RESEARCH REPORT

ADDICTION   SSA

Alcohol use in the year following approach bias modification during inpatient withdrawal: secondary outcomes from a double-blind, multi-site randomized controlled trial

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Abstract

Background and aims: Approach bias modification (ApBM) targeting alcohol approach bias has been previously shown to reduce likelihood of relapse during the first 2 weeks following inpatient withdrawal treatment (IWT). We tested whether ApBM's effects endure for a longer period by analysing alcohol use outcomes 3, 6 and 12 months post-discharge.

Design: A double-blind, sham-controlled randomized controlled trial.

Setting: Four IWT units in Melbourne, Australia.

Participants: Three hundred alcohol IWT patients (173 men, 126 women, 1 non-binary; mean age 43.5 years) were recruited between 4 June 2017 and 14 July 2019. Follow-up data collection was completed on 22 September 2020.

Intervention and control training: Four ApBM sessions were delivered during IWT. ApBM trained participants ($n = 147$) to avoid alcohol and approach non-alcohol beverage cues. Controls ($n = 153$) responded to the same stimuli, but without approach/avoidance training.

Measurements: Date of first lapse was recorded for non-abstinent participants to determine time to first lapse. Time-line follow-back interviews assessed past-month alcohol consumption at each follow-up, with participants reporting no alcohol consumption classified as abstinent. In analyses of past-month abstinence, non-abstinence was assumed in participants lost to follow-up. Number of past-month drinking days, standard drinks and heavy drinking days (five or more standard drinks for women or non-binary; six or more standard drinks for men) were calculated for non-abstinent participants at each follow-up.

Findings: ApBM significantly delayed time to first lapse [ApBM median: 53 days, 95% confidence interval (CI) = 21–61; controls = 12 days, 95% CI = 9–21, $P = 0.045$]. Past-month abstinence rates at 3-, 6- and 12-month follow-ups were 33/153 (21.6%), 30/153 (19.6%), and 24/153 (15.7%) in controls; and 51/147 (34.7%), 30/147 (20.4%) and 29/147 (19.7%) in the ApBM group, respectively. Past-month abstinence was significantly more likely in ApBM participants than controls at the 3-month follow-up [odds ratio (OR) = 1.93, 95% CI = 1.16–3.23, $P = 0.012$], but not at 6- or 12-month follow-ups

(6-month OR = 1.05, 95% CI = 0.60–1.95, P = 0.862; 12-month OR = 1.32, 95% CI = 0.73–2.40, P = 0.360). No significant group differences were found for indices of alcohol consumption in non-abstinent participants.

Conclusions: Approach bias modification for alcohol delivered during inpatient withdrawal treatment helps to prevent relapse, increasing rates of abstinence from alcohol for at least 3 months post-discharge.

KEYWORDS

Alcohol, alcohol use disorder, approach bias modification, cognitive bias modification, detoxification, relapse, withdrawal treatment

INTRODUCTION

Cognitive bias modification targeting approach bias, known as approach bias modification (ApBM), is a computerized training intervention that aims to reduce alcohol approach bias (i.e. a behavioural inclination to approach, rather than avoid, alcohol-associated stimuli) [1]. Multiple RCTs have shown that four to 12 ApBM sessions delivered during residential rehabilitation treatment for alcohol use disorder (AUD) significantly reduces rates of relapse by 8–13%, relative to sham-training or no-training control groups, at 12-month follow-up [2–5]. In a pilot RCT of ApBM delivered during inpatient withdrawal treatment (IWT), those who received the per-protocol four sessions of training had a significantly (30%) lower rate of relapse 2 weeks post discharge relative to sham-training controls [6]. These findings were recently replicated in a double-blind, multi-site RCT with 300 inpatients, where four sessions of ApBM reduced approach bias to alcohol cues and reduced rates of early relapse (defined as any drinking in the first 2 weeks post-discharge—primary outcome) by 12% (17% with per-protocol analysis), relative to sham-training controls [7].

However, the longer-term efficacy of ApBM delivered during IWT (i.e. beyond the initial 2 weeks post-discharge) and its comparability to effects when delivered during residential rehabilitation at 1-year follow-up has yet to be established. The previous ApBM trials have only assessed alcohol use outcomes at a single end-point (12 months post training in the residential rehabilitation-based studies; 2 weeks post training in studies conducted during IWT). As such, it is unclear if the strength of ApBM's relapse-prevention effects change over time, e.g. if some patients may benefit in the initial weeks or months following ApBM but relapse before the 12-month follow-up. Another limitation of these prior studies is their assessment of single, binary (abstinence/relapse) alcohol consumption outcomes, overlooking other drinking behaviours that may be altered by ApBM. In recognizing that recovery rarely has a linear trajectory and is characterized by set-backs and intermittent periods of use ('slips, lapses or relapses'), the inclusion of outcomes other than abstinence in treatment trials is being increasingly endorsed [8]. Indeed, understanding if ApBM affects these other drinking outcomes is important, given that many of those seeking treatment for AUD wish to reduce or control their use rather than stop drinking entirely [9].

To address these knowledge gaps, this report examines longer-term alcohol use outcomes from our multi-site RCT examining ApBM during alcohol IWT (the primary 2-week outcome has been previously reported [7] and noted above). These include time to first lapse (using survival analysis for the first time in the ApBM literature); rates of abstinence at later follow-ups (3, 6 and 12 months post-discharge); and other alcohol consumption outcomes among non-abstinent participants, including quantity of drinking (standard drinks), frequency of drinking (drinking days) and number of heavy drinking days.

METHOD

Trial design and study setting

The study used a double-blind, sham-controlled, parallel-group randomized clinical trial design with a 1:1 allocation ratio. Recruitment occurred at four alcohol and other drug IWT units in Melbourne, Australia. Training was delivered adjunctive to treatment as usual, which typically lasted approximately 1 week [mean of 7.3, standard deviation (SD) = 2.6 days among trial participants] and included pharmacological management of withdrawal symptoms, group therapeutic activities and referral to post-withdrawal psychosocial and/or pharmacological treatment as appropriate.

Participants

Three hundred alcohol IWT patients were randomized between 4 June 2017 and 14 July 2019 (with follow-ups completed on 22 September 2020). Inclusion criteria were: aged 18–65 years; meeting DSM-5 criteria for moderate or severe AUD; and at least 5 days' alcohol use in the 30 days prior to IWT admission. Exclusion criteria were: a diagnosed history of neurological illness, injury or concussion resulting in loss of consciousness exceeding 30 minutes; intellectual disability; or too mentally or physically impaired to provide informed consent or safely participate. Sample size calculation is detailed in the protocol report [10] and recruitment was ended following randomization of 300 participants based on this calculation.

Outcome measures

At each follow-up, participants were asked if they had consumed any alcohol since the previous follow-up (or since discharge if no previous

follow-up had been completed) and, if so, when they first consumed alcohol, to determine time to first lapse. The time-line follow-back (TLFB) interview method was used to quantify number of days of alcohol use and estimated standard drinks consumed [11] in the 30 days preceding inpatient admission at baseline and the 30 days prior to each of the follow-up interviews.

Interventions

ApBM condition

The ApBM training task has been described in detail previously [7, 10]. To summarize, participants were instructed to respond to images by pushing or pulling a joystick, based on the orientation of the 'frame' displayed around the image (pushing if landscape; pulling if portrait). The image shrank or expanded in response to push or pull joystick motions, respectively, to simulate 'avoidance' and 'approach'. Forty images of alcoholic and 40 images of non-alcoholic beverages were presented three times each (i.e. 240 total image presentations per session) in a random order; 95% of landscape-orientated frames contained alcoholic images. The remaining 5% of landscape-orientated presentations contained non-alcoholic images. Conversely, 95% of portrait-orientated images contained non-alcoholic images, and 5% contained alcohol-related images. As participants were required to 'push away' (avoid) images with landscape-orientated frames and 'pull' (approach) images with portrait-orientated frames, this meant that participants pushed away 95% of alcoholic images (and approached 95% of non-alcoholic images), implicitly training an avoidance response to alcohol.

Sham control condition

Sham training was identical to the ApBM training, except that each orientation (portrait or landscape) contained alcohol images in 50% of trials and non-alcohol images the other 50% of trials. Moreover, instead of instructing participants to respond with approach or avoidance movements, participants were instructed to respond with lateral movements of the joystick, according to picture orientation (left for landscape; right for portrait), causing the image to move to the left or right edge of the computer screen without changing size. The sham condition thereby controlled for participants' exposure to alcohol (and non-alcohol) images, and for the demand to attend to image orientation and to manipulate the image with a joystick based on orientation, without including the approach/avoidance component hypothesized to underlie the therapeutic effect of ApBM.

Randomization

Prior to commencing recruitment, a researcher not involved in recruitment or data collection generated site-specific randomization sequences using a random number generator, based on permuted

blocks of variable size. The allocation sequence for each site was incorporated into the training task programme on that site's task laptop, such that opening the programme and entering the participant number caused the programme to load the allocated training task. Researchers administering the intervention did not have access to the randomization sequences, so were unaware of the participant's assignment prior to commencement of the first session of training.

Procedure

Detailed description of the procedure can be found in the protocol [10] and on the Australian New Zealand Clinical Trials Registry (ANZCTR; registration number ACTRN12617001241325; registered 25 August 2017). Intake clinicians at participating sites conducted preliminary screening of patients at the time of admission. Those eligible and interested in trial participation met with a researcher, typically on the third day of IWT. If consent to participate was provided, baseline questionnaires confirming eligibility and assessing demographic and clinical characteristics were completed, followed by the first session of ApBM. Subsequent training sessions occurred over the next 3 days (i.e. 4 consecutive days of training in total, one session per day). A researcher not involved in administering the participant's training (and therefore blinded to their treatment allocation) conducted 3-, 6- and 12-month telephone follow-ups. Three-, 6- and 12-month follow-ups were conducted 83–129 (mean = 97.2) days, 179–278 (mean = 190.4) days and 361–488 (mean = 377.5) days post-discharge, respectively. T-tests showed that time to follow-up did not differ significantly between groups at any follow-up (all $P > 0.227$). Following intention-to-treat (ITT) principles, follow-ups were pursued with any participant who commenced training, regardless of whether or not they completed the four-session training protocol, and regardless of whether they had missed previous follow-ups, unless they withdrew consent to participate. Participants were given $30 (Australian dollars) supermarket gift cards for completing training and $10 gift cards for each follow-up they completed. This study was approved by the St Vincent's Hospital Melbourne Human Research Ethics Committee (HREC; reference number 030/17) and the Monash University HREC (project number 8447).

Statistical analysis

Analyses were conducted in SAS version 9.4 and SPSS version 27. Distributions of times to first lapse were estimated using the Kaplan–Meier product–limit method and groups were compared using the log-rank test (PROC LIFETEST in SAS version 9.4). Time to first lapse was coded as 0 days if the participant drank alcohol on the day of discharge, 1 day if they first drank alcohol on the day following discharge, etc. Time to first lapse was censored for participants who were continuously abstinent at the time of their final follow-up. Participants who completed no follow-ups were censored on day 0.

Odds of participants reporting past-month abstinence (i.e. no alcohol consumption in the past 30 days) at each time point analysed

(3-, 6- and 12-month follow-ups) were compared between groups using logistic regression. In analyses of past-month abstinence, participants who were lost to follow-up for any reason were assumed to have consumed alcohol, in accordance with an assumption that this outcome was missing not at random. Additional analyses of rates of continuous abstinence since discharge (i.e. no alcohol use at any point between completing withdrawal treatment and follow-up) are reported in Supporting Information.

Additional drinking outcomes among participants who were not past-month abstinent were analysed at each of the 3-, 6- and 12-month follow-ups. These included number of days on which alcohol was consumed in the past 30 days; total standard drinks consumed in the past 30 days; and number of 'heavy drinking days' (defined as consumption of at least five standard drinks in a day for women (or non-binary) or at least six standard drinks in a day for men—note that in Australia a standard drink is defined as 10 g (i.e. 12.7 ml) of pure ethanol). These variables were compared between groups using t-tests. These analyses only used data from participants who completed the follow-up being analysed (i.e. data were not imputed for participants lost to follow-up).

All participants who commenced at least one session of ApBM were included in the primary ITT analysis. We also conducted secondary 'per-protocol' analyses including only those participants who completed four training sessions, which are reported in Supporting Information. Additional, secondary sensitivity analyses are included in the Supporting Information which adjust for the number of previous withdrawal treatment episodes and whether participants had additional drugs of concern aside from alcohol and tobacco. Survival analysis of time to first lapse, analyses of past-month abstinence and analyses of past-month drinking days and standard drinks in non-abstinent participants were pre-registered in a statistical analysis plan (SAP) that was attached to the trial registration on ANZCTR on 6 February 2019, prior to completion of recruitment. Additional outcomes analysed herein (past-month heavy drinking days) or in supporting information (continuous abstinence since discharge at follow-ups)) were not included in the SAP and should be regarded as exploratory.

RESULTS

Sample characteristics and follow-ups

Numbers of patients screened, recruited, randomized and providing data at each follow-up are shown in Figure 1. Demographic and clinical characteristics of the sample are shown in Table 1. Participants' first day of ApBM/sham training was typically 3 days after admission (whole sample: mean = 3.0 days post-admission, SD = 0.9; controls: mean = 3.0, SD = 0.9; ApBM: mean = 3.0, SD = 0.8).

Survival analysis of time to first lapse

Estimated percentages of participants maintaining continuous abstinence, as a function of time since discharge, are shown in Figure 2.

While approximately one-third of participants in both groups lapsed within the first week following discharge, the groups then diverged, with the ApBM group maintaining a notably higher continuous abstinence rate than controls for several months afterwards. In Figure 2, this difference between groups is most visually apparent approximately 1–2 months following discharge, with groups' rates of continuous abstinence appearing to re-converge approximately 4–5 months post-discharge. Kaplan–Meier analysis confirmed a significant difference between groups (log-rank test $\chi^2 = 4.03$, $P = 0.045$). Time taken for 25%, 50% and 75% of the control group to lapse was 3 [95% confidence interval (CI) = 1–4], 12 (95% CI = 9–21) and 76 (95% CI = 50–134) days, respectively, while for the ApBM group, these values were 3 (95% CI = 2–5), 53 (95% CI = 21–61) and 127 (95% CI = 84–176). As such, median time to first lapse was more than four times as long in the ApBM group compared to the control group. The effect of group remained significant in per-protocol and adjusted sensitivity analyses described in the Supporting Information.

Past-month abstinence

Proportions of participants abstinent from alcohol at each follow-up are shown in Table 2. The rate of past-month abstinence was significantly (13.1%) higher in the ApBM group than controls at the 3-month follow-up. Between-group differences were non-significant at later (6- and 12-month) follow-ups, although abstinence rates remained slightly higher in the ApBM group, relative to controls, at both time-points. This general pattern (significant effect of group at 3-month follow-up, but not 6- or 12-month follow-ups) remained in per protocol (OR = 2.17) and adjusted sensitivity analyses (OR = 1.94) (see Supporting Information). Rates of continuous abstinence since discharge at each follow-up are shown in the Supporting Information and did not reveal significant between-group differences.

Alcohol use in participants who were not abstinent at each follow-up

Mean number of drinking days, standard drinks and heavy drinking days among participants who were not abstinent for the past month at each follow-up are shown in Table 3. While values of these variables were substantially lower than at baseline, there were no significant differences between groups at any follow-up. Per-protocol and adjusted sensitivity analyses also did not reveal significant effects of group for these outcomes (see Supporting Information).

Differences between participants completing follow-ups and those lost to follow-up

To test potential sources of bias in outcome measurement, we compared participants who completed follow-ups and those who did not
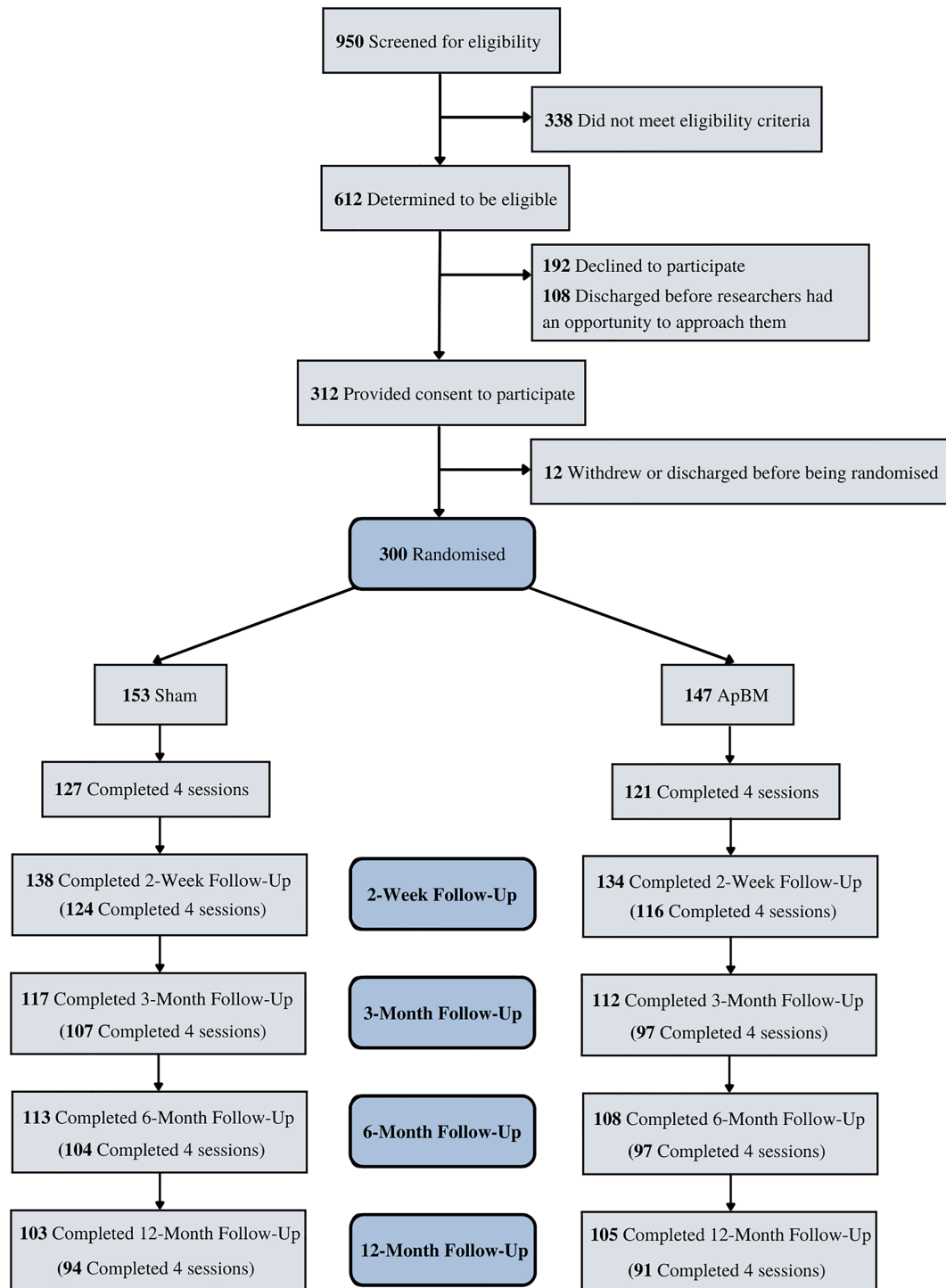
FIGURE 1   Number of patients screened, recruited, randomized and completing each follow-up

in terms of baseline demographic and clinical variables, as well as allocated group, at each follow-up. Variables tested included age, gender, age at which alcohol use became problematic, any previous withdrawal treatment episodes, current daily tobacco use, presence of additional drugs of concern other than alcohol or tobacco, number of days alcohol use in the 30 days prior to IWT admission, number of

standard drinks consumed in the 30 days prior to IWT admission and allocated group. The only significant differences detected were that completers were significantly older at the 3-month (completers mean = 44.3, SD = 10.1 years; non-completers mean = 40.7, SD = 11.0 years; $t_{(298)} = -2.56$, $P = 0.011$), 6-month (completers mean = 44.3, SD = 10.1 years; non-completers mean = 41.1,

TABLE 1 Participants' demographic, clinical and treatment characteristics

	Total sample (n = 300)	Controls (n = 153)	ApBM group (n = 147)
Age, mean (SD)	43.5 (10.4)	42.3 (10.7)	44.7 (10.1)
Gender			
Men, n (%)	173 (57.7)	97 (63.4)	76 (51.7)
Women, n (%)	126 (42.0)	55 (36.0)	71 (48.3)
Non-binary, n (%)	1 (0.3)	1 (0.6)	0
Born in Australia, n (%)	252 (84.0)	122 (79.7)	130 (88.4)
Aboriginal or Torres Strait Islander, n (%)	18 (6.0)	8 (5.2)	10 (6.8)
Age at which alcohol use first became problematic, mean (SD)	26.3 (10.6)	26.3 (10.9)	26.2 (10.2)
Number of DSM-5 AUD criteria met, mean (SD)	9.7 (1.4)	9.6 (1.4)	9.8 (1.4)
SADQ score, mean (SD)	32.2 (11.7)	32.0 (11.5)	32.4 (11.9)
Number of days alcohol use in 30 days prior to admission, mean (SD)	27.3 (5.0)	27.1 (5.2)	27.5 (4.7)
Number of standard drinks[a] consumed in 30 days prior to admission, mean (SD)	589.5 (344.9)	588.4 (343.2)	590.6 (347.9)
Number of heavy drinking days[b] in 30 days prior to admission, mean (SD)	26.5 (6.0)	26.2 (6.5)	26.8 (5.3)
Any previous withdrawal treatment episodes, n (%)	201 (67.0)	110 (71.9)	91 (61.9)
Number of previous withdrawal treatment episodes, mean (SD)	2.7 (4.1)	2.4 (3.6)	3.0 (4.6)
Current daily tobacco smoker, n (%)	215 (71.7)	111 (72.5)	104 (70.7)
Current drugs of concern other than alcohol and tobacco, n (%)	64 (21.3)	26 (23.5)	28 (19.1)
Current psychiatric diagnosis, n (%)	227 (75.7)	114 (74.5)	113 (76.9)
Benzodiazepines administered during IWT, n (%)	293 (97.7)	150 (98.0)	143 (97.3)
Anti-craving medications[c] administered during IWT, n (%)	148 (49.3)	75 (49.0)	73 (49.7)
Days spent in IWT, mean (SD)	7.3 (2.6)	7.3 (2.1)	7.4 (3.1)

ApBM, approach bias modification; AUD, alcohol use disorder; DSM-5, Diagnostic and Statistical Manual of Mental Disorders; IWT, inpatient withdrawal treatment; SADQ, Severity of Alcohol Dependence Questionnaire; SD, standard deviation.

[a]In Australia, a standard drink is defined at 10 g of pure ethanol.
[b]Heavy drinking days were defined as six or more standard drinks for men or five or more standard drinks for women and non-binary participants.
[c]Medication classified as anti-craving medications included acamprosate, naltrexone, baclofen and disulfiram.

SD = 11.2 years; $t_{(298)} = -2.34$, $P = 0.020$) and 12-month follow-ups (completers mean = 44.5, SD = 10.1 years; non-completers mean = 41.2, SD = 10.9 years; $t_{(298)} = -2.53$, $P = 0.012$).

DISCUSSION

The findings of this double-blind RCT demonstrate for the first time that four sessions of ApBM significantly delays the time to first drink among ApBM participants during the initial months post-discharge, extending median time to first lapse until day 53 (relative to day 12 in controls). Although visual examination of survival curves suggested some convergence in continuous abstinence rates after several months, past-month abstinence rates were still 13% higher among participants who received ApBM than among sham-trained controls

3 months after discharge from IWT. The finding that the effects of ApBM were detectable at least 3 months post-discharge is particularly encouraging in light of the brevity (totalling just 1 hour of training during detoxification), low cost and simplicity of the intervention. As ApBM was shown to significantly reduce alcohol approach bias in our earlier report on this trial's primary outcome [7] it is possible that automatic responses to alcohol cues, which are ubiquitous in the community in countries such as Australia, remain diminished for at least several months. Reducing vulnerability to cue-induced relapse during this post-discharge period may also facilitate participants' uptake and engagement in psychosocial and pharmacological treatments that can improve long-term outcomes [12–14].

However, in contrast to studies where ApBM was administered during longer-term residential rehabilitation treatment after withdrawal was completed [2–5], which found significant effects on
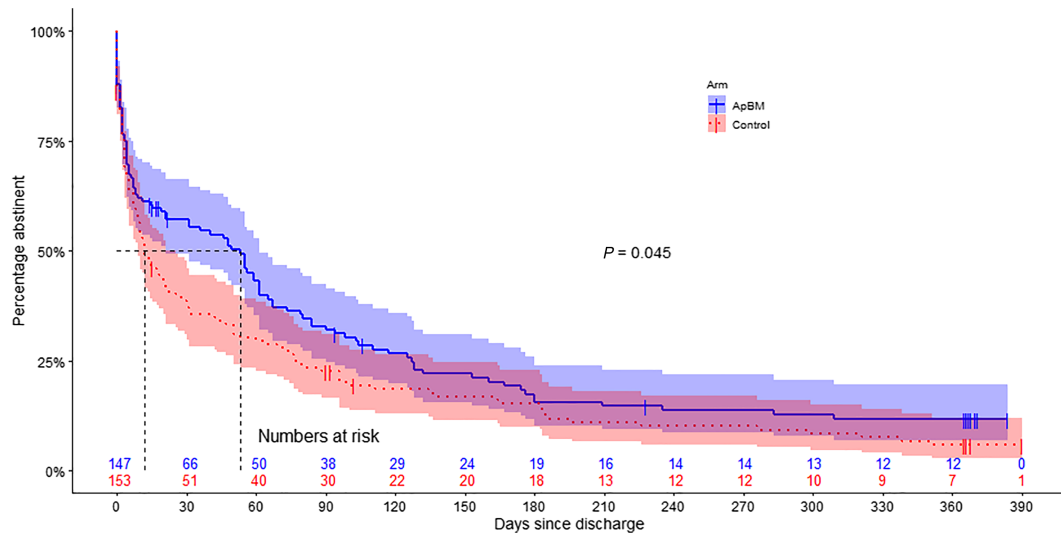
FIGURE 2 Percentage of participants in each group maintaining continuous abstinence since discharge as a function of days since discharge. Shading shows 95% confidence intervals. Vertical bars on the Kaplan–Meier curves indicate abstinent participants censored at their last assessment date. Dotted lines show time taken for 50% of participants in each group to lapse

TABLE 2 Numbers and percentages of participants abstinent for the past 30 days at each follow-up

Time	Control (n = 153)	ApBM (n = 147)	OR	95% CI of OR	P
3-month, n (%, 95% CI)	33 (21.6, 15.3–28.9)	51 (34.7, 27.0–43.0)	1.93	1.16–3.23	0.012*
6-month, n (%, 95% CI)	30 (19.6, 13.6–26.8)	30 (20.4, 14.2–27.8)	1.05	0.60–1.85	0.862
12-month, n (%, 95% CI)	24 (15.7, 10.3–22.4)	29 (19.7, 13.6–27.1)	1.32	0.73–2.40	0.360

ApBM, approach bias modification; CI, confidence interval; OR, odds ratio.
*P < 0.05.

TABLE 3 Alcohol use outcomes among participants who were not abstinent at each follow-up

Time	Drinking outcome	Control, mean (SD)	ApBM, mean (SD)	t	P
3-month	Drinking days	16.9 (11.0)	17.1 (10.9)	−0.09	0.929
	Standard drinks	220.3 (195.8)	229.6 (245.2)	−0.25	0.805
	Heavy drinking days	13.9 (11.0)	14.4 (11.6)	−0.24	0.809
6-month	Drinking days	17.1 (11.1)	17.8 (11.4)	−0.40	0.689
	Standard drinks	221.8 (215.9)	243.1 (253.1)	−0.57	0.571
	Heavy drinking days	13.8 (11.8)	15.9 (12.5)	−1.04	0.299
12-month	Drinking days	18.3 (10.3)	19.2 (11.2)	−0.51	0.611
	Standard drinks	216.6 (195.3)	247.0 (230.8)	−0.89	0.376
	Heavy drinking days	14.5 (11.4)	15.8 (12.9)	−0.65	0.518

ApBM, approach bias modification; SD, standard deviation.

abstinence rates a year after discharge, we found no significant differences between groups in rates of abstinence at 6- and 12-month follow-ups. This suggests that the durability of ApBM's effects may be lower when delivered in a more acute treatment setting and/or with a shorter and more compressed training schedule. Alternatively, the differences between our findings and those of studies based in rehabilitation settings may reflect differences in patient populations. With regard to other drinking outcomes (quantity and frequency of use) in non-abstinent participants, no significant group differences were found. This suggests that while ApBM had efficacy in preventing

or delaying the first drink following withdrawal treatment, once drinking had recommenced it had little or no effect on the quantity or frequency of consumption. One potential explanation for this is that drinking may reinstate approach bias that was present prior to ApBM, overriding expression of the avoidance bias learned during ApBM. This would be analogous to the drug-induced reinstatement of drug-seeking that has been reported following extinction of conditioned responding for drugs demonstrated in animal models of addiction [15–17]. Indeed, in an experimental study examining approach bias to smoking cues in tobacco smokers before and after smoking a cigarette, smoking caused an immediate increase in tobacco approach bias, relative to participants who were denied the opportunity to smoke between the two approach bias assessments, despite craving being reduced following smoking [18]. The reinstatement of alcohol approach bias following resumption of alcohol use may be further facilitated by contextual cues such as the social and physical environments where alcohol is obtained and consumed.

It is possible that the short-term relapse prevention effects of ApBM during IWT could be extended with further/booster ApBM sessions post-discharge. While repeated visits to treatment services to undertake training sessions may be impractical, there are remotely accessible ApBM formats, including online training, where drinking has been found to reduce following ApBM (although not to a greater extent than among sham-trained controls) [19]. Alternatively, smartphone-delivered ApBM has recently been explored in two uncontrolled single arm studies, with both demonstrating positive (and similar) findings in terms of significant reductions in drinking [20, 21]. Importantly, smartphone ApBM could allow patients to engage in post-discharge ApBM in multiple, naturalistic contexts, including those where alcohol could be consumed, which could reduce the potential for reinstatement/renewal effects.

Limitations of the study included all outcomes being assessed using self-report, although the TLFB interview method is considered a valid measure of recent substance use under conditions in which it was administered (i.e. by a researcher independent of the treatment team and with confidentiality ensured) [22, 23]. Another limitation is attrition, which reached 31% of participants by the 12-month follow-up, although this rate is typical of outcomes studies of this population [2, 24]. This could reduce precision of the findings as well as potentially biasing them, particularly since younger participants had a higher rate of attrition than older participants. However, at no time-point did rates of attrition differ significantly between groups, nor were there any other significant demographic or clinical characteristic differences, aside from age, between follow-up completers and those lost to follow-up. Finally, while we sought to maintain blinding by using a control condition which included the same stimuli and very similar task demands, we did not formally assess participants' blinding at follow-up. Although participants gave very similar post-intervention ratings of the two conditions in terms of how interesting the training was and how much they felt it affected their craving and attention (see Supporting Information in Manning *et al.* [7]), suggesting minimal subjective difference between the tasks, we did not explicitly ask them to which condition they believed they had been randomized. We therefore cannot rule out the possibility that placebo/expectancy effects resulting from blinding failure influenced our findings.

Despite these limitations, the trial has multiple strengths that have been absent in previous ApBM trials, including multiple outcomes assessed at multiple time-points. These findings provide increased clarity on the durability of ApBM relapse prevention effects following IWT, and suggest it tends to be strongest during the first few months following discharge and wanes over time. These outcomes add to our confidence that ApBM is a valuable relapse prevention tool when added to residential treatment, including inpatient withdrawal. Future research should examine the value of post-discharge booster sessions of ApBM as part of outpatient management following IWT to extend the durability of ApBM's effect.

CLINICAL TRIAL REGISTRATION

This trial was registered in the Australian New Zealand Clinical Trials Registry (ANZCTR; trial registration number ACTRN12617001241325) on 25 August 2017. Registration was completed 82 days after commencing recruitment (4 June 2017) and we had recruited 58 participants (19% of the eventual total sample of 300) by this time. No 3-, 6- or 12-month follow-ups had been completed, and we had not examined any data collected or conducted any interim/preliminary analyses at the time of registration.

DECLARATION OF INTERESTS

V.M. and H.P. are founders, directors and shareholders of Cognitive Training Solutions Pty Ltd, which recently began commercializing the 'SWiPE' smartphone application, which offers approach bias modification. D.I.L. has provided consultancy advice to Lundbeck and Indivior outside the submitted work; has received travel support and speaker honoraria from AstraZeneca, Camurus, Indivior, Janssen,

Lundbeck, Shire and Servier outside the submitted work; and has been an investigator on an untied education grant from Sequirus unrelated to the current work. J.R. has received grants from AbbVie outside the submitted work, being a former employee of Novartis AG (2009–2012), and holding shares in Novartis AG and ALCON. A.V.-G. has received personal fees from Servier and Elsevier outside the submitted work, and is part of the Scientific Advisory Board of Monclarity/Brainwell, which produces cognitive training games (but does not receive any honorarium for this role). M.L.-J. has received speaking honoraria from Indivior outside the submitted work. Y.B. has provided consultancy advice to Indivior and AbbVie outside the submitted work. She has been an investigator on a clinical trial for Zelira Therapeutics unrelated to the current work. No other authors have any conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.