

Protocol for “A randomised controlled trial of Cognitive Bias Modification training during early recovery from alcohol dependence”

BACKGROUND

One in five Australians will develop alcohol abuse or dependence (i.e. an alcohol use disorder) during their lifetime (Teesson *et al.*, 2010). Consumption of alcohol accounted for 4.7% of male and 3% of female deaths in Australia in 2010 (Gao *et al.*, 2014). Alcohol use disorders are associated with over 60 diseases and conditions and the associated social costs in Australia are estimated to exceed \$15 billion per annum (Collins & Lapsley, 2008). Given the costs of alcohol use disorders and increasing resource constraints in public healthcare, research into effective treatment is a priority investment.

Treatment for alcohol-dependent persons often commences with costly and intensive inpatient detoxification, followed by several weeks or months of outpatient counselling (AIHW, 2014). Yet despite decades of research on psychosocial and pharmacological treatments for alcohol use disorders, relapse unfortunately remains ‘the norm’. Research suggests that 80-90% of alcohol-dependent patients relapse after detoxification (Boothby & Doering, 2005; Sanghani *et al.*, 2015), often in the first few weeks or even days following detoxification (Miller & Kavanagh, 2011). Alcohol-dependent individuals typically undergo multiple episodes of inpatient withdrawal before achieving sustained recovery. Relapsing individuals therefore place considerable burden on an already overstretched healthcare system in their demand for subsequent costly inpatient detoxification treatments, their disproportionately higher use of acute health services due to alcohol-related injuries and illnesses, and extended periods of unemployment and related welfare support (Manning *et al.*, 2013). Hence there is an urgent need for novel and effective methods to reduce relapse following inpatient detoxification, as such interventions are likely to benefit those directly and indirectly affected by alcohol use disorders and generate substantial economic savings in terms of public spending.

According to contemporary “dual process” models of addiction, alcohol use disorders are maintained by an imbalance between two independent but interacting information processing systems (Bechara, 2005), of which one operates at least partly outside conscious control, rendering the drinker persistently vulnerable to relapse. One system, the impulsive/automated system, becomes sensitised towards alcohol-related stimuli in the environment (Strack & Deutsch, 2004). The other is the reflective/executive control system, which becomes less proficient at suppressing automated impulsive behaviours in favour of alternative/healthier responses (Wiers *et al.*, 2013). The interplay between these two interconnected systems is influenced (or unbalanced) by cognitive motivational biases. One such cognitive bias is termed ‘attentional bias’; the tendency for alcohol-related cues in the environment to selectively capture attention because of their increased incentive salience. Another relevant cognitive bias is ‘approach bias’; the automatically activated action tendencies to approach alcohol due to the motivational significance that is attributed to alcohol-related cues (Wiers *et al.*, 2009). These cognitive biases have been proposed to result in an individual’s behaviour becoming increasingly governed by alcohol-related cues in their environment, triggering the desire to consume alcohol (Wiers *et al.*, 2007). The resulting automatic approach tendency is then harder to inhibit because of a compromised executive control system that is impaired in its ability to steer the individual towards an alternative behavioural response (Czapla *et al.*, 2013; Stavro *et al.*, 2013).

Chronic alcohol use affects multiple brain circuits including those that underpin decision-making, reward and stress (Cui *et al.*, 2013). However there is mounting evidence of structural, functional and neurocognitive recovery and reorganisation during early withdrawal from alcohol (Bartsch *et al.*, 2007; van Eijk *et al.*, 2013; Willoughby *et al.*, 2015). This includes recovery in brain regions that underpin the motivational system and associated cognitive biases. Significant improvements in neurocognitive functioning have also been observed within the initial week (Manning *et al.*, 2008) and even days (Mann *et al.*, 1999) of detoxification. It is therefore possible that cognitive biases are also amenable to change at this time.

Cognitive-bias modification is an umbrella term used to describe computerised training programs designed to target and change maladaptive cognitive biases. To address approach bias towards alcohol, Wiers *et al.* (2010) developed the alcohol approach/avoidance task (alcohol-AAT). In this task, participants are presented with pictures of alcohol-related stimuli and neutral stimuli and are instructed to respond with an approach behaviour (pulling a joystick) or an avoidance behaviour (pushing a joystick). Pulling increases the size of the picture, while pushing decreases the size of the picture, essentially generating the sensation of approaching or avoiding alcohol-related stimuli. In a sample of social drinkers, those who were trained to avoid (push away) pictures of alcohol showed a reduced approach bias to untrained pictures in the same task, and consumed less alcohol in a subsequent taste test than those who were trained to approach (pull towards them) pictures of alcohol. Participants in clinical studies of the alcohol-AAT undergo numerous trials of the approach bias training delivered over multiple sessions (days), so that the automatic approach bias is weakened, and avoidance bias strengthened, in response to alcohol cues. Approach bias modification has been tested in outpatient alcohol-dependent samples, with promising results (Wiers *et al.*, 2011; Eberl *et al.*, 2013).

Surprisingly, despite evidence that CBM is efficacious in re-training cognitive biases and reducing relapse, and that early withdrawal is a time of neural recovery relevant to these biases, no published study has examined the impact of re-training approach biases during the acute detoxification phase. With respect to the dual process model of addiction, psychosocial treatments such as CBT, motivational interviewing etc. that typically follow detoxification address the faulty reflective processes by augmenting cognitive control to inhibit drinking behaviour. However, they fail to address the other faulty system, (i.e., the impulsive/automatic information processing system). We anticipate that by weakening approach bias during detoxification, their behaviour will become less driven by immediate alcohol-related representations. This should allow greater capacity to consider future consequences of their behaviour, thereby reducing the likelihood of relapse in those vulnerable days after leaving the supportive environment offered by inpatient settings.

Participants and recruitment:

Participants will be 300 alcohol-dependent patients (aged 18-65) admitted for inpatient detoxification at De Paul House (St. Vincent's Hospital Melbourne), Wellington House (Eastern Health) or Windana Drug and Alcohol Recovery. Inclusion criteria are:

1. Current moderate or severe DSM-5 alcohol use disorder (i.e. at least 4 alcohol use disorder criteria met within the past year, according to the Structured Clinical Interview for DSM-5 Disorders – Research Version (SCID-5-RV; First, Williams, Karg, & Spitzer, 2015)).
2. Report at least weekly use of alcohol in the past month.
3. Be able to understand English.

Exclusion criteria are:

1. History of neurological illness or injury or brain trauma involving loss of consciousness for longer than 30 minutes.
2. Intellectual disability.
3. Acutely unwell, as judged by clinical staff.

Clinicians at De Paul House, Wellington House, and Windana will be advised of the inclusion and exclusion criteria. They will advise eligible patients of the opportunity to participate in research and seek their permission for a researcher to contact the patient for further explanation if interested in participation. If a patient agrees to be approached, clinical staff will identify them to a researcher who will approach the patient on their 3rd day of detoxification to provide further information about the study. If a patient expresses a desire to participate and appears to have understood the information provided, they will be asked to sign a consent form. After providing informed consent, the researcher will administer the SCID-5-RV and the time-line follow-back (TLFB; Sobell & Sobell, 1996) to confirm that the participant meets alcohol use disorder and frequency of use criteria. Signing the consent form will also provide permission for the researcher to view the participant's clinical intake notes to confirm other inclusion and exclusion criteria.

Procedure:

Following provision of informed consent, the researcher will conduct a baseline questionnaire assessment. In addition to the SCID-5-RV (which will also be used to index the number of alcohol use disorder criteria met, in addition to eligibility) and the TLFB (which will also index tobacco, medication, and other drug use during the past 30 days, as well as alcohol use), this questionnaire will also include:

1. A demographic/clinical history questionnaire assessing date of birth, gender, country of birth, Aboriginal/Torres Strait Islander status, highest level of completed education, relationship status, employment status, housing status, age of onset of alcohol use, history of prior withdrawal treatment, other drugs of concern, family history of substance use disorders, psychiatric diagnoses, and any brain injuries, neurological disorders or other mental disorders.
2. The Alcohol Craving Questionnaire – Short Form – Revised (ACQ-SF-R; Singleton, Tiffany, & Henningfield, 2014) to assess craving for alcohol at the time of assessment.
3. The Brief Situational Confidence Questionnaire (BSCQ; Breslin, Sobell, Sobell, & Agrawal, 2000) to assess sense of self-efficacy for resisting urges to drink.

Following this, a baseline battery of computerised tests will be administered including:

1. A modified neutral version of the Alcohol-AAT (Wiers, Rinck, Kordts, Houben, & Strack, 2010) to measure approach bias towards alcohol. Participants are required to react to the format of pictures using a joystick (e.g. push landscape pictures, pull portrait pictures), irrespective of the content of the pictures. There are two categories of pictures; 10 different

alcoholic beverages and 10 different non-alcoholic beverages (images will differ from those used in the training task). Each image type is repeated 4 times, for a total of 80 trials. Every picture type appears in landscape and in portrait format 50% of the time. For both categories of pictures (alcohol, non-alcohol), the median reaction time (RT) for pull responses is subtracted from the median RT for pull responses to produce a measure of approach bias. A positive score indicating that a participant more readily approached that category of picture than avoided it, while a negative score indicates the opposite.

2. The Balloon Analogue Risk Task (BART; Lejuez *et al.*, 2002). In the BART game, participants are required to inflate a virtual balloon on a computer screen to accumulate money. This requires participants to make sequential decisions about whether or not to make a “pump”, whereby each pump is rewarded with an increasing sum of money, and participants can choose to cease pumping and “bank” this reward at any time. The participants are informed that the balloon can burst at any point and that the likelihood of a “burst” increases as they continue to pump. As such, every decision to pump the balloon is associated with an increasing degree of risk. The average number of inflations of unburst balloons over 30 trials provides an accurate estimation of the subject’s propensity towards risk-taking, which has been shown to be a strong and robust predictor of alcohol and drug use behaviours. The task takes approximately 5 minutes to complete.

3. A picture rating task designed to measure subjective desire elicited by beverage images. Participants will view 20 computerised images, 10 of alcoholic beverages and 10 of non-alcoholic beverages. Participants rate ‘wanting’ of images by marking a point along an accompanying 100 mm line with end caps either side indicating “I do not want this at all” to “I really want this”. Scores range from 0-100, based on the ‘mm’ distance between the participant’s mark and the lower end point (i.e. a score of 0 indicates no wanting at all; a score of 100 indicates maximal wanting). Within each of the two beverage categories (alcoholic; non-alcoholic), 5 of the 10 images are identical to images to be used in the training task (see below) and the other 5 are novel images not used in other study tasks. Thus, by repeating this task after the final session of training, we will therefore not only be able to measure whether the training task reduces cue-induced alcohol desire, but also whether this generalises to alcohol images that participants haven’t been trained to avoid.

Following these assessments, participants will commence either the cognitive bias modification (CBM) training task, or a sham-training version of this task, according to a randomisation sequence programmed into the laptop used for the training task.

1. In the intervention CBM task, participants will be exposed to 240 computerised images of 40 different alcoholic and 40 different non-alcoholic drinks and instructed to respond as quickly and accurately as possible with an approach or avoidance movement according to their orientation (landscape or portrait). While instructions are based on picture orientation, one orientation will contain alcoholic beverages 95% of the time (and non-alcoholic beverages 5% of the time) and will require an avoidance movement (pushing of a joystick, which decreases image size). The other orientation will contain non-alcoholic beverages 95% of the time and alcoholic beverages 5% of the time and will require an approach movement (pulling the joystick, which increases image size). The requirement to push away nearly all (95%) of alcohol images is intended to train participants to over-ride their pre-existing tendency to approach alcohol, and we hope that this will generalise to a reduced tendency to approach alcohol and its related cues following discharge from detoxification. This requirement will be reversed on 5% of trials to reduce the likelihood of participants being unblinded to the nature of the training. In each session, the 240 training trials will be preceded by 8 practice trials in which participants will be asked to respond to blank

rectangles (4 in landscape orientation and 4 in portrait orientation) to familiarise participants with (or remind them of) the task demands. In both practice and training trials, a red 'X' will be displayed if a participant makes an incorrect response, and they will be unable to proceed to the next trial until they respond correctly.

2. In the control sham-training task, 150 participants will be exposed to 240 computerised images 40 different alcoholic and 40 different non-alcoholic drinks and instructed to respond as quickly and accurately as possible by using the joystick to move the images to the left or right according to their orientation (landscape or portrait). Each orientation will contain images of alcohol beverages 50% of the time and non-alcoholic beverages 50% of the time. Thus, there will be an equal frequency of requirement to move alcoholic images to the left and to the right, and neither motion expands or shrinks the images, meaning participants in this condition are not systematically trained to either approach or avoid alcoholic images, though this training is matched to the CBM task in terms of exposure to images and requirement to respond to each one. Each session will begin with 12 practice trials, as in the CBM condition. As in the CBM condition, a red 'X' will be displayed if a participant makes an incorrect response, and they will be unable to proceed to the next trial until they respond correctly.

The training will be repeated on each of the three following days, such that the participant receives four consecutive days of training. Additional baseline questionnaire measures will be administered after training on days 2 and 3. These will not be administered on day 1 to avoid the initial session being too time-consuming, burdensome, or fatiguing. On day 2, the researcher will administer excerpts from a modified version of the Lifetime Drug Use History Questionnaire (LDUH) to record past-year use of acute health service and substance withdrawal treatment services. On day 3, the researcher will administer the Severity of Alcohol Dependence Questionnaire (SADQ; Stockwell, Sitharthan, McGrath, & Lang, 1994) to assess symptoms of physical dependence on alcohol.

Immediately before and following each CBM training session, participants will complete a single-item visual analogue scale measure of the current intensity of their craving for alcohol (ranging from "not at all" to "extreme"), to allow researchers to monitor whether the task has triggered increased cravings. If participants indicate high cravings at the end of the session (i.e. marking within the quarter of the scale closest to the "extreme" end), the researcher will offer the participant the SOBER intervention guide-sheet (a mindfulness-based set of activities, such as breathing exercises, designed to reduce cravings) and will ask the participant whether they feel they are at risk of relapse and whether they would like further support from clinical staff. If necessary, the researcher will alert withdrawal unit clinical staff to provide further support. The researcher will also remind the participant of their right to withdraw from the study without any consequences for their treatment if there are any indications that the task is distressing to the participant (e.g. a high score on the post-session craving measure or signs of tearfulness or agitation). If such signs of distress are severe or sustained, or if the participant expresses fears that they are highly likely to relapse due to uncontrollable cravings or distress, the researcher will terminate the session and seek immediate support from clinical staff. The researcher must document any time that additional support is sought from clinical staff, regardless of whether the participant withdraws from the study or not.

If a session must be terminated due to distress, the researcher will discuss with clinical staff the following day to check whether the participant still qualifies as not meeting exclusion criterion 3 ("acutely unwell, as judged by clinical staff"). If clinical staff feel the participant now meets this exclusion criterion, they will be withdrawn from the study. Otherwise, the

researcher will approach the participant to discuss whether they would like to continue with the study, while reminding them of their right to withdraw from the study without any consequences for their treatment.

Following the final training session, the ACQ-SF-R and BSCQ will be re-administered, as will the alcohol-AAT, BART, and picture rating tasks to measure possible changes in alcohol cravings, approach bias, impulsivity, and cue reactivity, respectively. All participants will also be asked to provide contact details to be used for follow-up assessments. To minimise loss to follow-up, we will request that the participant provide multiple points of contact (e.g. family, friends, agencies involved in ongoing treatment) in addition to the participants' contact details, if they are willing to do so. Participants' treatment agency, family and friends will only be contacted if participants are un-contactable at follow-up. In addition, participants will be asked to rate the following statements on a 5-point scale (ranging from "strongly disagree" to "strongly agree"): "I found the task improved my attention"; "I found the task decreased my craving for alcohol", and "I found the task interesting". At the conclusion of these assessments the participant will be given a \$30 supermarket voucher.

A researcher will also collect medication information (i.e. medications prescribed at admission and discharge, and doses of medications administered on each day of inpatient treatment), date of admission, and date of discharge from the participant's clinical notes. Demographic and clinical information in the participant's medical record will also be collected to confirm the participant's self-report, including: date of birth, country of birth, Aboriginal or Torres Strait Islander status, gender, education level, relationship status, employment status, housing status, substance dependence and psychiatric diagnoses, age of onset of alcohol use, presence of family history of substance use disorder, and history of brain injury or mental disability. Identifying information will be removed from any copies made of clinical notes, and replaced with the participant's assigned number to maintain participants' anonymity. All computerised information collected from participants will be stored on a password protected computer. Paper documents will be stored in a locked filing cabinet at the detoxification unit during until a participant is discharged, and these documents will then be moved to a locked filing cabinet at Turning Point following the participant's discharge. Locator forms, which contain identifiable information, will be stored in a separate locked filing cabinet to that used to store de-identified paper records and a Microsoft Excel file summarising re-identification information will be protected with a password different to that used to access the drives containing de-identified data.

A researcher will contact the participant to administer the TLFB, ACQ-SF-R, and LDUH two weeks, three months, six months and 12 months post-discharge. At the 2-week follow-up, the TLFB will only measure substance use during the time since discharge while, at further follow-ups, it will measure the previous 30 days. To index basic relapse-relevant information in periods missed by the TLFB at the 3-, 6-, and 12-month follow-ups (e.g. 3-5 months after discharge at the 6-month follow-up), participants who had still maintained continuous abstinence at the previous follow-up will be asked additional brief questions assessing whether they consumed any alcohol since the previous follow-up and, if so, the date of the first consumption of alcohol, whether they drank on more than 3 consecutive days at any time and, if so, the date of the first consumption of alcohol exceeding 3 consecutive days. For each follow-up that the participant completes, they will be sent a \$10 supermarket voucher by post.

Data analysis:

The primary endpoint is abstinence/relapse assessed at two-weeks post discharge. In the ITT analysis of the primary endpoint, the divisor for the proportion of abstinent participants in an arm will be the number randomized to that arm and individuals not assessed, for any reason, at 2 weeks will be deemed to have relapsed. These proportions will be compared using a two-sample binomial test (two-sided $\alpha=0.05$) and a 95% confidence interval for the difference in the proportions will also be reported. In a supportive analysis of the primary endpoint, participants who complete fewer than 4 training sessions or who miss the 2-week assessment, will be excluded from the denominator (and the numerator) when the proportion of abstinent patients is calculated in each arm. This “per-protocol” analysis will use the same statistical methods as the ITT analysis. Follow-up assessments at each of 3, 6 and 12 months will also be analysed in the same way as the ITT analysis of the primary (2-week) endpoint. In a supplementary analysis of all available assessments (from 2-weeks to 12-months) a logistic regression analysis, using the method of generalized estimating equations (GEE), will be used to compare the arms, and changes over time in the arms, adjusting, if need be, for sites. Additional exploratory analyses will also investigate adjusting the estimated difference between the arms for such covariates as pre-admission drinking days, mean drinks per drinking day and severity of alcohol dependence score. Full details will be given in the statistical analysis plan (SAP) that will be documented prior to the first analysis of the primary endpoint.

Logistic regression analyses (GEE method) will also be used to investigate the moderating effect of baseline approach bias score by including baseline scores as covariates in the model and testing the significance of all two-way interactions, as well as the three-way interaction, of treatment arm, time and the covariate. A similar approach will be used to test for a moderating effect of impulsivity, as measured by the BART. To determine the economic feasibility of CBM, in terms of savings to the treatment system (evidenced by fewer repeat inpatient detoxifications and episodes of acute health service use at the 12-month follow-up), we will compare net spending (cost of CBM intervention + cost of further detoxification/acute health service use for each participant) in the CBM group to net spending (cost of further detoxification/acute health service use) in the control group. The statistical significance of the difference between the groups will be assessed with a t-test and a variance-stabilising transformation, such as the logarithm, will likely be required. For cue-induced wanting, outcomes will be assessed with a repeated measures ANOVA assessing within-subjects variables of ‘time’ (pre-training/post-training), ‘picture-type’ (alcohol/non-alcohol), and ‘novelty’ (used in training/not used in training), with the between-subjects conditions of ‘group’ (CBM/Control). This will be followed up by separately testing effects of time, picture, type, and group at each level of novelty, i.e. conducting separate analyses for those images that were used in training and for those images that weren’t, to examine generalisability.

Hypotheses:

We hypothesise that:

H₁ - Compared to those receiving sham training, participants receiving CBM training will show significantly higher rates of abstinence from alcohol at each follow-up.

H₂ - Stronger baseline approach bias will be associated with a larger effect of CBM (i.e., baseline approach biases will moderate CBM’s effect on abstinence).

H₃ - Significant net cost saving in the CBM group compared to controls in terms of reduced cost of repeated inpatient detoxification treatment and acute health care use during the year

following discharge (after accounting for the costs of implementing CBM training in the CBM group).

H₄ - Compared to those receiving sham training, participants receiving CBM training will show significantly reduced cue-induced desire to alcohol images (but not to images of non-alcoholic beverages). We expect that this interaction will remain, with similar effect size, when analyses are restricted to images not included in the training task, demonstrating generalisation of reduced cue-induced desire beyond the specific stimuli that participants were trained to avoid.

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Data management plan and statistical analysis plan

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Data management

There are two types of data generated in this study: questionnaire data collected on paper, and data automatically generated as computer files based on participants' performance of computerised tasks and tests. Assuming proper functioning of computer equipment, the latter form of data will be error-free and will merely need to be extracted from individual task files and organised into a spreadsheet according to participant and time point to allow analyses. Questionnaire data that has been collected in paper form and entered later, however, may be subject to data entry errors. Therefore, prior to conducting analyses of these data, a careful process of data cleaning and verification will be required for these questionnaire data. This process will proceed in the following order, and will be conducted on the whole sample, prior to any unblinding:

1. Conduct range/content checks on all fields. This can be achieved by producing and examining frequency reports for each variable (where relevant – i.e. not applicable to “notes” variables containing explanatory text) to confirm the following:
 - a. Where data should be restricted to a specific numerical range (e.g. a questionnaire item with a restricted number of answer options), ensure that the minimum and maximum values are actually within this range. Correct any errors by referring to the paper records of the questionnaires.
 - b. Where data has been entered as words (e.g. medication names, some categorical variables), ensure consistent terminology, spelling, and capitalisation is used so these can be automatically converted to numerical variables without omission or error.
 - c. For variables with no specific upper or lower limit (e.g. alcohol standard drinks; diazepam doses), produce box-and-whisker plots and double-check extreme outliers against paper records, as extreme values are more likely to reflect data entry errors. For timeline follow-back (TLFB), calculate standard drinks per drinking day (divide total number of standard drinks and drinking days) and double-check any extreme outliers to ensure that number of drinking days and total number of standard drinks are correct in these cases.
 - d. Check that all medications (in both TLFB variables and in admission information variables derived from medication charts) are correctly categorised (e.g. antipsychotics not classified as antidepressants, etc.)
2. Conduct order checks for pairs/groups of variables in which the value of one conditions the possible values of the other(s):
 - a. For admission, recruitment, session, discharge, and follow-up dates, check to ensure they are:

- i. Within the actual recruitment/follow-up period (e.g. year hasn't been entered incorrectly).
 - ii. In the correct order (e.g. recruitment date is after admission date, discharge date is on or after final session date, etc.)
 - iii. Ensure that we've noted (in the "general notes" field) anyone who had 2 sessions on one day or had sessions spread out over more than 4 days.
 - b. Check age of first drink and age when alcohol became a problem to ensure former is not a higher number than the latter (i.e. you can't develop an alcohol problem until after you've first tried alcohol), and that both are lower than the participant's current age.
 - c. In TLFB, check that time to lapse/relapse is not longer than time to follow-up. If both lapse and relapse are present, ensure relapse is at least 2 days after lapse.
- 3. Check for consistency between fields that are paired by skip patterns or conditionality, or for which there should be consistency between pairs of variables:
 - a. Check site designation against participant code to ensure it's correct.
 - b. Check if the number of sessions commenced matches the number of sessions that are dated.
 - c. For fields detailing medications administered in detox:
 - i. Does data entered in "yes/no" fields correspond with subsequent fields?
 - ii. Do the number of days for which there's data on medications that were administered (i.e. where a zero or positive numerical figure is entered, rather than "n.a.") match the length of the admission?
 - d. Check if years of completed education match the text field describing education.
 - e. Ensure that, if "first detox episode" question is answered 'no', the number of prior detoxes >0; if "first detox episode" is answered 'yes', number of prior detoxes =0. Also, ensure that if number of prior detoxes =0, that the baseline service use section also lists 0 detox admissions.
 - f. Check for consistency between the "any other drugs of concern" variable and whether other drugs of concern are listed, and check that ranking of alcohol within drugs of concern matches its place in the list.
 - g. Check for consistency between presence of family history of substance use disorder (yes/no) and the content of the neighbouring text field.

- h. Check for consistency between presence of psychiatric disorder (yes/no) and content of following fields describing specific psychiatric disorders.
- i. Check for consistency between presence of neurological issues (yes/no) and the content of the following descriptive text field.
- j. Check whether the number of specific SCID criteria labelled “yes” corresponds to the numerical variable detailing total number of criteria met, and that the severity classification matches the number of criteria.
- k. Check if “yes/no” entries regarding use of medications in TLFB are consistent with subsequent info (i.e. “no” or “missing” followed by “n.a.” for remaining fields; “yes” followed by relevant information).
- l. For alcohol use at follow-ups: check for discrepancies between days of use and number of standard drinks (e.g. if one is ‘0’, other should be ‘0’ as well; if one is >0, other should be >0 as well).
- m. Check for discrepancies between presence of lapse/relapse and presence of alcohol use. At 2-week follow-up, if there is any lapse there should also be alcohol use, and if any relapse, at least 3 days alcohol use, while absence of lapse should correspond to 0 days use. At later follow-ups, prior lapse/relapse does not obviate the possibility of 0 days use in past 30 days, but absence of lapse is inconsistent with any alcohol use.
- n. Check that lapse and relapse times, when registered at one follow-up, are then entered as the same values for subsequent follow-up fields.
- o. Is there a reasonable correspondence between number of days tobacco use and number of cigarettes? Double-check TLFBs of any entries where number of cigarettes per day would be less than 1 or more than 30.
- p. Are the number of days using illicit drugs consistent with the subsequent descriptive text field (i.e. “no” followed by “n.a.”; “yes” followed by drug use information consistent with number of days of use).
- q. In service use sections, is there consistency between “yes/no” items, number of times using that service, and any subsequent fields describing specific service use episodes?
- r. For service use at 3-, 6-, and 12-month follow-ups:
 - i. Where there are no previous follow-ups, are fields related to previous follow-ups entered as “n.a.”?
 - ii. If participant was currently in a relevant service at the previous follow-up, is this correctly registered?

- iii. If participant is still in same admission (rehab or hospital inpatient) that they were in during the previous follow-up, is this simply noted as “yes” and further fields related to new admissions all just entered as “n.a.”?
 - s. In session craving ratings variables, check if there is consistency between “session referral for support” “yes/no” answer and subsequent text field.
 - t. Are session craving ratings entered for the same number of sessions as the participant completed?
- 4. Examine content in text fields (e.g. highest educational attainment, employment status, other classes of medications, other drugs, clinical notes) and discuss whether we want to create further categorical variables data based on these.

Data verification:

Following completion of data cleaning steps detailed above, the rate of remaining data entry errors will be assessed to test the accuracy of the data. For each field, a random selection of 10% of entries will be selected, and a separate spreadsheet will be created with only these values included (the “verification sample sheet”). These values will also be re-entered into a 3rd spreadsheet (the “re-entry sheet”, and excel will be used to detect discrepancies between the verification sample sheet and the re-entry sheet. Where discrepancies are detected, a researcher will examine the paper record and classify the discrepancy as either:

- Non-errors, where the original entry was correct, and the re-entry was incorrect or differed in a trivial way. (Trivial non-error differences only apply to some fields, e.g. non-categorical text fields where a slightly different wording was entered on re-entry, but conveyed essentially the same meaning).
- Non-trivial errors: errors in original entry that are genuinely incorrect
- Trivial errors (only applies to very restricted group of fields: number of standard drinks; Brief Situational Confidence Questionnaire (BSCQ) items; time to relapse or duration of treatment only where these are based on vague notes regarding participant self-report; and session craving ratings): a numerical difference of less than 5% that may be due to ambiguity in participant’s self-report and/or methods of calculation (e.g. calculation of standard drinks when it is unclear which specific brand or type of beverage the participant referred to; where assumptions were made to infer duration of treatment based on participant’s vague memory of timing of events), or minor measurement errors (calculating BSCQ and session cravings based on ruler measurements).

Detected errors (both trivial and non-trivial) will be corrected. For each field, rates of non-trivial errors will be calculated. For any field with a non-trivial error rate of more than 2%, complete double entry of that field will be conducted.

Decisions about including data:

Following data verification, decisions will need to be made regarding possible exclusion of certain data before proceeding to analyses. This must be done before analysis or unblinding, so decisions are not biased by knowing what results may be lost or gained by excluding data. This will be overseen by a 3-person committee composed of John Reynolds, Joshua Garfield, and Antonio Verdejo-Garcia, who will adjudicate grey-area cases and set exclusion parameters where necessary:

1. Some measures may be invalidated by performance issues in some individual participants (e.g. inattention to task demands; impatiently responding in a manner not consistent with task goals or questionnaire content, such as rushing through a questionnaire without reading it properly to speed up completion). These issues may affect computerised assessment tasks (the VAS picture rating task, BART, and AAT) and some self-administered questionnaires (particularly ACQ and BSCQ). These measures will be examined for outliers (multivariate in the case of VAS, ACQ, and BSCQ, using Mahalanobis distance; univariate outliers for AAT and BART) or for clusters of scores that sit outside the main distribution (e.g. multi-modal distributions involving clusters of scores suspiciously separate from the rest). Criteria for exclusion of data for each measure will be set based on examination of the degree of deviation, according to these indices, that appears to correspond to “suspect” patterns of responding, or to session notes documenting researchers’ impression that a participant was not “honestly” engaging in the task.
2. For per-protocol analysis (restricted to those who completed 4 sessions), there will be a need to define what protocol deviations can be tolerated for inclusion. Regarding timing of sessions, if sessions are spread out over more than 4 days (e.g. if there was a 2-day gap between the 3rd and 4th session), this will be considered acceptable, as long as 4 sessions are completed during the same withdrawal admission. If sessions are spread over less than 4 days (e.g. if both a morning and an evening session were run on the same day to allow a participant to complete 4 sessions before discharge, following a decision to discharge earlier than originally expected), this will also be considered acceptable as long as there is no more than 1 day on which this occurs, and no more than 2 sessions run on that 1 day. In cases where sessions were interrupted by technical problems or external events, participants will be considered to have completed 4 sessions if they commenced at least 4 separate sessions, and the total number of trials completed over these sessions was at least 816 (i.e. 85% of the 960 trials one would complete in four 240-trial sessions).
3. Following application of these steps, session notes for each measure will be reviewed for any other data validity issues raised and the aforementioned committee will decide on these, with each decision clearly documented.

Data management of computerised measures

BART, VAS, and AAT data will be examined for outliers. For BART and VAS data, outliers will be identified at the individual level (univariate outlier for BART and multivariate for VAS), and criteria for exclusion of data will be set, if applicable, prior to unblinding. For the AAT, outliers will be

examined both at the level of trials (to decide on criteria for exclusion of individual trials for being too fast or slow) and at the participant level (univariate for each of the 4 categories of pictures). For the AAT, participant data will be excluded from analyses if less than 75% of first responses to trials are correct and within the acceptable latency window (to be decided following examination of trial reaction time outliers) to eliminate those who are likely not attending well to task demands.

Statistical analysis plan (SAP)

Changes from the protocol

The protocol to which this SAP relates (version 4, dated August 1, 2017) states that we will conduct the primary outcome analysis on an intention-to-treat (ITT) basis, treating all participants who were randomised as having received their assigned condition, regardless of any deviation from, or failure to complete, the protocol following randomisation. It is necessary to clarify this further in this SAP, because an audit of the participant allocations conducted between September 19-24, 2018 (at which point 184 participants had been recruited) detected discrepancies between the executed allocations and the randomisation sequences programmed into the laptops being used to deliver the intervention. As noted in the protocol, the laptops were programmed so that, upon entering the participant number at the start of the intervention, the intervention programme would automatically assign the participant to the CBM or control condition according to the pre-programmed sequence. However, our audit comparing “as executed” participant allocations indicated in task files (containing stimulus and performance data, automatically generated after participants complete a session) in September 2018 discovered that 12 participants who, according to the pre-programmed randomisation sequence should have received the CBM condition, appeared to have received the control condition.

Further testing of the computer programme and examination of task files confirmed that the programme had malfunctioned for all 12 of these participants and delivered the control condition for all of these participants’ training sessions. We considered that the possibility of this type of software error was highly specific to the situation in which there were 2 different versions of the intervention, both of which were accessed through opening the same programme, and selected randomly according to the participant number, without any intervention by a clinician or researcher (other than typing in the participant number). We therefore concluded that this specific type of error would be extremely unlikely if the intervention were demonstrated to be effective and adopted in routine clinical practice, since there would be no reason to include a demonstrably-inferior “sham” version of the intervention in computer programmes used to deliver it, and even if multiple versions of the programme were present, selection of the appropriate version would presumably be performed deliberately by a clinician, rather than automatically according to a randomisation sequence. Thus, we decided it would be more scientifically valid, and more consistent with the spirit and intention of the ITT approach, to conduct the primary analyses using a modified ITT (mITT) approach in which we considered participants to belong to the condition they actually received (i.e. “as executed” by the computer), rather than the condition which they were supposed to be allocated to, according to the originally-generated randomisation sequence.

Definitions and general considerations

Time windows: 2-week follow-ups will not be conducted less than 14 days post-discharge. If a 2-week follow-up is accidentally conducted less than 14 days after discharge, and an outcome of abstinence is found, this will not be considered a valid observation. Typically, 2-week follow-ups are

pursued until it has been 30 days since discharge, but in rare cases participants who have failed to complete the follow-up within this period have then contacted the researcher later (before the 3-month follow-up is due), allowing the follow up to be completed even later. Thus, any follow-up completed within 60 days of discharge will be considered a 2-week follow-up. Regardless of how late the 2-week follow-up is conducted, however, the primary outcome (abstinence during the first 2 weeks after discharge) will use only the data from the first 14 days of the time-line follow-back, so that a standard interval of time is assessed for every participant for this outcome. Other outcomes will be measured at the time the follow-up is conducted. Where 2-week follow-ups are missed, but a later follow-up is completed, questions regarding presence and timing of lapses to alcohol consumption since discharge are asked, and where the participant is able to report this information with sufficient clarity to determine whether or not a lapse occurred in the first 14 days post-discharge, this information will be used as data for the primary outcome.

Attempts to contact a participant for the 3, 6, and 12 month follow-ups will occur 3-4, 6-8, and 12-16 months following discharge, respectively. Any follow-up conducted 61-150 days post-discharge will be considered a 3-month follow-up. A follow-up conducted 151-300 days post-discharge will be considered a 6-month follow-up. A follow-up conducted 301-550 days post-discharge will be considered a 12-month follow-up.

There will be 2 analysis sets for outcome analyses: the modified intention-to-treat (mITT) set and the per-protocol set. The mITT set will include all participants who were allocated to a condition (i.e. who at least commenced the first session of training). The per-protocol set will include only those participants who commenced at least 4 sessions, completed at least 816 trials of training, and for whom there was no more than 1 day on which 2 sessions were run on the same day.

Addressing missing items in multi-item questionnaires:

- ACQ-SF-R: This is a 12-item scale with four 3-item subscales. Total scores for the scale and its subscales are the mean of the single items (after reverse-scoring of items 3, 8, and 11). Personal communication from the author of this scale suggested that when items are missing, they use the mean of the non-missing items as the total score (i.e. essentially imputing the mean of the non-missing items as the score for the missing item), but provided no guidance on the maximum acceptable number of missing items. In this study, we will only calculate subscale scores if at least 2 of the 3 items are non-missing, and will only calculate total score for the scale if at least 8 of the 12 items are non-missing. Otherwise, total (sub)scale scores will be considered missing.
- SADQ: Personal communication from the author of the scale suggested that the whole scale score should only be calculated if there are responses recorded for at least 18 of the 20 items, but suggested no method for imputing missing items if 1 or 2 items were missing. Where only 1 or 2 items are missing, linear regression, with the non-missing items entered as predictors, will be used to generate predicted scores for the missing item (based on the scores of participants for whom the relevant item was not missing). The predicted score will be rounded to the nearest whole number between 0-3 before calculating a total score for the scale.

- BSCQ: Scores on this scale will be calculated based on the mean score of the 8 items. In addition, two 3-item affect-based subscales will be calculated: a “negative affect” subscale consisting of items 1, 2, and 6; and a “pleasant/social affect” subscale consisting of items 3, 7, and 8. Whole scale scores will not be calculated unless at least 6 items are non-missing, and affect subscale scores will not be calculated unless at least 2 items are non-missing. Where items are missing, linear regression, using all non-missing items in the measure, will be used to generate predicted scores for missing items (based on the scores of participants for whom the relevant item was not missing), which will then be used to calculate scale scores.

Addressing missing data:

We anticipate that rates of missing data for reasons other than failure to complete follow-ups will be low, and analyses involving moderators/covariates will be run using complete case analyses (i.e. without imputation of covariates, moderators, or outcomes).

Statistical analysis of main outcome:

The primary outcome is abstinence during the first 14 days post-discharge, assessed at the first follow-up. In the mITT analysis of the primary endpoint, the divisor for the proportion of abstinent participants in an arm will be the number randomised to that arm and individuals for whom alcohol use during the first 14 days post-discharge was not assessed, for any reason, will be deemed to not be abstinent. These proportions will be compared using a two-sample binomial test (two-sided $\alpha=0.05$) and a 95% confidence interval for the difference in the proportions will also be reported. The Cochran-Mantel-Haenszel Test, stratified by site, will be conducted as a supportive analysis. In a further supportive analysis of the primary endpoint, participants who complete fewer than 4 training sessions or who miss the 2-week assessment, will be excluded from the denominator (and the numerator) when the proportion of abstinent patients is calculated in each arm. This “per-protocol” analysis will use the same statistical methods as the mITT analysis. The moderating effect of baseline approach bias score on abstinence/relapse in the two weeks post discharge (i.e. the primary outcome) will be investigated by logistic regression models that include baseline scores as covariates in the model and tests of the significance of the two-way interaction of treatment arm with the covariate will be conducted. A similar approach will be used to test for a moderating effect of impulsivity, as measured by the BART.

Statistical analysis of secondary outcomes:

Assessments of abstinence in the 30 days prior to each of the 3, 6 and 12 month follow-ups will also be analysed in the same way as the mITT analysis of the primary (2-week) endpoint – participants not assessed for any reason will be deemed to not be abstinent. In a supplementary analysis of all available follow-up assessments (from 3 to 12-months), that assumes any missing follow-ups are missing completely at random, a logistic regression analysis, using the method of generalized

estimating equations (GEE), will be used to compare the arms, and changes over time in the arms, adjusting, if need be, for sites. An additional supplementary, missing not at random (MNAR), analysis will use a Bayesian approach, and Markov chain Monte Carlo (MCMC) to jointly model abstinence and missingness. The model will include a random effect for each participant and minimally-informative, normal prior distributions for parameters in the logistic models for abstinence and missingness. Parameter estimates and their associated 95% credible intervals, based on posterior distributions, will be reported. The MNAR approach will also be used to investigate the moderating effect of the baseline approach bias score. Additional exploratory analyses, also using the MNAR approach, will investigate adjusting the estimated difference between the arms for such covariates as age, gender, and severity of alcohol dependence score.

Continuous-scale outcome measures, and ordinal scale outcomes that have 5 or more ordered categories, will be analysed using mixed models, and the restricted maximum likelihood (REML) method, with random effects for participants and assessments within participant, and fixed effects for treatment arm, time and baseline covariates. Diagnostic plots of residuals will be examined and, if required, analyses will be conducted using a variance-stabilising transformation such as the log transformation or the empirical logit transformation.

To determine the economic feasibility of CBM, in terms of savings to the treatment system (evidenced by fewer repeat inpatient detoxifications and episodes of acute health service use at the 12-month follow-up), summary statistics for the whole 12-month follow-up period will be calculated from service use data collected at each follow-up (e.g. number of emergency department admissions at each follow-up will be summed to produce a total for the entire follow-up period, etc.), and costs of this treatment will be estimated. We will compare net spending (cost of CBM intervention + cost of further detoxification/acute health service use for each participant) in the CBM group to net spending (cost of further detoxification/acute health service use) in the control group. Since not all participants will complete their 12-month follow-up exactly 365 days following discharge, cost estimates will be converted according to the formula " $365 \times (\text{cost}/d)$ ", where "d" is the number of days between discharge and the final follow-up, to standardise cost estimates to a 365 day period. Using this formula will also allow inclusion of data from participants who complete the 3- and/or 6-month follow-up, but who fail to complete a 12-month follow-up, with "d" meaning the number of days between discharge and the final follow-up in these cases. However, these cases will be weighted in analyses (weighting = 0.25 or 0.5 if the final follow-up was the 3-month or 6-month, respectively) to reflect the fact that cost data were generated from a substantially shorter period of time and therefore may be less reliable. Data from participants who only completed the 2-week follow-up will not be included in these analyses. The statistical significance of the difference between the groups in estimated costs will be assessed with a t-test and a variance-stabilising transformation, such as the logarithm, will likely be required.

For cue-induced wanting, outcomes will be assessed with a repeated measures ANOVA assessing within-subjects variables of 'time' (pre-training/post-training), 'picture-type' (alcohol/non-alcohol), and 'novelty' (used in training/not used in training), with the between-subjects conditions of 'group' (CBM/Control). This will be followed up by separately testing effects of time, picture, type, and group at each level of novelty, i.e. conducting separate analyses for those images that were used in training and for those images that weren't, to examine generalisability.

Additional exploratory analyses:

To explore cross-sectional associations between approach bias and other measures relevant to alcohol cravings and dependence severity, we will use linear regression modelling to test whether baseline approach bias is predicted by measures including ACQ-SF-R, BSCQ, single-item VAS craving ratings, SADQ, number of previous withdrawal admissions, age of onset of alcohol problems, mean standard drinkers per drinking day, BART score. These analyses will utilise baseline data collected before randomisation, and thus use the whole sample. These analyses will also inform selection of measures to use in further potential exploratory analyses, which may include:

- Testing the hypothesis that BSCQ scores should increase following CBM training, and exploring whether any increase is specific to items measuring ability to resist drinking in response to pleasant vs. unpleasant affect, or to item 5 which is related to urges and cravings rather than affective situations. To this end, a repeated-measures analysis of variance will be conducted with time (pre vs. post-training) as the within-subjects independent variable and group (CBM vs. control) as the between-groups variable, testing BSCQ scores averaged across all items. To explore whether any such effects are specific to “pleasant” or “unpleasant” items, or item 5, this analysis will be separately conducted on the 2 affective subscales and item 5. In addition we propose to use structural equation modelling to test whether post-training BSCQ score mediates the effect of CBM on abstinence after discharge, and whether any such mediation effect is moderated by pre-training BSCQ score.
- Testing the hypothesis that CBM training should cause reduced ACQ-SF-R scores. For post-training ACQ-SF-R scores, this will be conducted using repeated-measures analysis of variance (RMANOVA) with time (pre vs. post-training) as the within-subjects independent variable and group (CBM vs. control) as the between-groups variable, testing ACQ-SF-R scores averaged across all items. Further exploratory analysis will test whether CBM’s impacts are specific to certain ACQ-SF-R subscales by testing ACQ subscales separately. In addition we propose to test whether CBM’s impact on likelihood of relapse is mediated by change in ACQ-SF-R scores, using a similar structural equation modelling approach as mentioned above for the BSCQ. ACQ-SF-R scores at follow-ups will also be analysed using RMANOVA with time (2-week, 3-month, 6-month, 12-month) as the within-subjects variable and group as the between-groups variable (adjusting for time to follow-up if necessary, as there will be some variability in the interval between discharge and follow-up, which may also affect craving scores). This analysis will be conducted separately from the analysis of scores collected during the detoxification admission because the different method of collection (self-administered using a visually-presented Likert scale in detox vs. interviewer-administered using a numerical scale at follow-up) may alter the psychometric properties of this scale.
- Testing whether declines in approach bias mediate the effects of CBM on alcohol use, using structural equation modelling.

In addition we also intend to explore other operationalisations of the alcohol use outcome, as well as other minor secondary outcomes including:

- Testing the hypothesis that CBM may reduce alcohol consumption at follow-ups among non-abstainers, using continuous measures (i.e. proportion of days measured by the TLFB on which there was alcohol consumption; average number of standard drinks per day). For each post-discharge time-point, non-abstinent participants will be included in a RMANOVA analysis with time (baseline vs. follow-up) as the within-subjects factor and group as the between-subjects factor.
- Testing the hypothesis that CBM delays time to first lapse (defined as number of days between discharge and first use of any alcohol) and relapse (defined as first time alcohol is consumed for 3 consecutive days). This will be conducted using Kaplan-Meier analysis or, if other variables are found to moderate the effect of CBM on abstinence, these variables, and their interaction with group, will be entered into Cox regression analysis.
- The single-item craving visual analogue scale (VAS) ratings will be explored with a 2 (group; between-groups) x 4 (day; within-subject) x 2 (pre/post-session; within-subject) repeated measures ANOVA to test the hypotheses that:
 - o Cravings tend to decrease over the 4 sessions (main effect of day).
 - o Cravings tend to increase between the pre-session and post-session ratings during the earlier sessions, but the degree of this within-session increase decreases over the course of the 4 sessions of training (2-way interaction between day and pre/post timing).
 - o CBM training is associated with a greater decrease in cravings over the 4 sessions (2-way interaction between group and day), and with a reduced tendency for there to be increases in cravings between pre- and post-session ratings (2-way interaction between group and pre/post timing; also possibly a 3-way interaction if CBM leads to a more marked tendency for within-session increases in craving to be reduced/reversed over the 4 days of training).
- Exploratory analysis of whether participants' task ratings differ by group, particularly to test the hypothesis that participants in the CBM group will tend to agree more strongly than those in the control group that the task reduced their cravings. For the purpose of this analysis, responses will be recoded as: "strongly disagree" = 1; "disagree" = 2; "unsure" = 3; "agree" = 4; "strongly agree" = 5, and this variable will then be analysed with a t-test.
- If sufficient participants who have drugs of concern other than alcohol are present in the dataset, we will explore the hypothesis that CBM's reduction of alcohol use will have flow-on effects of reducing use of other drugs of concern as well, using the same analytical methods as proposed for analyses of post-discharge alcohol consumption.
- To examine whether the effects of CBM depend on other participant characteristics, we intend to examine whether other factors moderate the effects of CBM, including demographic variables (e.g. age, sex); clinical treatment-related characteristics (e.g. number

of previous acute withdrawal treatment episodes; use of certain classes of psychiatric and anti-craving medications; engagement in further treatment following discharge, presence of certain psychiatric diagnoses; indicators of craving and dependence severity such as ACQ and SADQ scores; presence of other drugs of concern).

- We will examine whether abstinence at the first follow-up (2 weeks) mediates any effect of CBM on abstinence at later follow-ups (3, 6, and 12 months) to test whether avoiding early lapse is vital for any ongoing benefit from CBM, or whether people continue to benefit from CBM at later times even despite earlier lapses.
- Finally, we will explore, using structural equation modelling, whether engagement in further supportive AOD treatment following discharge (e.g. AOD counselling or rehab) mediates the effect of CBM on alcohol use, considering the possibility that CBM may facilitate post-discharge treatment engagement by reducing cravings or preventing relapse long enough for them to commence other treatments, and this post-discharge treatment may then confer additional benefits.

Table 1. Demographic and clinical characteristics of the sample at baseline

	Whole sample (N=)	Control group (n=)	CBM group (n=)
Age (mean, SD)			
Gender (% male)			
Born in Australia (%)			
Aboriginal or Torres Strait Islander (%)			
Years of completed education (mean, SD)			
Currently employed (%)			
Current unstable housing (%)			
Age at which alcohol use became problematic (mean, SD)			
Any previous acute withdrawal episodes (%)			
Current drugs of concern other than alcohol and tobacco (%)			
Current daily tobacco smoker (%)			
Substance use disorder in first degree relatives (%)			
Current psychiatric diagnosis (%)			
Number of SCID criteria met (mean, SD)			
SADQ score (mean, SD)			
Number of days alcohol consumption in 30 days prior to admission (mean, SD)			
Number of standard drinks consumed in 30 days prior to admission (mean, SD)			
Number of CBM sessions commenced (mean, SD)			

CBM: cognitive bias modification; SADQ: severity of alcohol dependence questionnaire; SCID: structured clinical interview for the DSM-5; SD: standard deviation;

Table 2. Percentage follow-up rates and reasons for loss to follow-up

	control group	CBM group	χ^2	p
2-week				
completed				
withdrawn/declined				
imprisoned				
deceased				
failed to contact or complete/unknown				
3-month				
completed				
withdrawn/declined				
imprisoned				
deceased				
failed to contact or complete/unknown				
6-month				
completed				
withdrawn/declined				
imprisoned				
deceased				
failed to contact or complete/unknown				
12-month				
completed				
withdrawn/declined				
imprisoned				
deceased				
failed to contact or complete/unknown				

Table 3. Logistic regression model testing the moderating effect of baseline approach bias on the effect of CBM on abstinence during the 2 weeks following discharge.

Predictor	beta	p	Exp(B)	95% CI
group				
approach bias				
approach bias * group				

Table 4. Logistic regression model testing the moderating effect of baseline BART score on the effect of CBM on abstinence during the 2 weeks following discharge.

Predictor	beta	p	Exp(B)	95% CI
group				
BART score				
BART * group				

Proposed figures:

1. Proportion of participants in each group reporting abstinence during the first 14 days following discharge (simple 2-bar graph with one bar for each group, y axis showing percentage).
2. Proportion of participants reporting abstinence at 3, 6, and 12-month follow-ups (line graph with separate line for each group, x axis showing time, and y axis showing percentage)
3. Survival curves for lapse/relapse outcome (graph displaying results of Kaplan-Meier/Cox regression analyses, with one curve for each group, time displayed on the x axis, and proportion not yet having (re)lapsed since discharge displayed on the y axis; may be 2 graphs if there is a good reason to show analyses for both 'lapse' and 'relapse' outcomes, or we may just choose to display the most illustrative outcome if results are very similar).
4. Cost to health system in the year following discharge (simple 2-bar graph with one bar for each group, y axis showing cost).
5. Changes in picture-induced 'wanting' ratings (2 separate panels, one for each group, each panel containing 4 lines (familiar alcohol pictures, novel alcohol pictures, familiar non-alcohol pictures, novel non-alcohol pictures), x axis shows time (before vs after training), while y axis shows mean rating.
6. Change in ACQ-SF-R scores between pre- and post-training assessments. (Line graph with separate lines for each group and 2 time-points on the x axis and cravings core on the y axis. If there are significant differences between subscales, or an interaction involving subscale and group, a supplementary 4-panel version of this graph may be produced with separate panels for each subscale.)
7. ACQ-SF-R scores at follow-ups. (Line graph with separate lines for each group, 4 time points on the x axis corresponding to the 4 follow-ups, and mean ACQ-SF-R score displayed on the y axis). If relevant, a supplementary 4-panel version of this graph will be produced showing each subscale of the ACQ-SF-R separately.)
8. BSCQ scores before and after training. (Line graph – depending on results it will either display just 2 lines (one for each group) or 4 lines (broken down by group and subscale). The x axis will display the 2 time points (before vs. after training) and the Y axis will show mean BSCQ score.)
9. Approach bias before and after training. (Line graph with separate lines for each group, with pre- and post-training time-points indicated on the x axis and approach bias score indicated on the y axis.
10. Single-item craving visual analogue scale ratings. (Composite line graph with 4 consecutive pairs of lines arranged horizontally, separate lines for each group. Thus, there will be 8 points on the x axis (session 1 pre-training; session 1 post-training; session 2 pre-training; ...), but only the pre- and post-training points for each session will be connected with a line, i.e. no line connecting the post-training score to the pre-training score of the next session. The y axis will display the mean VAS craving rating.)

11. Participants' ratings of the training task. (3 pairs of pie charts, one pair for each of the 3 ratings, and one chart for each group within each pair, showing the proportion of participants who "strongly agree", "agree", "unsure", "disagree", and "strongly disagree" with each