 month follow-up) compared to TAU (n=5, 25% baseline; n=4, 33.3% 12 month follow-up; Online Table 2) although this was not statistically significant ($\chi^2 = 3.5$, $p = 0.062$) . There was no evidence for differential changes in impulsivity or medication adherence by treatment arm over time (Online Tables 3-4).

Qualitative data on Acceptability

Participants who engaged with qualitative interviews were mainly bipolar 1, male (n=10), middle aged (mean 44.53, SD 13.82) and had attended 15-20 therapy sessions (see table 4)

(See Table 5 for illustrative quotes)

Participants indicated the MI-CBT intervention was helpful in addressing behaviours they identified as harmful and despite their concerns in advance of treatment, was experienced as collaborative rather than directive. It is of note that prior concerns reported included how services might respond if honest about current consumption, which led some participants to say that they had not done so at baseline. The MI-CBT approach facilitated engagement and sense of personal control and responsibility over the decisions made in treatment. Participants indicated that they became less likely to find alcohol use being triggered by stress or social events and that they were better able to cope with bipolar mood symptoms and improve functioning. Participants who had felt unable to be honest about their alcohol use at baseline reported therapy helped them develop strategies to reduce their drinking. In contrast to these positive comments, one participant experienced the intervention as more conversational than therapeutic and another felt that after gaining confidence in therapy they felt they tried to do too much during a period of elevated mood and then felt overloaded.

Secondary Outcomes

Key exploratory clinical outcomes for the MI-CBT study were frequency and quantity of alcohol use (see Table 3 & 6) and time to next bipolar recurrence (see Figure 2).

Alchohol Data - TLFB

Mean alcohol use and percentage binge days reduced, and percentage days abstinent increased from baseline in both arms. Table 5 shows the results from fitting repeated

measures models to these outcomes. None of the time by treatment interactions were significant but the overall treatment effect was significant for percentage days abstinent from alcohol (an estimated 12 % days lower on MI-CBT compared to TAU, P=0.04).

Episode recurrence

Thirty-seven percent (n=9) of MI-CBT and 25% (n=5) of TAU participants had a recurrence of depression (n=7 in MI-CBT and n=5 in TAU) or mania (n=2 in MI-CBT) during follow-up: a non-significant difference (hazard ratio 1.50, 95% CI, 0.49 to 4.58, $P = 0.478$). Kaplan-Meier plot for time to first recurrence among the two groups is shown in Figure 2.

Additional exploratory Self- and observer-rated outcome measures

Social functioning (PSP) remained within the same functioning categories for both arms across follow-up (Online Table 5). Mood states remained similar over the follow-up period in both arms as indicated by ISS (Bauer et al, 2000), except for a reduction in those in euthymia in TAU at 6 months and higher rates of mixed states at 12 months in both arms compared to baseline (Online Table 6). PHQ-9 scores indicated low rates of moderate to severe depression throughout, with reductions in the MI-CBT arm at follow-up (Online Table 7). Observer rated depression (HAM-D) and mania (MAS) remained in the normal range throughout (Online Table 1).

Discussion

This paper reports the first RCT feasibility and acceptability study of a new integrated psychological intervention for alcohol use issues in the context of BD. Trial design appears to be feasible with recruitment 92% of target and only 10.5% of those offered the opportunity to participate refusing. Of 76 individuals screened, 58% both met inclusion criteria and agreed to participate, an inclusion rate that is higher than previous individual CBT for bipolar disorder trials (Jones et al., 2015; Lam et al., 2003; Scott et al., 2006) and comparable with integrated group therapy interventions for substance use and BD (47-59%) (Weiss et al., 2007; 2009).

Retention to 12-months follow-up was 75%, and did not differ significantly between arms, suggesting that resentful demoralisation was not a significant issue for the TAU arm of this trial (Brewin & Bradley, 1989). This retention rate is similar to that reported for in-person data collection by Weiss et al. 2007/2009 (73.8-74.2%) but lower than their total retention to

follow-up when second tier data collection (95%: email/questionnaire) was included. It is likely that this is due to differences in inclusion criteria (current trial permitted inclusion of individuals not reporting high motivation to change or adherence to mood stabiliser medication) and longer follow up period (12 months from baseline compared with 6-8 months). Consistent with this, these retention rates compared favourably with the with other CBT trials for BD with comparable follow up periods (Jones et al., 2015; Scott et al., 2006).

Demographic characteristics of participants in the current trial were similar to those in the majority of RCT evaluations of psychological therapy for BD to date. Participants were predominantly over 40 years old, with a chronic course of BD and unemployed, despite most having education beyond GCSE level (Jones et al., 2015; Meyer & Hautzinger, 2012; Scott et al., 2006). We are not aware of any previous individual psychological therapy trials that have focussed specifically on alcohol use in BD, so there is no direct comparator with respect to severity of alcohol use. However, AUDIT scores for the current study indicated the majority of participants fell into the category of harmful/hazardous use; balance across arms was an issue here with 20% more falling into this category in MI-CBT compared with TAU at baseline.

The current trial also indicated that delivery of MI-CBT intervention is feasible. No participants refused the intervention, with an average attendance of 88% of sessions offered. This is higher than group therapy attendance in the Weiss et al. (2007; 2009) trials (54-74%), despite their exclusion of participants without confirmed motivation to change both substance use and bipolar symptoms. In-depth qualitative interviews with recipients of the MI-CBT intervention indicated that the intervention was positively received, with engagement enhanced by the collaborative flexible approach fundamental to MI and reports of meaningful improvements in alcohol use, mood, self-management and functioning including reengaging with work. Not all experiences were positive, however, including perception of sessions as 'nice' but not formal therapy and that confidence imbued through progress in therapy could interact with mood elevation and lead to over activity. This latter perception contrasts with reports of effective self-management strategies. Overall, these findings might suggest that additional provision of booster sessions might help capitalise on gains in self-management whilst mitigating potential risks linked to over-confidence.

As a feasibility and acceptability study, this was not designed to formally test the efficacy of MI-CBT in changing clinical outcomes. Therefore, although information was collected with

respect to alcohol use, mood, relapse and functioning, any estimates were imprecise. No significant differences were observed across groups with respect to mean alcohol use or percentage of binge days; in both cases, there was a pattern of general reduction in both arms. Number of days abstinent from alcohol increased in both arms. It is of note here that the focus of the MI-CBT intervention was based on collaborative goals around reduction and management of alcohol rather than eradication of use.

Overall, recurrence rate for episodes of mania or depression was approximately 31%, which is extremely low compared with previous individual therapy trials for BD (52-53% over 48-72 weeks; Lam et al., 2003; Scott et al., 2006) and did not significantly differ between arms. Very low levels of depression and mania at baseline may have influenced the recurrence rate observed.

Despite significant levels of risk in relation to alcohol consumption, the participants reported generally good social functioning and low levels of depression and mania symptoms at baseline. This pattern remained similar across the follow up period and did not differ significantly between groups.

Gold et al. (2018) indicated that of the 8 trials included in their review, only those of Weiss and colleagues (2007; 2009) showed consistent evidence of benefit in relation to substance use outcomes (and none showed consistent benefits for both mood and substance use. Compared with Weiss et al.'s (2007; 2009) studies of integrated group therapy, the current trial did not signal a benefit in relation to alcohol outcomes despite better attendance rates at therapy and high levels of satisfaction with therapy as indicated by qualitative interviews. As noted above, the current trial did not require participants to be taking a mood stabiliser or be actively seeking treatment for both substance and bipolar mood issues, in contrast to Weiss et al.'s (2007; 2009) studies. Other differences with respect to participants were that for the current study the majority of the participants were male, unemployed, and had lower rates of alcohol abstinence days (39% of days in previous month vs 66-72%) and much lower levels of depression and mania at baseline.. It would therefore be of interest to explore the extent to which integrated group therapy is of benefit to a less selected sample delivered outside a specialist treatment centre. With respect to the current MI-CBT intervention it appears that the intervention was feasible and acceptable and successfully engaged participants. However, it is possible that improved clinical outcomes might require further adaptation of the therapy including consideration of whether the intervention was of sufficient duration to address the

complexity of participants' longstanding problems. It would also be worth considering whether the promising findings in relation to acceptance and commitment approaches for smoking behaviour in BD (Heffner et al., 2013; 2015) might enhance the current approach by increasing willingness to experience discomfort to achieve personally valued change in behaviour.

There were some limitations to the current study. Sample size was selected to permit assessment of feasibility and acceptability outcomes for this trial and was not powered to test clinical outcomes. Therefore, findings with respect to clinical outcomes should be treated with caution. Measures of alcohol consumption were self-report/interview rather than through objective monitoring, which means that actual levels of use could not be formally validated. However previous research suggested high concordance between self-report and objective screening (Weiss et al., 2007). The overwhelming majority of participants had bipolar I so it is unclear how the current results relate to other subtypes of BD.

Strengths of the study include comprehensive assessment of participants, extended follow-up assessment from baselines and the evaluation of outcomes from both quantitative and qualitative perspectives.

Conclusion

Feasibility and acceptability of selection, recruitment and intervention procedures was demonstrated for the trial. Participants engaged with therapy when offered, and retention to follow-up was acceptable. Participants had significant levels of alcohol use problems at baseline but appeared to be comparatively well in terms of mood symptoms and social functioning. None of these outcomes changed differentially in the treatment group. The lack of change in some of these outcomes is likely to be associated with floor effects. Further investigation is required to identify how this intervention can be adapted to enhance clinical outcomes so that it efficacy matches the positive feasibility and acceptability data.

Trial Registration

This study has been registered with ISRCTN registry (ISRCTN14774583 – date of registration 14-03-2011).

Declarations

Acknowledgements

The views expressed by the authors do not necessarily reflect those of the National Institute for Health Research (NIHR), the National Health Service (NHS), or the Department of Health in England. We thank the service users who participated in the development of the MI-CBT and those individuals who took part in current trial.

Funding

This work was supported by the NIHR under its Programme Grants for Applied Research Programme (Reference Number RP-PG-0407-10389). The funding body had no role in study design, collection, analysis, and interpretation of data or writing the manuscript. Further support was received from primary care trusts, mental health trusts, the Mental Health Research Network and Comprehensive Local Research Networks in North West England.

Availability of data and materials

Data sharing requests submitted to the corresponding author will considered contingent on appropriate ethical approvals.

Author's contributions

SJ is Chief Investigator for the PARADES programme and worked closely with CB who was lead investigator for this study. SJ led the writing of this paper. HR, EW & LB contributed to assessment of participants and write up of the paper. LR coordinated the study as part of her role as PARADES trial manager aided by RO. RH, KB, MF & IW provided therapy to participants. CR and FH developed and actioned the statistical analysis plan for the paper. SP led the qualitative analysis plan. CH conducted qualitative interviews. RL provided service user oversight of all aspects of the study. All authors contributed to the writing of the paper and approved the final version.

Competing interests

The authors developed the intervention and as such could not be considered entirely independent. No other competing interests.

Consent for publication

Not applicable

Ethics approval and consent to participate

The study was reviewed and approved by the UK NHS Ethics Committee process (REC ref: 10/H1014/75), participants provided written informed consent.

References

Alloy LB, Bender RE, Wagner CA, Whitehouse WG, Abramson LY, Hogan ME, et al, 2009. Bipolar spectrum–substance use co-occurrence: Behavioral approach system (BAS) sensitivity and impulsiveness as shared personality vulnerabilities. J Pers Soc Psychol. 97:549-65.

Barrowclough CB, Haddock G, Tarrier N, Lewis SW, Moring L, O'Brien R, et al, 2001. Randomized controlled trial of motivational interviewing , cognitive behavior therapy and family intervention for patients with comorbid schizophrenia and substance use disorders. Am J Psychiatry.158:1706-13.

Bauer MS, Crits-Christoph P, Ball WA, Dewees E, McAllister T, Alahi P, et al, 1991 Independent assessment of manic and depressive symptoms by self-rating. Scale characteristics and implications for the study of mania. Arch Gen Psychiatry. 48:807-12.

Bech P, Rafaelsen OJ, Kramp P, Bolwig TG, 1978. The mania rating scale: scale construction and inter-observer agreement. Neuropharmacology.17:430-1.

Bellivier F, Yon L, Luquiens A, Azorin JM, Bertsch J, Gerard S, et al, 2011. Suicidal attempts in bipolar disorder: Results from an observational study (EMBLEM). Bipolar Disord.13:377-86.

Braun V, Clarke V, 2006. Using thematic analysis in psychology. Qual Res Psychol. 3:77-101.

Brewin CR, Bradley C, 1989. Patient Preferences and Randomized Clinical-Trials. Brit Med J. 299:313-5.

Burke BL, Arkowitz H, Menchola M, 2003. The efficacy of motivational interviewing: a meta-analysis of controlled clinical trials. J Consult Clin Psychol.71:843-61.

Burt VK, Rasgon N, 2004. Special considerations in treating bipolar disorder in women. Bipolar Disord. 6:2-13.

Cardoso BM, Kauer Sant'Anna M, Dias VV, Andreazza AC, Cereser KM, Kapczinski F, 2008. The impact of co-morbid alcohol use disorder in bipolar patients. Alcohol. 42:451-7.

Elbogen EB, Johnson SC, 2009. The intricate link between violence and mental disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 66:152-61.

Etain B, Mathieu F, Liquet S, Raust A, Cochet B, Richard JR, et al., 2013. Clinical features associated with trait-impulsiveness in euthymic bipolar disorder patients. J Affect Disord.144:240-7.

Farren CK, Snee L, Daly P, McElroy S, 2013. Prognostic factors of 2-year outcomes of patients with comorbid bipolar disorder or depression with alcohol dependence: Importance of early abstinence. Alcohol and Alcoholism. 48:93-8.

First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS, 1997. Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version, Patient Edition. Washington DC: American Psychiatric Press, Inc.

Frye MA, Salloum IM, 2006. Bipolar disorder and comorbid alcoholism: prevalence rate and treatment considerations Bipolar Disord. 8:677-85.

Gaudiano BA, Uebelacker LA, Miller IW, 2008. Impact of remitted substance use disorders on the future course of bipolar I disorder: Findings from a clinical trial. Psychiatry Research.160:63-71.

Gold AK, Otto MW, Deckersbach T, Sylvia LG, Nierenberg AA, Kinrys G, 2018. Substance use comorbidity in bipolar disorder: A qualitative review of treatment strategies and outcomes. Am J Addiction. 27:188-201.

Goldstein BI, Velyvis VP, Parikh SV, 2006. The association between moderate alcohol use and illness severity in bipolar disorder: a preliminary report. J Clin Psychiatry. 67:102-6.

Haddock G, Beardmore R, Earnshaw P, Fitzsimmons M, Nothard S, Butler R, et al., 2012. Assessing fidelity to integrated motivational interviewing and CBT therapy for psychosis and substance use: the MI-CBT fidelity scale (MI-CTS). J Ment Health. 21:38-48. Hamilton M. A rating scale for depression. Journal of Neurology and Psychiatry. 1960;23:59-62.

Heffner JL, Anthenelli RM, DelBello MP, Stahl L, Strakowski SM, 2013. Mood Management and Nicotine Patch for Smoking Cessation in Adults With Bipolar Disorder. Nicotine Tob Res.15:1805-6.

Heffner JL, McClure JB, Mull KE, Anthenelli RM, Bricker JB, 2015. Acceptance and Commitment Therapy and nicotine patch for smokers with bipolar disorder: preliminary evaluation of in-person and telephone-delivered treatment. Bipolar Disord.17:560-6.

Henna E, Hatch JP, Nicoletti M, Swann AC, Zunta-Soares G, Soares JC, 2013. Is impulsivity a common trait in bipolar and unipolar disorders? Bipolar Disord.15:223-7.

Jones SH, Barrowclough C, Allott R, Day C, Earnshaw P, Wilson I, 2011. Integrated motivational interviewing and cognitive–Behavioural therapy for bipolar disorder with comorbid substance use. Clin Psychol Psychother.18:426-37.

Jones SH, Smith G, Mulligan LD, Lobban F, Law H, Dunn G, et al., 2015. Recovery-focused cognitive-behavioural therapy for recent-onset bipolar disorder: randomised controlled pilot trial. Br J Psychiatry. 206:58-66.

Jones, S., Robinson, H., Riste, L., Roberts, C., Peters, S., Bateman, L., Weymouth,, E., Barrowclough, .C, 2018. Integrated psychological therapy for people with bipolar disorder and co-morbid alcohol use: A feasibility and acceptability randomised controlled trial. Contemporary and Clinical Trials Communications. 10: 193-198.

Keller MB, Lavori PW, Friedman B, Nielsen E, Endicott J, McDonald-Scott P, et al., 1987. The Longitudinal Interval Follow-up Evaluation. A comprehensive method for assessing outcome in prospective longitudinal studies. Archives of General Psychiatry. 44:540-8.

Kroenke K, Spitzer RL, Williams JBW, 2001. The PHQ-9 - Validity of a brief depression severity measure. J Gen Int Med.16(9):606-13.

Lam D, Watkins ER, Hayward P, Bright J, Wright K, Kerr N, et al., 2003. A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year. Arch Gen Psychiatry. 60:145-52.

Lancaster, G. A., Dodd, S., & Williamson, P. R. (2004). Design and analysis of pilot studies: recommendations for good practice. *Journal of Evaluation in Clinical Practice, 10*(2), 307-312.

Liebert RJ, 2013. A re-view of ambivalence in bipolar disorder research. Ethical Human Psychol and Psychiatry.15:180-94.

Marshall DF, Walker SJ, Ryan KA, Kamali M, Saunders EFH, Weldon AL, et al., 2012. Greater executive and visual memory dysfunction in comorbid bipolar disorder and substance use disorder. Psychiatry Research. 200:252-7.

MATCH P, 1997. Matching Alcoholism Treatments to Client Heterogeneity: Project MATCH posttreatment drinking outcomes. J Stud Alcohol. 58:7-29.

Mazza M, Mandelli L, Di Nicola M, Harnic D, Catalano V, Tedeschi D, et al., 2009. Clinical features, response to treatment and functional outcome of bipolar disorder patients with and without co-occurring substance use disorder: 1-year follow-up. J Affect Disord. 115:27-35.

Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al., 2007. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 64:543-52.

Merikangas KR, Jin R, He J-P, Kessler RC, Lee S, Sampson NA, et al., 2011. Prevalence and Correlates of Bipolar Spectrum Disorder in the World Mental Health Survey Initiative. Arch Gen Psychiatry. 68(3):241-51.

Meyer TD, Hautzinger M, 2012. Cognitive behaviour therapy and supportive therapy for bipolar disorders: relapse rates for treatment period and 2-year follow-up. Psychol Med. 42:1429-39.

Miller WR, Rollnick S, 2002. Motivational Interviewing: Preparing People for Change. Second ed. New York: Guilford Press.

Morosini PL, Magliano L, Brambilla L, Ugolini S, Pioli R, 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. Acta Psychiatr Scand. 101:323-9.

NICE, 2012. Alcohol: Facts and Figures. London: National Institute for Health and Care Excellence.

Oquendo MA, Currier D, Liu S, Hasin DS, Grant BF, Blanco C, 2010. Increased risk for suicidal behavior in comorbid bipolar disorder and alcohol use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). J Clin Psychiatry. 71:902-9.

Prochaska JO, DiClemente CC, 1986. Toward a comprehensive model of change. In: Miller WR, Heather N, editors. Treating Addictive Behaviors: Process of Change. New York: Plenum.

Rakofsky JJ, Dunlop B, 2013. Do alcohol use disorders destabilize the course of bipolar disorder? J Affect Disord. 145(1):1-10.

Rehm J, Shield KD, Rehm MX, Guel G, Frick U, 2012. Alcohol consumption, alcohol dependence, and attributable burden of disease in Europe: Potential gains from effective interventions for alcohol dependence. Toronto: CAMH.

Rollnick S, Heather N, Gold R, Hall W, 1992. Development of a short 'readiness to change' questionnaire for use in brief, opportunistic interventions among excessive drinkers. Br J Addict. 87:743-54.

Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M, 1993. Development of the Alcohol Use Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. Addiction. 88:791-804.

Schmitz JM, Averill P, Sayre S, McCleary P, Moeller FG, Swann A, 2002. Cognitive-Behavioral Treatment of Bipolar Disorder and Substance Abuse: A Preliminary Randomized Study. Addictive Disord and Their Treatment. 1:17-24.

Schulz KF, Altman DG, Moher D, 2010. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 340:c332.

Scott J, Colom F, Vieta E, 2007. A meta-analysis of relapse rates with adjunctive psychological therapies compared to usual psychiatric treatment for bipolar disorders. Int J of Neuropsychopharmacol. 10:123-9.

Scott J, Paykel E, Morriss R, Bentall R, Kinderman P, Johnson T, et al., 2006. Cognitive-behavioural therapy for bipolar disorder. B J Psychiatry. 188: 488-489.

Sobell LC, Sobell MB, 1992. Timeline follow-back: A technique for assessing self-reported alcohol consumption. In: Litten RZ, Allen J, editors. Measuring Alcohol Consumptiom: Psychosocial and Biological Methods. New Jersey: Humana. p. 41-72.

Stephenson BJ, Rowe BH, Haynes RB, Macharia WM, Leon G, 1993. The rational clinical examination. Is this patient taking the treatment as prescribed? JAMA. 269:2779-81.

Swann AC, Dougherty DM, Pazzaglia PJ, Pham M, Moeller FG, 2004. Impulsivity: a link between bipolar disorder and substance abuse. Bipolar Disord. 6:204-12.

Swann AC, Gerard MF, Steinberg JL, 2007. Manic symptoms and impulsivity during bipolar depressive episodes Bipolar Disorders. 9:206-12.

Taves DR, 1974. Minimization: a new method of assigning patients to treatment and control groups. Clin Pharmacol Ther. 15:443-53.

Tracey TJ, Kokotovic AM, 1989. Factor structure of the working alliance inventory. Psychol Assess. 1:207–10.

van Zaane J, van den Brink W, Draisma S, Smit JH, Nolen WA, 2010. The effect of moderate and excessive alcohol use on the course and outcome of patients with bipolar disorders: A prospective cohort study. J Clin Psychiatry. 71:885-93.

Weiss RD, Griffin ML, Jaffee WB, Bender RE, Graff FS, Gallop RJ, et al., 2009. A “community-friendly” version of integrated group therapy for patients with bipolar disorder and substance dependence: A randomized controlled trial. Drug and Alcohol Dep. 104:212-9.

Weiss RD, Griffin ML, Kolodziej ME, Greenfield SF, Najavits LM, Daley DC, et al., 2007. A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. Am J Psychiatry. 164:100-7.

Weiss RD, Najavits LM, Greenfield SF, 1999. A relapse prevention group for patients with bipolar and substance use disorders. J Subst Abuse Treat. 16:47-54.

Figure Titles/Legends

Figure 1. Study CONSORT diagram

Figure 2. Kaplan-Meier estimates of time to first depression or mania-type bipolar episode

Table 1. Schedule of Assessments

Assessment	Baseline	3 months	6 months	9 months	12 months
Primary Outcome Measures					
Time Line Follow Back	✓	✓	✓	✓	✓
SCID Life	✓	✓	✓	✓	✓
Secondary Outcome Measures					
Hamilton Depression Rating Scale	✓	✓	✓	✓	✓
Bech-Rafaelsen Mania Scale	✓	✓	✓	✓	✓
Internal State Scale	✓		✓		✓
Personal and Social Performance Scale	✓		✓		✓
Stephenson Medication Adherence Interview	✓		✓		✓
Euroquol Scale	✓		✓		✓
Patient Health Questionnaire,	✓		✓		✓
State-Trait Anxiety Inventory for Adults	✓		✓		✓
Barratt Impulsiveness Scale	✓		✓		✓
Readiness to change questionnaire - Alcohol	✓		✓		✓

Table 2. Baseline demographic and clinical characteristics

Characteristic	MI-CBT (*n* = 24), No. (%)	TAU (*n* = 20), No. (%)
Sex		
Male	14 (58.3)	9 (45.0)
Female	10 (41.7)	11 (55.0)
Previous episodes		
<12	9 (37.5)	8 (40.0)
12 or more	15 (62.5)	12 (60.0)
AUDIT score		
8-15	8 (33.3)	11 (55.0)
16 or more	16 (66.7)	9 (45.0)
Ethnicity		
White British	24 (100.0)	16 (80.0)
Other white	0	1 (5.0)
Black British	0	2 (10.0)
Asian	0	1 (5.0)
Marital status		
Divorced/annulled/separated	8 (33.3)	6 (30.0)
Never married	11 (45.8)	11 (55.0)
Married or cohabiting	5 (20.8)	3 (15.0)
Number of children		
0	11 (45.8)	10 (50.0)
1	5 (20.8)	7 (35.0)
2	2 (8.3)	3 (15.0)
3	5 (20.8)	0
Not stated	1 (4.2)	0
Education		
Year 7-11 (No GCSEs)	4 (17.4)	2 (10.0)
GCSEs or equivalent	4 (17.4)	7 (35.0)
Further education not completed	1 (4.3)	2 (10.0)
Further education completed	4 (17.4)	2 (10.0)
Higher education not completed	2 (8.7)	1 (5.0)
Higher education completed	5 (21.7)	3 (15.0)
Postgraduate not completed	2 (8.7)	1 (5.0)
Postgraduate completed	1 (4.3)	2 (10.0)
Working		
No	17 (70.8)	16 (80.0)
Yes (includes 1 volunteer)	7 (29.2)	4 (20.0)
Type of work		
Employed full-time	2 (8.3)	2 (10.0)
Employed part-time	3 (12.5)	0

Voluntary	0	1 (5.0)
Self employed	1 (4.2)	1 (5.0)
Unemployed	3 (12.5)	1 (5.0)
Sick/disability	11 (45.8)	12 (60.0)
Retired	2 (8.3)	1 (5.0)
Student	1 (4.2)	2 (10.0)
Not stated	1 (4.2)	0
Bipolar Status		
Bipolar I	21 (87.5)	19 (95.0)
Bipolar II	3 (12.5)	1 (5.0)
Alcohol abuse		
Overall	20 (83.3)	12 (60.0)
In the past month	11 (55.0)	7 (58.3)
Alcohol Dependence		
Overall	15 (62.5)	12 (60.0)
In the past month	7 (46.7)	7 (58.3)
Substance Abuse		
Overall	4 (16.7)	4 (20.0)
In the past month	0	1 (25.0)
Substance Dependence		
In the last 12 months	8 (33.3)	4 (20.0)
In the past month	2 (25.0)	1 (25.0)

Table 3. Summary statistics on frequency of alcohol use (timeline follow back) over 30 days

	MI-CBT			TAU		
Visit (months) [a]	*M*	SD	*n*	*M*	SD	*n*
			Mean Alcohol units/day			
0	7.5	5.3	24	6.0	3.5	20
3	7.4	7.8	22	5.5	4.3	17
6	6.1	4.8	19	4.1	3.6	14
9	6.5	5.7	18	4.1	4.6	14
12	5.7	5.5	19	4.2	4.1	14
			% days abstinent alcohol			
0	39.3	26.3	24	43.3	24.0	20
3	45.2	32.0	22	48.2	30.1	17
6	45.8	33.7	19	60.2	31.1	14
9	41.3	37.7	18	62.1	30.6	14
12	47.4	35.0	19	61.7	23.3	14
			% binge days			
0	48.3	3.4	24	43.9	28.6	20
3	43.5	32.6	22	41.6	36.3	17
6	41.4	34.7	19	30.5	31.3	14
9	42.0	39.0	18	30.7	34.1	14
12	36.5	34.3	19	31.7	24.8	14

Table 4**.** Demographic and clinical characteristics of qualitative interviewees

Pt. No.	Sex	Age	Employment status	Bipolar Status	No. of sessions attended
AB001	M	30	working	Bipolar 1	20
AB002	M	28	Unemployed	Bipolar 1	20
AB003	F	47	Unemployed	Bipolar 1	19
AB004	F	49	Unemployed	Bipolar 1	20
AB005	M	66	Retired	Bipolar 1	18
AB006	M	31	Unemployed	Bipolar 1	20
AB007	M	24	Unemployed	Bipolar 2	20
AB008	M	52	Unemployed	Bipolar 1	20
AB009	M	54	Unemployed	Bipolar 1	20

AB010	F	37	Working	Bipolar 1	18
AB011	M	67	Retired	Bipolar 1	16
AB012	F	58	Working	Bipolar 1	20
AB013	M	52	Retired	Bipolar 1	15
AB014	M	40	Working	Bipolar 1	19
AB015	F	33	Unemployed	Bipolar 1	20

Table 5. Illustrative quotes from qualitative interviews with MI-CBT participants

Theme	Illustrative Quotes
Helpfulness of intervention overall	*'The fact that it's worked, and it has worked for somebody who well self-confessed is really, really cut up, messed up, scarred like you know I was totally destroying myself, and the fact that it has managed to work on someone like me*' (AB002) *'The therapy without wanting to sound melodramatic I would probably say it was fairly life changing for me to be honest.'* (AB001)
Pre-therapy concern about being told what to do	*"I had actually lied to the researchers; I had scaled down how much I was drinking. I had lied because of I thought because I am a single parent, and my son is everything to me, and I was really, really worried about the implications of admitted how much I was drinking." AB003* *'I was worried… that it was going to be like, writing thou shalt not drink, I thought it was going to be a bit of a finger wagging erm... because I can't give up alcohol, I can't, because by giving up alcohol I*

	would give up my whole social existence.' (AB008) *'There is probably elements of things that we didn't cover, not necessarily because there wasn't time but because I didn't want to cover them at that time. Erm… I think [therapist] touched on a couple of things that, quite emotional things for me, erm… as I was growing up and things like, that we didn't touch on because I found it too stressful at the time.'* (AB010)
Engagement with MI-CBT	*'[Therapist] never came across as superior so to speak or anything like that it was like on a one-to-one equal basis. And I never felt put down by saying certain, you know things other people might find stupid, hearing things and things like that it wasn't ever; I didn't feel embarrassed to say anything whatever.'* (AB010) *'The biggest thing that I became aware of, out of all the therapy and speaking to you and everything, everybody who has ever come and seen me, it is down to me, it is down to me, it is not about the people who come and sit and you discuss it with them who were really kind to me and*

	what have you it's not at the end of the day the buck stops with me.' (AB008)
Benefits in relation to alcohol and mood	*"the therapy really took off, and I was able to put into place plans to make changes to my drinking from the therapy and it was excellent at that. I am so glad I have gone through the process, I have even made my own file and plan of action, of how I was going to cut down, cut down on my drinking."* (AB003)
	'I feel it's much more manageable it is not my go-to place, so it is not the first thing that I go right I need a drink… because always there is a reason to drink, there is a funeral, there is a wedding, you are happy, you are sad, you are stressed you are on holiday, you could link it as much as you want to, erm… so I feel that I have extricated myself from [that].' (AB015)
	'I have been great. I have not had any erm... more episodes and I have stayed out of hospital, and I have started a little job actually.' (AB006)
	'having a one-to-one and feel that it's safe to talk, about your problems, well made me, give me the courage a bit, to go forward rather than backwards' (AB009)

	'[my daughter] understands how I feel now rather than just mom is not well today, erm… she understands it, she even jokes about it now.' (AB010)
Negative comments on MI-CBT	*I couldn't actually say that you know I felt it was therapeutic. The conversation was therapeutic because it's always nice to be involved in a conversation but you know apart from that you know I couldn't say it was a therapy.'* (AB011) *'as time went on and what I had set out to do I had achieved, I actually started to get overconfident, and then towards the end of the therapy I was going a bit up and trying to do too much so I got ahead of myself, and that ended up with me just overloading myself and then hitting a bit of a crisis.'* (AB013)

Table 6. Repeated measures model analyses for the TLFB outcomes

Outcome measure, model	Month	Treatment Effect	95% CI lower	95% CI upper	*P*-value
Mean Alcohol/day					
Model 1	3	0.98	-2.04	4.00	
	6	0.92	-1.15	3.00	
	8	0.72	-1.38	2.82	
	12	0.06	-2.96	3.09	
time*treatment interaction					0.955
linear trend test					0.641
Model 2 - no interaction		0.68	-0.77	2.14	0.358
% days abstinent alcohol					
Model 1	3	-5.39	-21.5	10.7	
	6	-16.0	-32.1	0.12	
	9	-16.7	-36.3	2.89	
	12	-14.9	-31.6	1.81	
time*treatment interaction					0.500
linear trend test					0.395
Model 2 - no interaction		-12.0	-23.5	-0.48	0.041
% days abstinent all substances					
Model 1	3	0.77	-15.3	16.8	
	6	-15.1	-31.1	0.90	
	9	-15.7	-34.9	3.41	
	12	-10.2	-26.5	6.14	
time*treatment interaction					0.226
linear trend test					0.335
Model 2 - no interaction		-9.0	-19.8	1.87	0.105
% binge days					
Model 1	3	-0.46	(-14.5	13.6)	
	6	7.55	(-4.80	19.9)	
	9	1.86	-15.2	19.0	
	12	-1.78	-19.5	16.0	
time*treatment interaction					0.569
linear trend test					0.775
Model 2 - no interaction		2.16	-6.93	11.26	0.641