Author's manuscript

Note: This is a pre-print research manuscript. The final published version of this work will be available in a forthcoming edition of the Journal of Substance Abuse Treatment.

Cite this article as follows:
Delgadillo, J., Gore, S., Ali, S., Ekers, D., Gilbody, S., Gilchrist, G., McMillan, D., and Hughes, E. (2015). Feasibility randomized controlled trial of cognitive and behavioral interventions for depression symptoms in patients accessing drug and alcohol treatment. Journal of Substance Abuse Treatment.
http://dx.doi.org/10.1016/j.jsat.2015.02.008

Feasibility randomized controlled trial of cognitive and behavioral interventions for depression symptoms in patients accessing drug and alcohol treatment

Jaime Delgadillo*[1], Stuart Gore[2], Shehzad Ali[3], David Ekers[4], Simon Gilbody[5], Gail Gilchrist[6], Dean McMillan[5] and Elizabeth Hughes[7]

1. Leeds Community Healthcare NHS Trust and Department of Health Sciences, University of York
2. City & South Community Drugs Treatment Service, St. Anne's Community Services
3. Department of Health Sciences, University of York
4. Wolfson Research Institute for Health and Wellbeing, Durham University
5. Hull York Medical School and Department of Health Sciences, University of York
6. Institute of Psychiatry, King's College London
7. University of Huddersfield, South West Yorkshire Partnership NHS Foundation Trust and University of York

Declaration of interest: None.

Acknowledgements
This trial was supported by a research capability funding (RCF) grant awarded by Leeds Community Healthcare NHS Trust, United Kingdom. We gratefully acknowledge our clinical collaborators Omar Moreea, Geraldine Greenwood, Helen Stocks, Susan Watson, Jodi Clark, Julio Mendoza, Iain Cullum, Jo Craven, Tony Hargreaves, Zoe Patterson and Melanie Senior. Helen Stocks assisted with writing the application for NHS research ethics approval. Rebecca Forster assisted with independent randomization. Stuart Fahey, Rachel Bos and Emma Ferguson provided administrative support. We also thank colleagues who assisted the research team with advice and organizational support: Ann Sunter, Anna Tassell, Susanna Lawrence, Bill Owen, the Leeds Dual Diagnosis Project and the Leeds Dual Diagnosis Expert Reference Group.

* Corresponding author: jaime.delgadillo@nhs.net

Abstract

Depressed mood often co-exists with frequent drug and alcohol use. This trial examined the feasibility of screening, recruiting, randomizing and engaging drug and alcohol users in psychological interventions for depression symptoms. A total of 50 patients involved in community drugs and alcohol treatment (CDAT) were randomly allocated to behavioral activation delivered by psychological therapists (n = 23) or to cognitive behavioral therapy based self-help introduced by CDAT workers (n = 27). We examined recruitment and engagement rates, as well as changes in depression (PHQ-9) symptoms and changes in percent days abstinent (PDA within last month) at 24 weeks follow-up. The ratio of screened to recruited participants was 4 to 1, and the randomization schedule successfully generated 2 groups with comparable characteristics. Follow-up was possible with 78% of participants post-treatment. Overall engagement in psychological interventions was low; only 42% of randomized participants attended at least 1 therapy session. Patients offered therapy appointments co-located in CDAT clinics were more likely to engage with treatment (Odds ratio = 7.14, p = .04) compared to those offered appointments in community psychological care clinics. Intention-to-treat analyses indicated no significant between-group differences at follow-up in mean PHQ-9 change scores (p = .59) or in PDA (p = .08). Overall, it was feasible to conduct a pragmatic trial within busy CDAT services, maximizing external validity of study results. Modest and comparable improvements in depression symptoms over time were observed for participants in both treatment groups.

Highlights

- It was feasible to apply a high volume, stepwise screening method in routine addiction treatment
- Patients offered therapy appointments 'co-located' in addiction clinics were more likely to engage with treatment compared to those offered 'parallel' appointments in other mental health clinics
- Poly-substance users were less likely to engage with treatment
- No significant differences were found between behavioral activation and CBT based guided self-help in terms of depression symptom reductions or percent days abstinence
- Both interventions were associated with moderate depression symptom improvements over time

Key words: depression, comorbidity, drugs, alcohol, cognitive behavioral therapy

Study acronym: COBID (**CO**morbidity and **B**rief **I**nterventions for **D**epression)

Website: http://www.isrctn.com/ISRCTN26937594

1. Introduction

There is considerable evidence that common mental health problems like depression and anxiety often co-occur with problematic alcohol and drug use (Marsden, Gossop, Stewart, Rolfe & Farrell, 2000; Strathdee, et al., 2002; Weaver et al., 2003). People who frequently use substances are 2 times at greater risk of having a comorbid depression or anxiety disorder, and this increases to 5 times greater risk for dependent substance users (Merikangas et al., 1998). This combination of problems often complicates treatment and can result in greater functional impairment (Johnson et al., 1995), reduced treatment adherence (Carroll, Power, Bryant, & Rounsaville, 1993; Ford, Snowden & Walser, 1991), poor health outcomes (Hasin et al., 2002; McKay et al., 2002) and increased risk of suicide (Harris & Barraclough, 1997).

The detection of such comorbid disorders has historically been inconsistent in routine treatment in the United Kingdom (Weaver et al., 2003). Consequently, it has been estimated that only 1 in 5 people (20%) involved with community drugs services tend to access mental health treatment (Marsden et al., 2000). Even if comorbid mental health problems are adequately detected, treatment options for this client group seem to have fairly modest benefits. Pharmacological treatments for depression in alcohol and drug users appear to have mixed evidence, with some reviews that indicate a beneficial effect (Iovieno, Tedeschini, Bentley, Evins, & Papakostas, 2011; Nunes & Levin, 2004) and other reviews that question their efficacy (Lingford-Hughes, Welch & Nutt, 2012; Pedrelli et al., 2011; Torrens, Fonseca, Mateu & Farré, 2005). In view of such evidence, exploring the potential of psychological treatments may be a fruitful avenue for research and practice.

Published trials of psychological treatments for depression and anxiety in substance users suggest that cognitive behavioral therapy (CBT) may be an effective treatment (Baillie & Sannibale, 2007; Baker et al., 2010; Brown et al., 2006; Brown, Evans, Miller, Burgess & Mueller, 1997; Hides, Samet, & Lubman, 2010; Hunter et al., 2012; Kay-Lambkin, Baker, Lewin & Carr, 2009; Kay-Lambkin, Baker, Kelly & Lewin, 2011; Watkins, Paddock, Zhang, & Wells, 2006; Watkins et al., 2011). There is, however, scarce research on the application of contemporary behavioral activation (BA) models of treatment in clinical populations of substance users. BA is an intervention that alleviates depression by focusing primarily on changing maladaptive behaviors (such as avoidance, rumination, coping strategies that have unintended negative consequences) that are posited to maintain a cycle of low mood (Martell, Addis, & Jacobson, 2001). BA shares some conceptual underpinnings with CBT such as behavior modification and learning theories, but it does not emphasize the direct modification of thoughts and beliefs as in CBT. The efficacy of BA for the treatment of depression in adults has been endorsed by several meta-analyses of clinical trials (Cuijpers, van Straten, & Warmerdam, 2007; Ekers, Richards, & Gilbody, 2008; Ekers et al., 2014; Mazzucchelli, Kane, Rees, 2009). However, to our knowledge, only one published controlled trial has tested the efficacy of BA with a clinical sample of dependent substance users (Daughters et al., 2008). This trial concluded that augmenting inpatient addiction treatment with BA leads to greater reductions in depression symptoms compared to usual inpatient care.

Considering the prevalence and impact of common mental health problems in drug and alcohol users, and the emerging evidence-base for cognitive and behavioral interventions, we conducted a trial to investigate the feasibility of delivering BA and CBT based guided self-help for depression as part of routine community drugs and alcohol treatment (CDAT). Given our focus on feasibility, the study design also aimed to assess whether co-locating BA within CDAT clinics may enhance engagement with therapy, by comparison to offering this intervention in external mental health clinics as in usual practice. This aspect of the trial was informed by policy guidelines (Department of Health, 2002) that promote integration and close partnership work between substance use and mental health professionals. Though this seems like a sensible policy, we are not aware of empirical evidence specifically supporting the co-location of psychological interventions within CDAT settings and we therefore considered it worthy of further investigation.

2. Methods

2.1. Study design

This was a phase I feasibility randomized controlled trial embedded within CDAT services in Leeds, United Kingdom. Consistent with the medical research council (MRC) guidelines for the development of complex interventions (Craig et al., 2008), the central objective was to examine the feasibility of screening, recruiting, randomizing and engaging patients in psychological interventions for depression symptoms. In this context, we defined engagement as having attended at least one therapy session post-randomization. As part of the design, half of the patients assigned to BA were offered appointments in clinics co-located in CDAT services, and the other half were offered appointments in external clinics - which we refer to as 'parallel' care. A secondary objective was to compare the proportion of cases that engaged with BA treatment in the co-located versus parallel clinics. Finally, we also aimed to estimate comparative effect sizes to inform the sample size calculation for a fully powered efficacy trial.

Ethical approval for this trial was granted by a National Health Service research ethics committee (REC Reference: 12/YH/0096, Registration: ISRCTN26937594).

2.2. Inclusion criteria

Outpatients accessing five CDAT teams were screened for eligibility to take part in the trial. Patients were included if (a) they were currently registered with CDAT and engaged with these services within the last month; (b) they screened positive for clinically significant depression symptoms as defined by the Patient Health Questionnaire (PHQ-9); (c) they had mild-to-moderate symptoms of alcohol or drug dependence as defined by the Severity of Dependence Scale (SDS). Patients who did not meet the above criteria were excluded from the study, as were those who had a current diagnosis of a psychotic, bipolar, or severe anxiety disorder (this was established based on clinical records, screening tools and interview). People who were in treatment but were now free from psychoactive substances (abstinent for at least 4 weeks) were excluded as we were interested in the feasibility of recruiting, retaining and providing psychological treatment for those who were current and recent substance users.

2.3. Screening, recruitment and randomization

A stepwise screening and recruitment method was applied during 18 months, using the following steps:

(1) All patients currently in treatment in the participating services completed the Treatment Outcomes Profile (TOP) questionnaire as part of regular outcome monitoring.

(2) Those that screened positive for a possible common mental health problem using the TOP psychological health scale (TOP item 4a) were then immediately screened with more specific depression (PHQ-9), anxiety (GAD-7) and severity of dependence (SDS) questionnaires by their case managers.

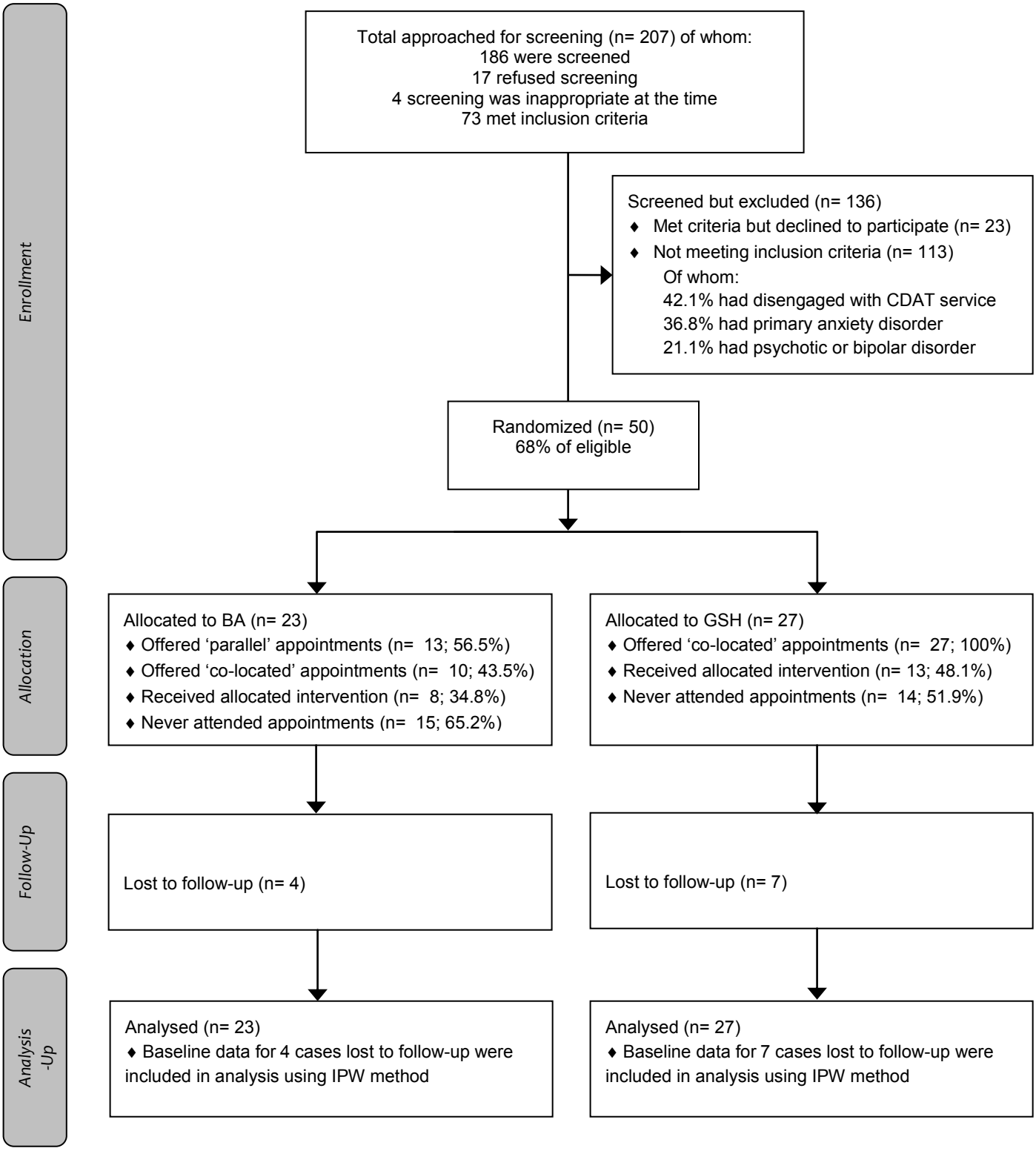
(3) Those who met inclusion criteria based on step 2 were informed about the study by their case manager and consent to be contacted by the study co-ordinator was obtained.

(4) The contact details of consenting patients were passed on to the study co-ordinator who contacted them to conduct an eligibility and recruitment interview. Informed consent was obtained for participation in the trial at the time of these interviews.

The first 3 steps were conducted in routine practice by the usual case managers and support workers, and step 4 was conducted by the study co-ordinator. The co-ordinator was a researcher with experience in screening and diagnostic assessment, who was not involved in the direct delivery of the trial interventions. In order to minimize the chances that case managers in CDAT teams may be selective about the patients they approached for mental health screening, the study co-ordinator performed regular searches in the clinical database to identify potential participants who had recently completed a TOP questionnaire and who screened positive on TOP item 4a. Electronic reminders were sent (via email and online team calendar) on a weekly basis to case managers to undertake step 2 of the screening method.

Eligible and consenting patients were assigned unique participant codes by the co-ordinator and these codes were then emailed to an independent assistant employed by the National Health Service who performed the random allocation. Randomisation was conducted using a computer generated random sequence which was concealed from the clinical teams and the study co-ordinator who undertook recruitment interviews. Participants were either randomized to receive BA or CBT based guided self-help, and this outcome was communicated to clinical administrators who then made contact with participants to offer them a treatment appointment. Outcomes data were collected by the study co-ordinator at 6, 12 and 24 week follow-up to maximize data completeness. This follow-up method ensured that post-treatment outcomes were not collected by the therapists who delivered the intervention. The CONSORT diagram in Figure 1 summarizes all of the above steps and illustrates the flow of participants through the screening, randomization, treatment and follow-up phases.

Figure 1. CONSORT diagram



2.4. Interventions

2.4.1. Behavioral activation (BA)

A 12-session BA intervention was delivered by qualified (to post-graduate level in structured guided self-help interventions, 1 year supervised clinical training course) and experienced psychological wellbeing practitioners offering low intensity treatments in a Primary Care Mental Health Service aligned to the English *Improving Access to Psychological Therapies* (IAPT) programme. BA is a structured intervention for depression based on principles of operant conditioning, functional analysis of behavior and problem solving (Hopko, Lejuez, Ruggiaro & Eifert, 2003; Martell, Addis & Jacobson, 2001). Essentially, it consists of: (a) self-monitoring to identify depressive and maladaptive behaviors; (b) graded scheduling of activities aiming to increase and reinforce adaptive behavior patterns; (c) reducing the frequency of avoidant behaviors, rumination and maladaptive coping strategies. The intervention followed a structured treatment manual developed by our collaborators for use in clinical trials of BA (Ekers, Richards, McMillan, Bland & Gilbody, 2011), with some additional examples and worksheets that are relevant to working with drug and alcohol users (timeline assessment of addiction and emotional problems, decisional balance sheets) drawn from a previous trial of dual diagnosis interventions (Hughes et al., 2008).

BA was delivered in two settings. During the first half of the study, participants assigned to this intervention were offered appointments in primary care mental health clinics across the city (we called this 'parallel' care) as is usual for patients who access the IAPT programme. During the second half of the study, new BA participants were offered appointments in clinic rooms that were based within the CDAT services (we called this 'co-located' care). This aspect of the study design enabled us to investigate whether the location of care made any difference to engagement with therapy. For logistical reasons (e.g. the need to obtain and regularly use a clinic room in addiction settings, the impact of travelling on psychological therapists' time and wider caseloads), it was more practical to switch to co-located care halfway through the study, rather than to individually randomize BA participants to parallel vs. co-located treatments.

2.4.2. Guided self-help (GSH)

The GSH intervention was much more minimal in terms of length and intensity, since it involved a single 1 hour session delivered by a non mental health specialist. This involved asking trained case managers employed by CDAT services to provide, describe and encourage participants to apply a self-help booklet for depression based on principles of CBT (Newcastle North Tyneside and Northumberland Mental Health NHS Trust, 2012). In brief, the booklet introduces readers to common thinking biases, thought challenging techniques, self-monitoring and goal setting. The intervention concludes with homework assignments (e.g. to finish reading the booklet and to apply it on a daily basis). All GSH appointments were 'co-located' in usual CDAT clinics.

2.5. Measures

The Patient Health Questionnaire (PHQ-9) was used to screen for symptoms of depression and as a primary outcome measure. This is a nine-item self-completed questionnaire based on the Diagnostic and Statistical Manual (DSM-IV) diagnostic criteria for major depressive disorder (Kroenke, Spitzer & Williams, 2001). Each item is rated on a 0 to 3 scale relating to the frequency of depressive

symptoms over the last two weeks (0 = 'not at all' to 3 = 'nearly every day'). Scores range from 0 to 27 with higher scores indicating greater severity. A cut-off score ≥ 12 has been found to have adequate sensitivity (81%) and specificity (75%) for the detection of a current depressive episode in routine addiction treatment; the measure also has reliable temporal stability (ICC = .78) in this setting which supports its use for outcome monitoring (Delgadillo et al., 2011).

Given that anxiety symptoms commonly co-occur with depression and impact on clinical outcome (Barlow, 2002), we also included the seven-item GAD-7 questionnaire (Spitzer, Kroenke, Williams & Lowe, 2006) to screen potential participants for a severe anxiety disorder which may render them ineligible for the trial interventions. The GAD-7 is scored in the same way as the PHQ-9, with a range between 0 – 21. This scale has been established as a valid and reliable case-finding measure for a variety of anxiety disorders in alcohol and drug users using a cut-off ≥ 9 (Delgadillo, 2012a).

The Treatment Outcomes Profile (TOP) is a validated questionnaire that captures information about substance use in the last 4 week period using the timeline follow-back method (Marsden et al., 2008). This questionnaire is routinely applied at regular intervals (e.g. 3 months) to monitor outcomes in addiction services (National Treatment Agency for Substance Misuse, 2012). The TOP also includes a brief psychological health scale (TOP item 4a) that has been demonstrated to reliably detect the presence of a diagnosable common mental disorder (cut-off ≤ 12, sensitivity = 83%, specificity = 71%) when compared to a structured diagnostic interview (Delgadillo, Payne, Gilbody, & Godfrey, 2013).

Severity of dependence to the primary drug used was assessed using the 5-item Severity of Dependence Scale (Gossop et al., 1995) which has been widely validated as a reliable case-finder for substance use disorders (Castillo, Saiz, Rojas, Vazquez & Lerma, 2010; Kaye & Darke, 2002; Lawrinson, Copeland, Gerber & Gilmour, 2007; Swift, Copeland & Hall, 1998). This scale renders a continuous severity score ranging from 0 – 15, where a score of 0 to 10 denotes mild-to-moderate psychological dependence.

2.6. Training and supervision

Qualified BA therapists accessed 2 training days delivered by practitioners with expertise in behavior therapy (DE) and dual diagnosis (JD, LH), and had access to group and individual supervision (led by JD; 2 hours every 6 weeks) which was additional to their weekly clinical supervision in primary care. CDAT workers who delivered GSH accessed ½ day training with a counseling psychologist (SG) who also led their supervision group (1.5 hours every 6 weeks). All therapists were required to keep written records of sessions, which were inspected by the relevant supervisors. Due to limited study resources, no additional fidelity checks (such as independent analysis of recorded sessions) were possible.

2.7. Data analysis

2.7.1. Feasibility analysis

Screening, recruitment, random allocation and treatment engagement data were summarized using a CONSORT diagram (Figure 1). In order to assess the integrity of randomization, demographic and clinical characteristics were compared between groups using chi-square tests for categorical variables, t-tests for normally distributed continuous variables and non-parametric Mann-Whitney U-tests for continuous variables with skewed distributions.

In order to quantitatively assess the feasibility of screening, recruitment and successful treatment, we estimated the number needed to screen (NNS) in order to obtain one additional recruit and the number needed to treat (NNT) in order to attain reliable and clinically significant improvement with one patient. We were also interested in exploring potential predictors of engagement with psychological interventions, which was defined as having attended at least 1 therapy appointment. To this end, we applied multivariate logistic regression models predicting engagement (coded = 1) versus non-engagement (coded = 0), using backward elimination of variables with an alpha level of $p > .05$. Backward elimination was considered appropriate given the small number of participants and hence the likelihood that sample power would be insufficient to apply models that control for several variables. Potential predictors were demographics (age in quartiles, gender, ethnicity), treatment group (BA vs. GSH), appointment modality (co-located vs. parallel care), baseline symptom severity (PHQ-9, SDS), and baseline substance use variables (use of opiate substitute medication, PDA, binary marker for poly-substance use). Goodness-of-fit in these analyses was assessed using the Hosmer-Lemeshow test and by examining residual plots.

2.7.2. Secondary analyses

The outcome variable, change in the severity of depression symptoms (PHQ-9) at endpoint follow-up, was compared between groups using analysis of covariance (ANCOVA). Since we expected difficulties with attrition and follow-up as is common in routine addiction treatment, the study design with multiple follow-up assessments enabled us to use the last available assessment as the endpoint for each participant (applying a *last observation carried forward* method). PHQ-9 change scores were taken as the dependent variable in ANCOVA models. Change scores were calculated as the baseline minus the endpoint measure to make interpretation more intuitive, such that a positive score denotes improvement and a negative score denotes deterioration in depression symptoms. Group (BA vs. GSH) was entered as a fixed factor; baseline PHQ-9 score, age (categorized into quartiles), gender and time were entered as covariates. The time variable denoted the time interval (in weeks) between the baseline and final available measurement for each participant, which was variable considering differences in attrition and follow-up. The main analysis was conducted based on *intention-to-treat* principles. To account for cases with completely missing follow-up data (N = 11; 22.0%), inverse probability weighting (IPW) was used in the ANCOVA model as a sensitivity analysis. IPW has been recommended as an appropriate method to minimize bias that is common in complete-case analysis and is often preferable to multiple imputation (Hernán & Hernández-Díaz, 2012; Seaman & White, 2013). Between-group differences were estimated, both in terms of mean and adjusted PHQ-9 change scores and as standardized effect sizes (Cohen's *d*). Within-group effect sizes were also calculated using the method proposed by Minami et al. (2008); this estimate is comparable to Cohen's *d*, computed for repeated measures and weighted by sample size.

Reliable and clinically significant improvement (RCSI) rates were calculated following the criteria proposed by Jacobson and Traux (1991) and based on a PHQ-9 reliable change index (≥7) and cut-point (<12) calibrated for clinical samples of alcohol and drug users (Delgadillo, 2012). Between-group RCSI rates were compared using chi-square analysis.

Changes in substance use (measured with TOP) were explored by estimating percent days abstinent (PDA) over the last 4 weeks for each case. Endpoint PDA change scores were calculated as described above and taken as the dependent variable in ANCOVA; with group as a fixed factor; and controlling for age (quartiles), gender, time, baseline SDS and baseline PDA. In this analysis, a negative change score would denote a reduction and a positive score would denote an increase in substance use. Associations between PDA and PHQ-9 change scores at follow-up were explored using Pearson's correlations. Conventional assumptions to undertake ANCOVA analyses were verified using formal tests for homogeneity of variance and by inspecting residual plots.

3. Results

3.1. Sample characteristics and feasibility

As shown in Figure 1, a total of 207 patients were approached for mental health screening during an 18 month period, based on their response to the TOP questionnaire which indicated that they potentially met criteria for a common mental disorder (TOP item 4a). More detailed screening using PHQ-9 was feasible with 186 patients (89.9% of 207), out of whom 73 (39.2% of screened cases) met criteria for the study but only 50 (68.5% of eligible cases) consented to participate. Based on these observations, we estimate that it is necessary to screen 4 patients to successfully recruit and randomize one consenting and eligible participant (207 / 50 = 4.14 = number needed to screen).

Consenting participants were mostly white British (72.0%) males (68.0%), with a mean age of 37.2 (SD = 6.6), most of whom were currently prescribed opiate substitute medication (92.0%) and anti-depressants (64.0%). The most commonly used substances in this sample were alcohol (50.0%), heroin (34.0%), crack (22.0%) and cannabis (22.0%). Table 1 presents detailed sample characteristics and demonstrates that there were no significant differences between the BA (N = 23) and GSH (N = 27) groups in any of these characteristics, except for mean baseline SDS which appeared to be higher in the BA group; $U(50) = 202.00$, $p = .03$. Importantly, there were no significant differences in baseline PHQ-9 between those who provided follow-up data (mean = 16.72, SD = 4.48) and those who did not (mean = 17.91, SD = 3.75); $t(48) = -0.80$, $p = .42$. There were no significant differences in mean PDA estimates between participants who were followed-up (mean = 0.38, SD = 0.38) and those who were lost to follow-up (mean = 0.19, SD = 0.24); $t(26) = 1.96$, $p = .06$. Overall, the randomization process successfully produced two groups with comparable baseline characteristics, and there was no evidence of bias introduced by cases lost to follow-up.

Only 21 participants (42.0%) actually engaged with their allocated intervention (defined as attending at least one session). There were no significant differences in engagement between the BA (N = 8; 34.8%) and GSH (N = 13; 48.1%) groups; $x^2(1) = 0.91$, $p = .34$. Those who engaged with BA attended a mean number of 3.13 sessions (SD = 1.73, mode = 5). A closer examination of the group of BA participants that engaged in treatment revealed that those offered co-located care (N = 5; 62.5%) attended a higher mean number of total therapy sessions (mean = 4.20, SD = 1.10) compared to those offered parallel care (N = 3, 37.5%, mean = 1.33, SD = .58); however the small numbers did not allow us to formally apply tests of statistical significance. All of those who engaged with GSH had only 1 session (as per protocol), except for one participant who required 2 sessions to work through

the self-help booklet due to obstacles with concentration and literacy. We explored potential predictors of engagement using multivariate logistic regression. The final logistic regression model reached through a two-step process of backward elimination of variables is presented in Table 2. According to this model, poly-substance users were significantly less likely to engage with therapy (Odds ratio = .15, p = .02) and patients offered 'co-located' appointments in a CDAT clinic (who accessed GSH or co-located BA) were at least 7 times more likely to engage compared to participants offered BA in general primary care mental health clinics (Odds ratio = 7.14, p = .04).

Table 1.
Sample characteristics and comparisons between randomly assigned groups

	Full sample N=50 (100%)	**BA N=23 (46%)**	**GSH N=27 (54%)**	**test statistic**	***p***
Demographics					
Males	34 (68.0)	18 (78.3)	16 (59.3)	$x^2(1)=2.06$	.15
Mean age (SD)	37.2 (6.6)	38.4 (6.2)	36.2 (6.8)	t(48)=1.23	.22
Ethnicity					
White British	36 (72.0)	16 (69.6)	20 (74.1)	$x^2(1)=0.13$	.72
Other	14 (28.0)	7 (30.4)	7 (25.9)		
Substances used in the last month					
Alcohol	25 (50.0)	14 (60.9)	11 (40.7)	$x^2(1)=2.01$	.16
Mean units per week (SD)	42.9 (56.4)**	53.9 (73.3)**	30.9 (30.0)**	U(23)=61.00	.76
Heroin	17 (34.0)	5 (21.7)	12 (44.4)	$x^2(1)=2.85$	.09
Mean g. per week (SD)	.29 (.33)**	.15 (.13)**	.34 (.37)**	U(16)=32.50	.27
Crack	11 (22.0)	3 (13.0)	8 (29.6)	$x^2(1)=1.99$	.16
Mean g. per week (SD)	.19 (.13)**	.10 (.00)**	.22 (.14)**	U(11)=19.50	.09
Cannabis	11 (22.0)	6 (26.1)	5 (18.5)	$x^2(1)=0.42$	.52
Mean spliffs per week (SD)	10.3 (9.4)**	7.7 (10.3)**	13.4 (8.1)**	U(11)=22.50	.17
Other	4 (8.0)	4 (17.4)	0	-	
Poly-substance use	18 (36.0)	7 (30.4)	11 (40.7)	$x^2(1)=0.72$	.40
Injecting	6 (13.6)*	3 (15.0)*	3 (12.5)*	-	
Abstinent	9 (18.0)	4 (17.4)	5 (18.5)	-	
Severity of dependence and psychological symptoms at screening					
SDS mean (SD)	6.1 (3.7)	7.3 (3.8)	5.1 (3.4)	U(50)=202.00	**.03**
PHQ-9 mean (SD)	16.9 (4.3)	17.61 (4.7)	16.4 (4.0)	t(48)=-0.95	.35
GAD-7 mean (SD)	11.9 (4.7)	12.3 (4.0)	11.6 (5.3)	t(48)=0.50	.62
TOP-4a mean (SD)	8.5 (3.5)*	8.7 (3.6)	8.3 (3.4)*	t(47)=0.39	.70
Treatment					
Mean no. weeks in treatment (SD)	195.3 (119.1)*	202.9 (126.5)*	189.3 (115.1)*	t(43)=0.38	.71
Using opiate substitute prescription	46 (92.0)	21 (91.3)	25 (92.6)	-	
Using antidepressants	32 (64.0)	14 (60.9)	18 (66.7)	$x^2(1)=0.18$	.67
Engaged with trial intervention†	21 (42.0)	8 (34.8)	13 (48.1)	$x^2(1)=0.91$	.34

* Estimates exclude missing data; ** estimates exclude abstainers from each substance; † refers to participants who attended at least 1 session of allocated intervention; t = Student's t-test; U -Whitney U test; x^2 = Chi-square test; - denotes missing estimates due to violation of test assumptions

Table 2.
Step-wise logistic regression modelling strategy to identify predictors of engagement* with psychological interventions

	Step 1				Step 2			
	pseudo R^2 = .45				pseudo R^2 = .35			
Variable	**B**	**SE**	**β**	***p***	**B**	**SE**	**β**	***p***
(Constant)	-23.59	28235.63	<.001	.99	-1.42	1.15	.24	.22
Gender †	1.34	1.26	3.82	.29	.53	.82	1.70	.51
Age lowest quartile (≤32)				.60				.77
Age quartile 2 (33-36)	-.28	1.52	.76	.85	-.09	1.02	.92	.93
Age quartile 3 (37-43)	1.65	1.54	5.19	.28	.27	1.01	1.31	.79
Age quartile 4 (≥44)	.99	1.45	2.69	.50	1.07	1.17	2.90	.36
Poly-substance use †	-2.35	1.18	.10	**.04**	-1.90	.79	.15	**.02**
Modality †	3.47	1.73	31.98	**.04**	1.97	.98	7.14	**.04**
Psychological treatment group †	1.26	1.53	3.53	.41				
Ethnicity †	-1.40	1.45	.25	.33				
Opiate substitute treatment †	19.37	28235.63	258202165.3	.99				
Baseline PHQ-9	.03	.14	1.03	.82				
Baseline SDS	.01	.15	1.01	.97				
Baseline PDA	1.22	1.51	3.39	.42				

* Engagement is defined as having accessed at least one session of the allocated intervention; step 1 entered all potential predictors of engagement, while step 2 presents a more parsimonious model in which non-significant predictors were removed by backward elimination;
† Reference categories: Gender = male; Age = lowest quartile; poly-substance use = non poly-use; modality = parallel care; psychological treatment group = CBT guided self-help; ethnicity = white British; opiate substitute treatment = not using; β = odds ratio

3.2. Depression symptom outcomes

The intention-to-treat (ITT) ANCOVA analysis predicting change in depression symptoms (PHQ-9) at follow-up found no significant main effects for treatment group after controlling for covariates; $F(1, 33) = .29$, $p = .59$. The sensitivity analysis applying inverse probability weighting (IPW) to assess the influence of missing data also confirmed the same result; $F(1, 33) = .06$, $p = .81$. Only baseline PHQ-9 was a significant predictor of change in depression symptoms in the ANCOVA models; ITT model, $F(1, 33) = 8.89$, $p < .01$; IPW model, $F(1, 33) = 9.66$, $p < .01$. Table 3 presents unadjusted and adjusted mean estimates of PHQ-9 change scores for each group. The mean difference -1.06 (95% CI = -5.05, 2.92) reflects an approximate between-groups effect size of $d = -0.64$ favoring GSH, although this was not statistically significant ($p = .59$). Baseline and endpoint mean scores and standard deviations reported in Table 3 were used to estimate within-group effect sizes weighted by sample size; these were $d = .49$ for BA and $d = .63$ for GSH. The proportions of patients meeting criteria for reliable and clinically significant improvement (RCSI) were 11.8% for BA and 22.2% for GSH, although differences were not statistically significant; $x^2(1) = 0.67$, $p = .41$. The overall proportion of participants meeting RCSI criteria across both treatment groups was 17.1%, and the approximate number needed to treat in order to obtain full recovery with one patient was 6 (NNT = 5.83).

3.3. Substance use outcomes

The ITT ANCOVA model predicting change in percentage days abstinent (PDA in the last month) at follow-up found no significant main effects for treatment group after controlling for covariates; F(1, 28) = 3.32, p = .08. This finding was corroborated by the IPW ANCOVA model; F(1, 28) = 3.82, p = .06. Baseline PDA significantly predicted changes in endpoint PDA estimates in the ANCOVA models; ITT model, F(1, 28) = 12.10, p < .01; IPW model, F(1, 28) = 10.29, p < .01. The mean difference shown in Table 3 was .25 (95% CI = -.03, .52), which reflects an approximate between-groups effect size of d = 1.52 favoring BA, although this was not statistically significant (p = .08). Baseline and endpoint estimates reported in Table 3 were used to calculate within-group effect sizes weighted by sample size; these were d = .40 for BA and d = .02 for GSH. No significant associations were found between PDA change and PHQ-9 change scores at follow-up; r = 0.10, p = .57.

Table 3.
Change in depression (PHQ-9) and percentage days abstinent (PDA) in each of the treatment conditions

Group	Baseline mean (SD)	End-point mean (SD)	Unadjusted mean change score (SE)	Adjusted* mean change score (SE)	Mean Difference (95% CI)	*p*
Depression (PHQ-9)						
BA (N = 19)	17.61 (4.66)	15.21 (5.41)	1.79 (1.48)	1.69 (1.32)	-1.06 (-5.05, 2.92)	.59
GSH (N = 20)	16.44 (4.02)	13.80 (5.36)	2.65 (1.20)	2.75 (1.28)		
Percentage days abstinent during the last month (PDA)						
BA (N = 15)	.38 (.40)	.55 (.45)	.12 (.13)	.17 (.10)	.25 (-.03, .52)	.08
GSH (N = 20)	.30 (.33)	.30 (.34)	-.04 (.08)	-.08 (.08)		

* Adjusted for PHQ-9 baseline severity, age, gender, follow-up time, using intention-to-treat analysis; BA = Behavioural Activation; GSH = Guided self-help based on cognitive behavioural therapy booklet; SE = standard error; CI = 95% confidence intervals; N = denotes the total number of respondents with complete follow-up data per group and outcome of interest

4. Discussion

4.1. Main findings

This phase I feasibility trial applied a high volume, structured and stepwise mental health screening method to identify CDAT patients with clinically significant depression symptoms. Based on this strategy, the ratio of screened to recruited patients was 4 to 1. Our results demonstrated the integrity of the random allocation method and it was possible to follow up 78% of study participants post-treatment. Overall, it was feasible to conduct a trial embedded within busy clinical settings, maximizing the external validity of the study design. A noteworthy aspect of the study design is the demonstration that high volume screening of mental health problems can be feasibly embedded within routine CDAT services, and linked with evidence-based psychological treatments. The first point potentially offers an important advance, since consistent and reliable mental health screening

is known to be lacking in routine addiction services (Weaver et al., 2003). Our pragmatic approach also resembles recent studies aiming to train addiction treatment workers to use screening tools and to offer brief interventions for depressed substance users (e.g. see Lee et al., 2011; Watkins, Paddock, Zhang, & Wells, 2006).

The greatest difficulty we encountered was the high attrition rate resulting in poor engagement with treatment. This was in spite of the additional administrative support available to the research team which was used to proactively chase up study participants to try to maximize engagement. Our findings revealed that poly-substance use was a risk factor for non-engagement in this sample. Most poly-substance users in this study were combining heroin and crack-cocaine, which is consistent with research indicating that this combination of drugs is associated with treatment discontinuation (Leri, Bruneau, & Stewart, 2003). However, readers should also consider that other studies have yielded mixed evidence about the associations between treatment attrition and quantity, frequency and type of substance use (e.g. see review by Stark, 1992). It may be that poly-substance use could be a marker for other complex factors that influence engagement with treatment, for example impulsivity, involvement in criminal activity, impairments in social adjustment, etc. Such potential associations warrant further investigation. We also found that offering appointments co-located in the CDAT setting considerably increased the likelihood of engagement. Furthermore, it appears that co-located care may also result in greater number of attended therapy sessions by comparison to parallel care. A possible explanation may be that co-location in a familiar setting minimizes clients' concerns about privacy or stigma related to mental health problems. For instance, concerns about privacy have been previously endorsed by patients as a reason for dropping out of addictions treatment (Ball, Carroll, Canning-Ball, Rounsaville, 2006). Another possibility is that co-location simply makes access to treatment more convenient, especially if patients may have limited financial resources to travel to various appointments in different locations.

The preliminary outcomes analysis evidenced modest improvements in depression symptoms over time, with moderate within-group effect sizes (d = .49 to .63). These effects are comparable in magnitude to the BA trial conducted by Daughters et al. (2008), where the approximate within-group pre-post effect sizes for the BA intervention were d = 0.49 for the Hamilton Depression Scale and d = 0.91 for the Beck II Depression measure. Considering the wider literature in this area, Hesse (2009) reported aggregated depression symptom effect sizes in the region of d = -0.58 (95% CI -1.10 to -0.06) in a meta-analysis favoring integrated psychological and substance use disorder treatments compared to non-integrated control conditions. A more recent meta-analysis (Riper et al., 2014) which specifically focused on integrated CBT and motivational interviewing trials (iCBT) reported a more modest aggregated effect size for depression symptoms favoring iCBT versus usual care (g = 0.27, 95% CI 0.13 to 0.41).

As noted by Hides et al. (2010) trials comparing CBT to active control conditions in depressed substance users mostly report non-significant differences. Similarly, we found no significant differences in depression symptom outcomes between groups, which was remarkable considering that the GSH intervention was delivered over a considerably briefer duration (1 session). However, this finding should be taken as preliminary since this study was not sufficiently powered to undertake a non-inferiority analysis. It is also possible that the non-significant

differences may be explained by the relatively low number of mean treatment sessions (mean = 3.13, mode = 5) attended by participants in the BA group. We note that the PDA estimate increased by 17% in the BA group after treatment, indicating reduction in substance use, whereas no change in substance use was apparent in the GSH group. This finding requires replication in a larger sample since the mean difference between groups did not reach statistical significance. It nevertheless raises an interesting question about the potential benefit of BA in the reduction of problematic substance use, which is comparable in effect to the average 14.1% PDA gain reported in the meta-analysis by Hesse and collaborators (Hesse, 2009) favoring integrated psychological interventions.

4.2. Implications for practice and research

The psychological care of dependent substance users has historically tended to be a neglected area of practice and research. The present study draws attention to the feasibility of high volume mental health screening, and the co-location of psychological and substance use interventions.

Co-location of mental health and addiction specialists appears to enhance engagement with treatment and is consistent with policy developments urging professionals to co-ordinate care and break down barriers for people with complex needs and co-morbidities (Department of Health, 2002; Mental Health Foundation, 2013). We underline two further points about co-location. First, future trials could investigate whether it is possible to maximize the benefit of co-location by applying principles of contingency management (CM), which involves the provision of incentives (e.g. vouchers, or prescriptions) to enhance treatment adherence. CM has a robust evidence base in addictions treatment and is recommended by clinical guidelines (National Institute for Health and Clinical Excellence, 2007). For example, co-located depression treatment appointments followed by CM specifically aimed to incentivize (a) attendance and (b) abstinence may provide the best possible context to enable patients to self-manage their mental health. Secondly, the parallel care offered in our trial was far more costly and less efficient due to lost clinical time, additional administrative burden invested in chasing participants up and additional clinical time invested in calling and liaising with workers in CDAT services. Future trials and indeed clinical practice should consider either co-locating mental health specialists within CDAT services or training and supervising addiction workers to deliver evidence-based interventions for depression symptoms.

4.3. Limitations

The stepwise screening method may have excluded some potentially eligible participants simply due to the limitations of the TOP item 4a scale which was applied as the first step, since some 'false negatives' may have been excluded from screening with PHQ-9. This is a plausible limitation; however, our decision to apply a pragmatic stepwise method is congruent with our prior observations that some patients can find detailed screening intrusive and emotionally challenging (Delgadillo et al., 2012b). We therefore argue that stepwise screening achieves an adequate balance between reliability, acceptability and feasibility in busy clinical settings. It is also possible that the study sample may be less representative of more severely distressed and impaired substance users, since we excluded those patients with severe symptoms of dependence (defined by the SDS measure). The rationale for this exclusion was to ensure that participants were reasonably stable

on medication and engaged in addiction treatment by the time they had an opportunity to take part in the study. A further consideration about the screening and recruitment method is that our pragmatic case-finding and recruitment strategy introduced a low threshold for inclusion in the study, since we set out to find participants that may not otherwise have been treatment seekers. Indeed, this low threshold meant that we had to exclude a number of patients who were screened but turned out to have primary anxiety, psychotic or bipolar disorders as illustrated in Figure 1. We also note that nearly half of the patients that were screened but excluded from participating in the trial had either declined therapy or generally disengaged with the wider CDAT intervention.

Despite the considerable number of participants who did not engage with treatment, we managed to obtain follow-up data from 78% using a *last observation carried forward* (LOCF) method. It is of course possible that our estimations of end-point outcomes may be inaccurate since the LOCF method assumes that no change has occurred since the last available assessment. Missing follow-up data is a common limitation in clinical trials involving substance users with mental health problems (Hesse, 2009). Nevertheless, we ensured a robust analysis by applying intention-to-treat principles and inverse probability weighting to account for missing data. A further limitation concerns the lack of formal fidelity checks over and above regular case reviews and supervision, which was not possible to undertake within the financial constraints of this study.

4.4. Concluding remarks

Overall, this study demonstrates that integrating stepwise mental health screening in routine addiction treatment is feasible and can be linked with cognitive and behavioral interventions, ideally co-located in the same setting to maximize engagement. As others have argued (Morisano, Babor & Robaina, 2014; Torrens, Rossi, Martinez-Riera, Martinez-Sanvisens & Bulbena, 2012) we take the view that system level, public health oriented, screening and psychological interventions integrated within CDAT are needed to improve the mental health and functioning of patients.

References

Baillie, A., & Sannibale, C. (2007). Anxiety and drug and alcohol problems. In: Baker A, Velleman R, eds. *Clinical handbook of co-existing mental health and drug and alcohol problems*. London: Brunner-Routledge, 195–214.

Ball, S.A., Carroll, K.M., Canning-Ball, M., Rounsaville, B.J. (2006). Reasons for dropout from drug abuse treatment: Symptoms, personality, and motivation. *Addictive Behaviors, 31*, 320–330

Baker, A.L., Kavanagh, D.J., Kay-Lambkin, F.J., Hunt, S.A., Lewin, T.J., Carr, & V.J., et al. (2010). Randomized controlled trial of cognitive–behavioral therapy for coexisting depression and alcohol problems: short-term outcome. *Addiction, 105*, 87–99.

Barlow, D.H. (2002). *Anxiety and its Disorders: The Nature and Treatment of Anxiety and Panic*. Second Edition. New York: Guilford Press.

Brown, S.A., Glasner-Edwards, S.V., Tate, S.R., McQuaid, J.R., Chalekian, J., & Granholm, E. (2006). Integrated cognitive behavioral therapy versus twelve-step facilitation therapy for substance-dependent adults with depressive disorders. *Journal of Psychoactive Drugs*, *38*, 449-460.

Carroll, K.M., Power, M.E., Bryant, K.J., & Rounsaville, B.J. (1993). One-year follow-up status of treatment-seeking cocaine abusers: *Psychopathology and dependence severity as predictors of outcome*, *181*, 71–79.

Castillo, I.I., Saiz, F.G., Rojas, O.L., Vazquez, M.A.L., & Lerma, J.M.J. (2010). Estimation of cutoff for the Severity of Dependence Scale (SDS) for opiate dependence by ROC analysis. *Actas Espanolas de Psiquiatria, 38*, 270-277.

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *British Medical Journal, 337*, a1655.

Cuijpers, P., van Straten, A., Warmerdam, L. (2007). Behavioral activation treatments of depression: A meta-analysis. *Clinical Psychology Review, 27*(3), 318–326.

Daughters, S.B., Braun, A.R., Sargeant, M.N., Reynolds, E.K., Hopko, D.R., & Blanco, C. at al. (2008). Effectiveness of a brief behavioral treatment for inner-city illicit drug users with elevated depressive symptoms: the life enhancement treatment for substance use (LETS Act!). *Journal of Clinical Psychiatry, 69*, 122-129.

Delgadillo, J., Payne, S., Gilbody, S., Godfrey, C., Gore, S., & Jessop, D., et al. (2011). How reliable is depression screening in alcohol & drug users? A validation of brief and ultra-brief questionnaires. *Journal of Affective Disorders, 134*, 266–271.

Delgadillo, J. (2012). Depression and anxiety symptoms: Measuring reliable change in alcohol and drug users. *Advances in Dual Diagnosis, 5*, 102–114.

Delgadillo, J., Payne, S., Gilbody, S., Godfrey, C., Gore, S., & Jessop, D., et al. (2012a). Brief case finding tools for anxiety disorders: validation of GAD-7 and GAD-2 in addictions treatment. *Drug and Alcohol Dependence, 125,* 37-42.

Delgadillo, J., Gore, S., Jessop, D., Payne, S., Singleton, P., Gilbody, S. (2012b). Acceptability of mental health screening in routine addictions treatment. *General Hospital Psychiatry, 34,* 415–422.

Delgadillo, J., Payne, S., Gilbody, S., & Godfrey, C. (2013). Psychometric properties of the Treatment Outcomes Profile (TOP) psychological health scale. *Mental Health and Substance Use, 6*, 140-149.

Department of Health. (2002). *Mental health policy implementation guide: Dual Diagnosis Good Practice Guide*. London: Department of Health.

Ekers, D., Richards, D., Gilbody, S. (2008) A Meta Analysis of Behavioural Therapy for Depression. *Psychological Medicine, 38*, 611–623.

Ekers, D., Richards, D., McMillan, D., Bland, J.M., & Gilbody, S. (2011). Behavioral activation delivered by the non-specialist: phase II randomized controlled trial. *British Journal of Psychiatry, 198*, 66-72.

Ekers, D., Webster, L., van Straten, A., Cuijpers, P., Richards, D., Gilbody, S. (2014). Behavioural Activation for Depression; An Update of Meta-Analysis of Effectiveness and Sub Group Analysis. *PLoS ONE,* 9(6), e100100. doi:10.1371/journal.pone.0100100

Ford, L., Snowden, L.R., Walser, E.J. (1991). Outpatient mental health and the dual-diagnosis patient: Utilization of services and community adjustment. *Evaluation and Program Planning, 14*, 291-298.

Gossop, M., Darke, S., Griffiths, P., Hando, J., Powis, B., & Hall, W., et al. (1995). The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction, 90*, 607-614.

Harris, E.C., & Barraclough, B. (1997). Suicide as an outcome for mental disorders. A meta-analysis. *British Journal of Psychiatry, 170*, 205-228.

Hasin, D., Liu, X., Nunes, E., McCloud, S., Samet, S., & Endicott, J. (2002). Effects of major depression on remission and relapse of substance dependence. *Archives of General Psychiatry, 59*, 375–380.

Hernán, M.A., & Hernández-Díaz, S. (2012). Beyond the intention-to-treat in comparative effectiveness research. *Clinical Trials, 9*, 48-55.

Hesse, M. (2009). Integrated psychological treatment for substance use and co-morbid anxiety or depression vs. treatment for substance use alone. A systematic review of the published literature. *BMC Psychiatry, 9*, 6.

Hides, L., Samet, S., & Lubman, D.I. (2010). Cognitive behavior therapy (CBT) for the treatment of co-occurring depression and substance use: current evidence and directions for future research. *Drug and Alcohol Review, 29*, 508-17.

Hopko, D., Lejuez, C., Ruggiaro, K., Eifert, G. (2003). Contemporary behavioral activation treatments for depression: procedures, principles and progress. *Clinical Psychology Review*, *23*, 699–717.

Hughes, E., Wanigaratne, S., Gournay, K., Johnson, S., Thornicroft, G., & Finch, E., et al. (2008). Training in dual diagnosis interventions (the COMO Study): Randomized controlled trial. *BMC Psychiatry, 8*, 12.

Hunter, S.B., Watkins, K.E., Hepner, K.A., Paddock, S.M., Ewing, B.A., & Osilla, K.C. et al. (2012). Treating depression and substance use: A randomized controlled trial. *Journal of Substance Abuse Treatment, 43*, 137-151.

Iovieno, N., Tedeschini, E., Bentley, K.H., Evins, A.E, Papakostas, G.I. (2011). Antidepressants for major depressive disorder and dysthymic disorder in patients with comorbid alcohol use disorders: a meta-analysis of placebo-controlled randomized trials. *Journal of Clinical Psychiatry, 72*(8), 1144-1151.

Jacobson, N., & Truax, P. (1991). Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology, 59*, 12–19.

Johnson, J.G., Spitzer, R.L., Williams, J.B.W., Linzer, M., deGruy, F., & Kroenke, K., et al. (1995). Psychiatric comorbidity, health status, and functional impairment associated with alcohol abuse and dependence in primary care patients: Findings of the PRIME MD-1000 study. *Jounal of Consulting and Clinical Psychology***,** *63*, 133– 140.

Kay-Lambkin, F.J., Baker, A.L., Lewin, T.J., & Carr, V.J. (2009). Computer based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy. *Addiction, 104*, 378–388.

Kay-Lambkin, F.J., Baker, A.L., Kelly, B., & Lewin, T.J. (2011). Clinician-assisted computerised versus therapist-delivered treatment for depressive and addictive disorders: a randomized controlled trial. *Medical Journal of Australia, 195*, 44–50.

Kaye, S., & Darke, S. (2002). Determining a diagnostic cut-off on the Severity of Dependence Scale (SDS) for cocaine dependence. *Addiction, 97*, 727-31.

Kroenke, K., Spitzer, R.L., & Williams, J.B.W. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medical*, *16*, 606-613.

Lawrinson, P., Copeland, J., Gerber, S., & Gilmour, S. (2007). Determining a cut-off on the Severity of Dependence Scale (SDS) for alcohol dependence. *Addictive Behaviors, 32*, 1474-9.

Lee, N., Jenner, L., Baker, A., Ritter, A., Hides, L., Norman, J., Kay-Lambkin, F., Hall, K., Dann, F., Cameron, J. (2011). Screening and intervention for mental health problems in alcohol and other drug settings: Can training change practitioner behavior? *Drugs: Education, Prevention & Policy. 18*(2), 157-160.

Leri, F., Bruneau, J., & Stewart, J. (2003). Understanding polydrug use: review of heroin and cocaine co-use. *Addiction, 98*, 7–22.

Lingford-Hughes, A.R., Welch, S., & Nutt, D.J. (2012). Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology, 18*, 293–335.

Marsden, J., Farrell, M., Bradbury, C., Dale-Perera, A., Eastwood, B., & Roxburgh, M., et al. (2008). Development of the Treatment Outcomes Profile. *Addiction, 103*, 1450-60.

Marsden, J., Gossop, M., Stewart, D., Rolfe, A., & Farrell, M. (2000). Psychiatric symptoms among clients seeking treatment for drug dependence: Intake data from the National Treatment Outcome Research Study. *British Journal of Psychiatry*; *176*, 285-289.

Martell, C., Addis, M., & Jacobson, N. (2001). *Depression in Context. Strategies for Guided Action*. Norton.

Mazzucchelli, T., Kane, R., Rees, C. (2009). Behavioral Activation Treatments for Depression in Adults: A Meta-analysis and Review. *Clinical Psychology: Science and Practice, 16*(4), 383–411.

McKay, J.R., Pettinati, H.M., Morrison, R., Feeley, M., Mulvaney, F.D., & Gallop, R. (2002). Relation of depression diagnoses to 2-year outcomes in cocaine-dependent patients in a randomized continuing care study. *Psychology of Addictive Behaviors, 16*, 225–235.

Mental Health Foundation. (2013). *Crossing boundaries. Improving integrated care for people with mental health problems.* London: Mental Health Foundation.

Merikangas, K. R., Mehta, R. L., Molnar, B. E., Walters, E. E., Swendsen, J. D., & Aguilar-Gaziola, S., et al. (1998). Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. *Addictive Bahaviors*, *23*, 893-907.

Minami, T., Serlin, R.C., Wampold, B.E., Kircher, J.C., & Brown, G.S. (2008). Using clinical trials to benchmark effects produced in clinical practice. *Quality and Quantity*, *42*, 513–525.

Morisano, D., Babor, T.F., & Robaina, K.A. (2014) Co-occurrence of substance use disorders with other psychiatric disorders: Implications for treatment services. *NAD, 31*, 5-25.

National Institute for Health and Clinical Excellence. (2007). *Drug Misuse: Psychosocial Interventions*. NICE Clinical Guideline 51. London: NICE.

National Treatment Agency for Substance Misuse. (2012). *The National Drug Treatment Monitoring System*. Available at: https://www.ndtms.net/Default.aspx [Accessed 2 April 2014].

Newcastle North Tyneside and Northumberland Mental Health NHS Trust. (2012). *Depression and Low Mood: a self-help guide*. Newcastle: Department of Design and Communication.

Nunes, E.V., Levin, F.R. (2004). Treatment of Depression in Patients With Alcohol or Other Drug Dependence. *JAMA, 291*(15), 1887-1896.

Pedrelli, P., Iovieno, N., Vitali, M., Tedeschini, E., Bentley, K.H., Papakostas, G.I. (2011). Treatment of Major Depressive Disorder and Dysthymic Disorder With Antidepressants in Patients With Comorbid Opiate Use Disorders Enrolled in Methadone Maintenance Therapy: A Meta-Analysis. *Journal of Clinical Psychopharmacology, 31*(5), 582-586.

Riper, H., Andersson, G., Hunter, S.B., de Wit, J., Berking, M., & Cuijpers, P. (2014). Treatment of comorbid alcohol use disorders and depression with cognitive-behavioral therapy and motivational interviewing: a meta-analysis. *Addiction, 109*, 394–406.

Seaman, S.R., & White, I.R. (2013). Review of inverse probability weighting for dealing with missing data. *Statistical Methods in Medical Research*, *22*, 278-295.

Spitzer, R., Kroenke, K., Williams, J.B.W., & Lowe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 66*, 1092–1097.

Srark, M.J. (1992). Dropping out of substance abuse treatment: A clinically oriented review. *Clinical Psychology Review, 12*, 93-116.

Strathdee, G., Manning, V., Best, D., Keaney, F., Bhui, K., & Witton, J., et al. (2002). *Dual diagnosis in a primary care group (PCG): a step-by-step epidemiological needs assessment and design of a training and service response model*. London: Department of Health.

Swift, W., Copeland, J., & Hall, W. (1998). Choosing a diagnostic cut-off for cannabis dependence. *Addiction*, *93*, 1681-1692.

Torrens, M., Fonseca, F., Mateu, G., & Farré, M. (2005). Efficacy of antidepressants in substance use disorders with and without comorbid depression. A systematic review and meta-analysis. *Drug and Alcohol Dependence*, *78*, 1-22.

Torrens, M., Rossi, P.C., Martinez-Riera, R., Martinez-Sanvisens, D., & Bulbena, A. (2012). Psychiatric Co-Morbidity and Substance Use Disorders: Treatment in Parallel Systems or in One Integrated System? *Substance Use and Misuse*, *47*, 1005-1014.

Watkins, K.E., Paddock, S.M., Zhang, L., Wells, KB. (2006). Improving care for depression in patients with comorbid substance misuse. *American Journal of Psychiatry, 163*(1), 125-
132.

Watkins, K.E., Hunter, S.B., Hepner, K.A., Paddock, S.M., de la Cruz, E., Zhou, A.J., Gilmore, J. (2011). An Effectiveness Trial of Group Cognitive Behavioral Therapy for Patients With Persistent Depressive Symptoms in Substance Abuse Treatment. *Archives of General Psychiatry, 68*(6), 577-584.

Weaver, T., Madden, P., Charles, V., Stimson, G., Renton, A., & Tyrer, P., et al. (2003). Comorbidity of substance misuse and mental illness in community mental health and substance misuse services. *British Journal of Psychiatry*, *183*, 304-313.