Protocol scientific title: The AAT-App outpatient trial: A randomised controlled trial of a novel approach bias modification smartphone application to reduce alcohol use and craving among clients accessing outpatient treatment for alcohol use disorder

Public title: AAT-App Trial: A clinical trial of a "brain-training" smartphone app to help reduce alcohol use in people accessing outpatient alcohol treatment

Version 2

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Countries of recruitment: Australia

Composition, roles, and responsibilities of trial governance bodies

Coordinating Principal Investigator (CPI): Victoria Manning, who is also the principal investigator (PI) for Turning Point, Eastern Health. Responsibilities include convening the steering committee and supervising the coordinating centre, and ensuring the responsibilities of these bodies (as detailed below) are carried out.

Steering Committee: Comprised of Victoria Manning; the PIs of each other site (David Jacka for Monash Health Drug and Alcohol Service, Peter Matthews for Odyssey House Victoria, Yvonne Bonomo for Saint Vincent's Hospital Melbourne Department of Addiction Medicine, Silvia Violante for Star Health, and Shannon Bell for Uniting Vic Tas Alcohol and Other Drug Services); and the project manager, Joshua Garfield. Responsibilities include general oversight of the trial, including approval of the protocol, monitoring of recruitment, and decision-making regarding publication, dissemination, and implementation of findings.

Coordinating centre: Comprised of Victoria Manning, Joshua Garfield, and Hugh Piercy. Responsibilities include: correspondence with ethics and governance committees, trial registration, recruitment and contacting participants, data collection and management, and ensuring analyses are conducted.

Other roles: Samuel Campbell is responsible for generating randomisation sequences. Ellie McSheedy will be provided with randomisation sequences to facilitate planning of qualitative interviews.

Background

Alcohol is a leading cause of injury, chronic disease and mortality, contributing to 3 million deaths each year, and accounting for 5.1% of the global burden of disease (World Health Organization, 2018). In 2020 there were 1,452 alcohol-induced deaths in Australia, an 8.3% increase in the age-standardised rate of alcohol-induced deaths since 2019 (Australian Bureau of Statistics, 2021). In Australia, approximately one in five adults have met criteria for an alcohol use disorder (AUD) during their lifetime (Slade et al., 2016). Alcohol is the most common drug of concern among people accessing publicly-funded alcohol and other drug (AOD) treatment services in Australia. In 2019-20, over 42,000 clients received over 75,000 episodes of treatment where alcohol was the primary drug of concern, with nearly 23,000 additional episodes in clients where alcohol was a secondary drug of concern (Australian Institute of Health and Welfare, 2021). Alcohol was therefore involved in 45% of all episodes of treatment delivered by publicly-funded Australian AOD services. Outpatient interventions formed the majority of the treatment provided to these clients. Excluding episodes that involved assessment only, counselling accounted for 46%, support and case management for 16%, information and education for 7%, and pharmacotherapy for 1% of all treatment episodes in which alcohol was the primary drug of concern. However, a recent large US study of people receiving outpatient psychosocial interventions for AUD found that 65% of clients experienced relapse in the year following treatment (Maisto, Hallgren, Roos, & Witkiewitz, 2018).

While there are numerous factors that may contribute to the difficulty many heavy drinkers face in avoiding relapse after ceasing heavy drinking, one important factor is likely to be strongly ingrained 'cognitive biases' that develop with repeated heavy drinking. The highly-influential incentive-sensitisation model (Robinson & Berridge, 1993) posits that, at least in some people, repeated use of

addictive drugs sensitises neural processes underlying the incentive salience of the drug. Through associative learning, stimuli associated with substance use (such as physical and social contexts, sights, sounds, scents, etc., which have often been present during drinking episodes) also gain incentive salience. This incentive salience is often equated with 'wanting' the drug, or cue-induced craving (Carter & Tiffany, 1999), but may also be reflected in less conscious 'cognitive biases', such as attention bias (the exaggerated tendency for drug-associated cues to capture attention) and approach bias (the automatic action tendency to approach drug-related cues) (Reinout Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013). Indeed, Berridge and Robinson (2016) posit that the less-conscious aspects of incentive salience may influence behaviour in the absence of conscious 'wanting', or even in the presence of conscious desire to *not* use the drug. Thus, while there is some evidence that alcohol craving and cognitive biases are associated with each other (Field, Kiernan, Eastwood, & Child, 2008; Field, Mogg, & Bradley, 2005), cognitive biases may also influence alcohol consumption even when a drinker does not consciously 'want' alcohol. In any case, craving (Schneekloth et al., 2012; Sinha et al., 2011), approach bias (Martin Braunstein, Kuerbis, Ochsner, & Morgenstern, 2016), and attention bias (Cox, Hogan, Kristian, & Race, 2002) have all been reported as predictors of alcohol use in people with AUD seeking to cease or reduce their drinking. Since alcohol-related cues are ubiquitous in Australian society, and largely unavoidable, the craving and cognitive bias that can be elicited by these cues is likely to pose a serious challenge for people seeking to reduce or cease drinking.

In addition to cognitive biases, other deleterious neural effects of heavy alcohol use are likely to exacerbate the difficulty experienced by heavy drinkers wishing to reduce their alcohol use. The neurotoxic effects of heavy alcohol consumption impair numerous cognitive functions, including the "reflective" processes responsible for decision-making, inhibition of maladaptive impulses, and long-term planning, and these deficits persist after cessation of drinking (Crowe, Cammisuli, & Stranks, 2019). This results in an "imbalance", whereby impulsive urges and cravings for alcohol (triggered by alcohol-related cues) are *strengthened*, and can more easily override the brain's *weakened* ability to inhibit these impulses in favour of more adaptive choices (Gladwin, Figner, Crone, & Wiers, 2011). Typical psychotherapeutic interventions for AUD, such as cognitive behavioural therapy (Magill et al., 2019) and motivational interviewing (Smedslund et al., 2011) aim to strengthen reflective processes, but don't necessarily have any direct impact on the less conscious cue-triggered cognitive biases. Cognitive bias therefore may remain a vulnerability to relapse long after cessation of drinking, especially when reflective processes remain impaired chronically (e.g., due to neurotoxic effects of alcohol or other brain injuries) or become impaired at a later time (e.g., during times of acute stress).

In the past 20 years, interventions have been developed which aim to reduce or reverse various types of cognitive biases, including attention bias, approach bias, and inhibitory control (Batschelet, Stein, Tschuemperlin, Soravia, & Moggi, 2020). In treatment-seeking samples, the only 'cognitive bias modification' approach with consistent evidence of efficacy is approach bias modification (ApBM). ApBM involves repeatedly presenting individuals with alcohol-related pictures to which they must make an 'avoidance' movement and non-alcoholic images to which they must make an 'approach' movement. In the major trials that have demonstrated its efficacy, this has been delivered by presenting images on a computer screen, and requiring participants to 'push' or 'pull' them using a joystick which causes the images to shrink or expand, respectively, to simulate 'avoidance' and 'approach'. Over time, individuals learn to automatically 'avoid' alcohol-related cues, with several studies demonstrating reductions in approach bias, or even its reversal (becoming an avoidance bias) after ApBM (Eberl et al., 2013; Garfield et al., 2021; R. W. Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 2011), including in patients with major neurocognitive impairment (Loijen et al., 2018). In one study, completing just six 15-minute ApBM training sessions reduced cue-induced neural activity in the amygdala in male AUD patients, and this reduction in neural activation was associated with reduced self-reported alcohol craving (C. E. Wiers et al., 2015). Importantly, several

randomised controlled trials (RCTs) have shown that, when delivered as an adjunctive intervention during residential AUD treatment, 4-12 sessions of ApBM can reduce likelihood of post-treatment relapse (Eberl et al., 2013; Manning et al., 2021; Manning et al., 2016; Rinck, Wiers, Becker, & Lindenmeyer, 2018; Salemink, Rinck, Becker, Wiers, & Lindenmeyer, 2021; R. W. Wiers et al., 2011).

Residential treatment, such as acute withdrawal management, or longer-term rehabilitation, is appropriate for people with very severe AUD. However, many people cannot access, or are unable to engage in, these highly-intensive types of treatment. Many others have an AUD which is not severe enough to warrant residential treatment, but which still poses substantial risks to health and quality of life, and can benefit from less intensive interventions. If ApBM could be shown to be feasible and effective in other settings (e.g., among people receiving outpatient treatment), it could benefit a much larger population of people with AUD. However, in non-residential settings, the 'computer-and-joystick' method of delivering ApBM may be less appropriate than it is during residential treatment. Outpatient clients may not have additional time to engage in ApBM sessions before or after appointments. Appointments may be too infrequent (e.g., weekly or fortnightly) to deliver multiple sessions of ApBM per week. AOD services might not have sufficient facilities (e.g., space in which clients can engage in ApBM sessions without distraction; computers on which to do ApBM training). Clients may not even attend these sites in person, e.g., if they are receiving treatment via telehealth.

Delivering ApBM via a smartphone app may address all these limitations, as well as allowing clients to freely access ApBM training when it is convenient for them, or when they feel it is most needed (e.g., during acute cravings). However, thus far, we are aware of only three studies examining ApBM smartphone apps for alcohol use, all of which delivered it to people recruited from the general community (i.e., not necessarily seeking treatment) who were drinking at hazardous levels. In the UK, Crane, Garnett, Michie, West and Brown (2018) tested apps containing various combinations of 5 different modules (including an ApBM module) among people drinking at hazardous levels. Despite initially reporting that combining ApBM with normative feedback reduced participants' weekly alcohol consumption (Crane et al., 2018), they later reported a lack of evidence for efficacy after re-analysing outcomes with a larger sample (Garnett, Michie, West, & Brown, 2019). In the Netherlands, Laurens et al. (2020) pilot-tested an ApBM app in people who were concerned about, or wished to reduce, their drinking. Participants were encouraged to complete at least 2 ApBM sessions per week over a 3-week period. Among those who completed the post-training questionnaire, weekly alcohol consumption declined over the 3-week intervention period by a mean of 7.2 standard drinks, and even further at a 3-month follow-up (an additional 6.2 standard drinks, or 13.4 standard drinks per week in total, relative to pre-training) (Laurens et al., 2020). Participant feedback was generally positive, though participants noted the lack of personalisation, monotony and repetitiveness of the ApBM training, and suggested that game-like features could make it more engaging.

Participants' criticisms of Laurens et al.'s (2020) app are understandable given that all participants were trained using the same standardised set of beverage images. In our research on AUD treatment-seekers (Manning et al., 2021; Manning et al., 2019; Manning et al., 2016), we have observed that participants tend to drink a limited range of beverages. Thus, when ApBM programs use a standard image set of beverages for all participants, many images may have little relevance to most individuals (e.g., being repeatedly trained to avoid images of beer may have little impact for someone who only drinks wine). Since approach bias is the product of repeated associative conditioning experiences (Stacy & Wiers, 2010), it is likely to be specific to stimuli resembling the drinks frequently consumed by an individual. Designing ApBM tasks where individuals can use their own "personalised" images is therefore likely to be more engaging (as previously suggested by others (Laurens et al., 2020; R. W. Wiers, Boffo, & Field, 2018)), as well as potentially more "potent" at reducing approach bias.

It is not only the "avoidance" stimuli that could be personalised. In almost all alcohol ApBM research to date (Crane et al., 2018; Eberl et al., 2013; Laurens et al., 2020; Manning et al., 2021; Manning et al., 2019; Manning et al., 2016; Rinck et al., 2018; Salemink et al., 2021; R. W. Wiers et al., 2011), participants have been systematically trained to approach non-alcoholic beverages. These serve as relatively neutral stimuli, well-matched to alcohol-related stimuli in terms of content, and are therefore ideal for laboratory studies examining the psychological mechanisms of ApBM. However, they are likely to be monotonous and of relatively little personal relevance to patients (Laurens et al., 2020), and thus may not be ideal for clinical application. Recently, we have begun exploring the use of images representing positive, personal goals or personally-preferred healthy sources of pleasure (e.g., images symbolising friends, family, social connection, pets, exercise, financial gain, etc.) as "approach" stimuli in ApBM training for substance use disorders (Garfield et al., 2021). This responds to recommendations that these should align with patients' goals for behavioural change or offer alternative strategies to manage cravings (Kopetz, MacPherson, Mitchell, Houston-Ludlam, & Wiers, 2017; R. Wiers, Becker, Holland, Moggi, & Lejuez, 2016; R. Wiers, Zerhouni, den Uyl, & Boffo, 2020; R. W. Wiers et al., 2018). In this way, personalised ApBM can simultaneously be used to weaken motivations to drink and reinforce positive goals, which may further increase its overall therapeutic benefit.

Following this reasoning, we recently developed the first personalised, gamified ApBM smartphone app, called "SWiPE" (Manning, Piercy, Garfield, & Lubman, 2020). In SWiPE, ApBM sessions utilise 12 images in the training (6 alcohol, 6 positive), each presented 13 times (i.e., 156 trials per session in total). However, unlike previous alcohol ApBM programmes, these images are selected by the individual app user, who is provided with the option to either use photographs stored on their phone (e.g., photographs of alcoholic drinks they wish to avoid; photographs of friends, family, pets, enjoyable activities as positive "approach" images), or to select photographs from a library of 72 alcohol and 72 positive images provided in the app. In a pre-registered (ANZCTR trial number ACTRN12620000638932) open-label feasibility study of SWiPE conducted among people recruited from the general community who scored at least 8 on the Alcohol Use Disorders Identification Test (AUDIT), indicative of hazardous drinking, we encouraged participants to complete 2 sessions of ApBM on SWiPE per week for 4 weeks (Manning et al., In press). Of the 1309 participants who commenced using SWiPE, participants completed a median of 5 sessions, with 31% completing at least the recommended 8 sessions. Participants who completed the post-training questionnaire gave positive mean ratings of the app's functionality, aesthetics, and quality on the Mobile Application Rating Scale. Importantly, there were statistically significant reductions between baseline and post-training assessments in mean past-week drinking days (reduced from 5.1 to 4.2), past-week standard drinks (32.8 to 24.7), Craving Experience Questionnaire frequency score (4.5 to 2.8) and Severity of Dependence Scale score (7.7 to 6.0). Among the 254 participants who provided an additional follow-up report of alcohol use 1 month after the post-training questionnaire, mean past-week alcohol use days and standard drinks suggested that the reductions achieved during the intervention period were maintained over the following month.

However, as this was primarily designed to be a feasibility and acceptability study, this study did not include a control group, and it is therefore unclear whether reductions in alcohol use, craving, and dependence severity) were due to completing ApBM sessions or instead due to other non-specific factors. Moreover, the sample was largely a non-treatment-seeking sample (only 9% were currently accessing formal treatment for AUD), and it is therefore unclear whether these findings would generalise to people accessing alcohol treatment. Thus, in the present project, we will conduct a randomised controlled trial of SWiPE (Re-named "AAT-App" to preserve blinding, following publicity that SWiPE has received), comparing it to a minimal version of the app which does not include ApBM training sessions, in people accessing outpatient treatment for alcohol use from AOD services in the Melbourne metropolitan region.

There is no clear consensus regarding appropriate control conditions to use in alcohol reduction app (Staiger, O'Donnell, Liknaitzky, Bush, & Milward, 2020) or ApBM research (Kakoschke, Kemps, & Tiggemann, 2018). In designing our control condition, a primary consideration was controlling for the effect of self-monitoring, since the data collection aspects of AAT-App involve regular self-report of alcohol use, and such self-monitoring behaviours may themselves assist with reducing alcohol use (Michie et al., 2012). To control for this effect, and thereby ensure that we can specifically attribute any positive effects to the inclusion of ApBM training (and not merely the effects of the data collection, which may not be present in a final version of the app that would be implemented clinically), the control version of the app includes the same self-report requirements as the ApBM version. A second consideration was ensuring blinding: if participants in the control condition know they are in a control condition, this may bias outcomes both due to expectancy effects and due to differential rates of drop-out (as participants may be less likely to remain motivated to continue participating if they know they are not receiving an intervention). If control participants were only asked to self-report weekly alcohol use, it is likely they may guess they are not in an intervention condition and, as such we have included a weekly sham-training task (which also functions as an approach bias measurement task), so that participants in both conditions can be told they are completing an "attention control" task.

Aims and Hypotheses

We aim to determine whether providing the "active" version of AAT-App (including ApBM) to people accessing outpatient alcohol treatment from AOD services, is effective, relative to a minimal version of the app which does not include ApBM training, at reducing alcohol use, cravings, and severity of dependence. We also aim to test the psychometric properties of the mobile phone approach bias measure we developed, and whether engaging in AAT-App significantly reduces approach bias, relative to the minimal control condition. We also aim to explore user experiences of AAT-App's, perceived alignment with treatment, and suggested improvements, using qualitative interviews in a subset of participants, to guide further future improvements to the app and its implementation.

We hypothesise that:

Primary outcome:

1. Participants randomised to ApBM will consume significantly fewer standard drinks per week than participants in the minimal condition, as measured using self-report 4 weeks after commencing training (post-intervention; primary endpoint), and at 1-month and 3-month follow-ups (secondary endpoints).

Secondary outcomes:

2. Participants randomised to ApBM will show significantly larger declines, compared to those in the minimal condition, in past-week frequency of alcohol craving at post-intervention and follow-up assessments (relative to baseline craving frequency), as assessed by the frequency scale of the Craving Experience Questionnaire.
3. Participants randomised to ApBM will show significantly larger declines than those in the minimal condition in Severity of Dependence Scale scores at post-intervention and follow-up assessments (relative to baseline craving frequency).
4. Participants randomised to ApBM will show significantly larger declines than those in the minimal condition in Alcohol Use Disorders Identification Test (AUDIT) scores at the 3-month follow-up (relative to baseline scores).
5. Participants randomised to ApBM will have significantly fewer past-week heavy drinking days (HDDs, defined as $\geq$ 5 standard drinks in a day) than participants in the minimal

condition, as measured using self-report at post-intervention, 1-month, and 3-month follow-ups. Past-month HDDs will also be analysed post-intervention.

6. Participants randomised to ApBM will have significantly fewer past-month drinking days (i.e., days on which any alcohol is consumed) post-intervention and at 1- and 3-month follow-ups.
7. The proportion of participants reporting complete abstinence (i.e., 0 days on which any alcohol was consumed – both past week and past month will be analysed) will be significantly higher among participants in the ApBM than among those in the minimal condition at post-intervention and follow-up assessments.
8. Participants receiving ApBM will experience larger increases than those in the minimal condition in quality of life and health (assessed with 3 Australian Treatment Outcome Profile items) at post-intervention and follow-up assessments (relative to baseline).
9. There will be a significantly greater reduction in approach bias, as measured by the alcohol approach avoidance task, in participants assigned to the ApBM condition, compared to those in the minimal condition, between baseline and post-intervention.

Methods

Design & Setting: We will conduct a double-blind, randomised, parallel-group controlled superiority trial with alcohol treatment outpatients at 6 AOD treatment services in Melbourne, Victoria. Participants will be randomised to one of 2 groups with a 1:1 allocation ratio. Both participants and researchers completing the follow-up interviews will be unaware (blinded) of the condition to which they have been randomly allocated.

Participants: We aim to recruit at least 300 participants receiving outpatient interventions for alcohol use disorder at the participating services. To be eligible, participants must, at the time of the screening interview:

- Be aged 18+
- Own an Android or iOS smartphone with an Australian mobile number
- Be currently accessing outpatient treatment for alcohol problems. (There is no requirement that alcohol be the *only* substance for which they are seeking treatment, and as such participants with multiple drugs of concern are eligible as long as alcohol is one of the drugs of concern for the current episode of treatment.)
- Have an Alcohol Use Disorders Identification Test (AUDIT) score of at least 8
- Not have been in residential rehabilitation within the past 4 weeks.
- Not have been in any form of inpatient treatment (e.g. hospital or residential withdrawal treatment) within the past week.
- Not entering inpatient/residential treatment within the next month.

The target sample size was determined based on practical considerations (likely recruitment rate, time available for recruitment), as there was little prior basis to estimate likely effect size of a personalised ApBM smartphone app in an outpatient client population. Nevertheless, a calculation conducted in GPower 3.1 suggested that the primary analysis (across 4 repeated measures) would have 90% power to detect a small time x group interaction effect size (partial eta squared of .01) with a sample of 178 participants (i.e., 59% retention at follow-ups). If recruitment proceeds quickly enough, we will aim to recruit more than 300 participants, to allow for increased statistical power in case attrition is larger than expected.

Measures:

Demographic information: Participants will be asked to enter their gender, the AOD service where they were recruited from, the date they began the current episode of treatment they are receiving from that service, and drugs of concern, in an online survey hosted on Qualtrics.

Alcohol problem severity: The Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) will be used at baseline to measure the severity of alcohol use and related problems. The AUDIT consists of 10 items, each scored 0-4, and total scores are calculated based on the sum of individual item scores. The AUDIT has shown strong evidence for internal consistency, with meta-analyses suggesting it is above 0.8 (Reinert & Allen, 2007). Test-retest reliability over 1-week to 1-month intervals has ranged from .87-.95 in several general population samples, and test-retest reliability of the dichotomous categorisation using the hazardous drinking cut-off score (8 or above) is also strong (Reinert & Allen, 2007). This cut-off score has 92% sensitivity and 94% specificity for detecting hazardous or harmful alcohol use when compared to classification obtained through structured clinical interview and examination (Saunders et al., 1993). While the AUDIT usually enquires about drinking and related problems in the past year, wording of instructions and questions will be modified to ask participants to base answers on the past 3 months so that equivalent, non-overlapping periods can be assessed at both baseline and the 3-month follow-up.

The Severity of Dependence Scale (SDS) (Gossop et al., 1995) will be used to measure severity of psychological dependence on alcohol in the past month. The SDS is a 5-item scale, with each item scored 0-3, and total scores are calculated by summing individual item scores. Since the SDS was initially developed to measure dependence on heroin, cocaine, and amphetamines, wording of some items will be slightly modified to enhance its relevance to alcohol, similar to the wording used by Gossop, Marsden, and Stewart (2002) when they validated the SDS for measuring alcohol dependence. Gossop et al. (2002) reported that this version of the SDS had high internal consistency (Chronbach's α=0.86 among substance use treatment patients who had endorsed at least one SDS item for their alcohol use) and SDS scores correlated moderately with frequency of drinking, indicating its validity.

Alcohol craving: The Craving Experience Questionnaire frequency scale (CEQ-F) (May et al., 2014) will be used to measure the frequency of alcohol cravings over the past week. This is a 10-item scale, with each item rated on a scale of 0-10. Total scores are calculated based on the mean of individual items. Items can also be broken down into 3 subscales: "intensity" (3 items), "imagery" (4 items), and "intrusiveness" (3 items). The CEQ-F has an internal consistency of .94 and intercorrelations within each sub-scale range from .63-.73 (May et al., 2014).

In addition to the CEQ, we will also utilise a single-item visual analogue scale (VAS) to measure current intensity of alcohol craving immediately before and after each ApBM and AAT session. Participants will be asked "How strongly are you craving alcohol right now?", with a line displayed below the question and a slider that they can place between ends anchored with the words "not at all" on the left end and "extremely" on the right. A participants' placement of the slider will be converted to a number ranging from 0-100 for data storage. If participants provide a score of 90 or higher on the post-test VAS (i.e., immediately after completing an ApBM or AAT session), the app will prompt users with an additional support dialogue which links users to the National Alcohol and Other Drug Hotline and Counselling Online (www.counsellingonline.org.au).

Alcohol consumption: At baseline, participants will be asked to estimate the number of days on which they consumed alcohol out of the past 28 days and the number of standard drinks consumed on each day of the past week. To do this, they will be shown a calendar chart displaying the past 4 weeks, which will first be displayed with the most recent week in this period (i.e., 1-7 days ago) highlighted. For each day in this week, they will be asked to select a number ranging from 0-80 to indicate their estimate of how many standard drinks they consumed on that day in that week. Past-

week standard drinks will therefore be calculated using the sum of values entered for each of the past 7 days, and past-week drinking days will be derived from the number of days in the past week for which the participant provided a non-zero value for standard drinks. Participants will then be shown the calendar chart with the previous week highlighted (8-14 days ago), where they will be asked to select a number ranging from 0-7 to indicate their estimate of how many days they consumed alcohol in that week. This will then be repeated with the previous week (15-21 days ago) and then the week previous to that (22-28 days ago). Baseline past-month drinking days will be calculated by summing past-week drinking days with the number of drinking days indicated for each of the 3 preceding weeks. The app will automatically prompt participants to repeat the past-week standard drinks assessment 7, 14, 21, and 28 days after they complete this baseline assessment, to provide complete standard drink and drinking days data for the intervention period. Drinking assessments at 1-month and 3-month follow-ups will be identical to the baseline assessment. The past-week drinking assessment closely resembles the computerised 7-day timeline follow-back assessment used by Simons, Wills, Emery, and Marks (2015), which showed 87% concordance with an objective transdermal measure of alcohol use in terms of drinking days.

Alcohol approach bias: At baseline and post-test, participants will be required to complete an adapted, irrelevant-feature, smartphone version of the alcohol approach-avoidance task (AAT) (R. W. Wiers, Rinck, Dictus, & van den Wildenberg, 2009). Each session of the AAT is immediately preceded and followed by the VAS craving measure. Participants in the minimal condition will also complete 3 additional sessions of the AAT at the end of week 1, week 2 and week 3 (directly after completing the weekly alcohol consumption questions at each timepoint) in order to maintain blinding.

In the AAT, participants are presented with 20 images of alcohol and 20 neutral images (e.g., stationary, office ware, road signs, kitchenware, etc.) which are presented once in a white landscape orientation picture frame, and once in a white portrait orientation frame (for a total of 80 image presentations). Images are presented one by one, in a quasi-random order (with a maximum of three consecutive images appearing in the same category or orientation), and images are fixed (i.e., there is no option to personalise/select which images are presented in the task). When the frame is in landscape orientation, the participant is required to swipe downwards (i.e., towards themself), which (if the movement is at least 40 pixels downward) causes the picture to expand, increasing to 600 x 600 pixels over a period of 500 milliseconds (ms), as if the participant has “pulled” the picture “towards” themselves. When the frame is in portrait orientation, the participant is instructed to swipe upwards (i.e., away from themself), which (if the movement is at least 40 pixels upwards) causes the picture to shrink until it disappears, which takes 500 ms, as if they have “pushed” it “away”. If the participant swipes (at least 40 pixels) in the wrong direction, a red “X” is displayed to inform them that they made an error. After the picture expands/shrinks to its maximum/minimum extent, there is a 250 ms inter-stimulus interval before presentation of the next picture.

Upon commencing the AAT, task instructions are displayed to participants, and they then complete 10 practice trials (including 5 images in portrait frames and 5 in landscape frames, in random order) to familiarise themselves with the task. Participants then respond to the 80 image presentations, and reaction time (ms) data for each image trial and its response category (alcohol-portrait, alcohol-landscape, neutral-portrait and neutral-landscape) is recorded.

AAT trials will be considered valid if the initial response (i.e., swiping up or down) is correct and the reaction time is within 300-3000ms. Median reaction times of valid trials will be calculated separately for each of the 4 picture-response categories (i.e., alcohol-portrait, alcohol-landscape, neutral-portrait, neutral-landscape), if at least 70% of trials were valid. If less than 70% of trials are valid, the median for that picture-response category will be considered missing. For each picture type (alcohol or neutral), the median reaction time for "swipe-down" responses will be subtracted

from the median reaction time for "swipe-up" responses to quantify approach bias. As the psychometric properties of an AAT delivered via smartphone have not been previously established, and prior analyses of the psychometric properties of the AAT using other modes of delivery have yielded highly variable results (Kersbergen, Woud, & Field, 2015; Rinck et al., 2018), we will conduct our own analyses of this AAT's psychometric properties (described further below).

Quality of life and health: Participants will be asked to complete 3 items adapted from the Australian Treatment Outcomes Profile (ATOP) (Ryan et al., 2014) assessing psychological health, physical health, and overall quality of life over the past 28 days. Participants will be shown questions asking:

- "This question is about your psychological health during the past 4 weeks – this includes your overall mood, anxiety, depression, or any emotions or feelings that have been troubling you. How would you rate your psychological health?"
- "This question is about your physical health. Please think in an overall way about physical health problems, symptoms or illnesses that have bothered you during the past four weeks – this includes pain, breathing, stomach, sleep, mobility problems or other physical symptoms. How would you rate your physical health?"
- "This question is about how you see your overall quality of life. Please think in an overall way about your living conditions and circumstances, your family and other relationships, work and financial aspects of your life and your overall social situation. How would you rate your quality of life?"

Each item will be rated on a scale from zero to ten, where zero is poor and ten is good. Each rating will be treated as a separate variable in analyses (i.e., no composite score will be derived from the 3 separate items). These items have shown moderate-strong concurrent validity (correlation absolute values ranging from .51-.72) with relevant gold-standard multi-instrument measures of psychological health, physical health, and quality of life (Ryan et al., 2014). Mammen et al. (2021) found that a cut-off score of 5 or below had optimal sensitivity and specificity for indicating clinically significant problems.

App acceptability: At the end of the 4-week intervention period, participants will be asked to complete the "functionality" and "aesthetics" sub-scales and the "app subjective quality" section of the user version of the Mobile Application Rating Scale (uMARS) (Stoyanov, Hides, Kavanagh, & Wilson, 2016). Additionally, participants will have the option to enter free text comments in response to 3 open-ended questions: "What did you like about this app?", "what did you not like about the app?", "any further comments about the app?". Participants will also be asked to rate the statements: "The app helped me reduce my alcohol use", "The app increased my alcohol consumption", "The app helped reduce my cravings for alcohol" and "The app increased my cravings for alcohol". Responses will be assessed using a 5-point Likert scale ranging from "strongly agree" to "strongly disagree".

Qualitative interview: After completing the 1-month follow-up, a representative subset of participants (*n*=20) who had been randomised to the active ApBM condition will be contacted by an unblinded researcher and invited to complete an approximately 30-minute semi-structured qualitative interview about their experiences using the app, its perceived alignment with their treatment, and suggestions for improvement. Interviews will be audio-recorded, and recordings will be transcribed using a trusted transcription service. Participants will be reimbursed with a $40 supermarket voucher upon completion of the interview. See Appendix 1 for the qualitative interview schedule.

Randomisation and blinding of allocation: Six computer-generated randomisation sequences (one for each recruitment site) will be produced by a data scientist who is not otherwise involved in recruitment or data collection, processing, or analysis, using a 1:1 allocation ratio, based on blocks of

variable size (ranging from 2-6). As such, randomisation will be stratified by site. The app developers (ANT Development Studios Ltd.) will provide the data scientist with two lists of app access codes which will direct participants to either the intervention or minimal version of AAT-App when they first download and open the app. Using these lists and the randomisation sequence, the data scientist will generate a separate spreadsheet of access codes for each site (based on the site-stratified randomisation sequence). Researchers will send these codes to participants as they are recruited from each respective site. Researchers involved in recruitment will only have access to a spreadsheet displaying a single list of codes to be sent to participants at each respective site, while the randomisation sequence will be stored in a password-protected file provided to the trial statistician and to one research officer who will remain unblinded to assist with coordinating qualitative interviews. Neither the randomisation file, nor its password will be provided to any other staff (including the principal investigator, Victoria Manning, and research officer, Hugh Piercy) involved in recruitment or in pursuing follow-ups or quantitative data management until all data analysis is complete.

Intervention: Prior to commencing the intervention, participants will be prompted to select 6 alcohol-related pictures that represent the drinks they most frequently consume. Participants can either select from their own photographs stored on their phone, take photographs of alcoholic beverages using the app, or select pictures from a library of 67 alcohol-related images chosen to represent a broad range of alcoholic beverages commonly consumed in Australia. Participants will then be prompted to select 6 pictures that "represent your goals and motivations". Again, participants can either select their own photographs, take photographs, or select pictures from a library of 68 pictures representing a range of healthy activities or positive goals and sources of pleasure (including family or friends enjoying time together; financial success; employment; exercise, sports, and recreational activities; healthy foods; pets; travel and holidays) which do not contain any depictions of alcohol. If participants take/use their own photographs, they will be reminded to ensure that positive images do not contain depictions of alcohol.

Once the participant selects their 12 pictures, they will complete the pre-training VAS craving task before they are presented with instructions for the ApBM task. Pictures (200 x 200 pixels) will be displayed with a white "frame" around them which will be in either landscape or portrait orientation. When the frame is in landscape orientation, the participant is required to swipe downwards (i.e., towards themself), which (if the movement is at least 40 pixels downward) causes the picture to expand, increasing to 600 x 600 pixels over a period of 500 milliseconds (ms), as if the participant has "pulled" the picture "towards" themselves. When the frame is in portrait orientation, the participant is instructed to swipe upwards (i.e., away from themself), which (if the movement is at least 40 pixels upwards) causes the picture to shrink until it disappears, which takes 500 ms, as if they have "pushed" it "away". If the participant swipes (at least 40 pixels) in the wrong direction, a red "X" is displayed to inform them that they made an error. After the picture expands/shrinks to its maximum/minimum extent, there is a 250 ms inter-stimulus interval before presentation of the next picture.

Following the display of the instructions, participants complete 10 practise trials (including 5 images in portrait frames and 5 in landscape frames, in random order) to familiarise themselves with the task before commencing scored trials. Following the practise trials, participants will complete the first session of ApBM. Each session consists of 156 trials, comprising 13 presentations of each picture. For alcohol pictures, 12 of the 13 presentations are framed in portrait orientation, and one is framed in landscape orientation. This is reversed for positive pictures, whereby 12 of the 13 presentations of each positive picture are framed in landscape orientation, while one is framed in portrait orientation. Thus, participants are supposed to push away 92.3% of alcohol images and pull 92.3% of positive images towards themselves. If participants make the incorrect response, they are informed that it was an error, but the trial is not repeated.

To increase engagement and encourage participants to respond both quickly and accurately, the task is gamified with a scoring system. Each time the participant swipes an image in the correct direction, they are awarded 10 points. Additionally, they score 'bonus points' for correct responses if their response is fast enough. If they swipe correctly and within 500 milliseconds (ms) of picture onset, they receive 30 bonus points (yielding a total of 40 points for that trial). If they swipe correctly within 501-1000 ms of picture onset they receive 20 bonus points (i.e., 30 points total). If they respond correctly within 1001-1500ms they receive 10 bonus points (i.e., 20 points total). Correct responses that are slower than 1500 ms following picture onset earn only 10 points. If they swipe an image incorrectly (i.e., swipe down for portrait or swipe up for landscape), they lose 100 points, regardless of their reaction time. Note that reaction time is recorded as the time taken to complete the swipe movement (i.e., the interval between picture display and the time at which the participant has moved their finger at least 40 pixels upwards/downwards).

Participants' score will be displayed at the top of the screen as they perform the task, and their progression through the task is displayed in a progress bar along the bottom of the screen. Upon completion of the task, the final point score is displayed and participants are required to complete the post-training VAS craving task. On the second, and subsequent, sessions, participants' previous session score, and the score of their highest-scoring session, will be displayed prior to commencing the task, to encourage them to try to score higher. At the end of these sessions, their final score for that session will be shown (and, if it is not their first session, their previous personal best score will also be displayed, so they can compare their performance). On the second and subsequent sessions, participants are offered the opportunity to review the task instructions and complete the 10 practise trials, but from the second session onwards they are provided with the option to skip these steps.

Minimal (control) group: Control participants will receive a minimal version of AAT-App which does not include any ApBM training or picture selection component, and only includes the weekly alcohol consumption questions, a weekly AAT task, and the VAS craving measure. Upon opening the app for the first time, participants are informed that they will be using "an app designed to target their alcohol use and awareness". Instead, participants are told that the "brain-training" will involve completing one training task at the end of each week, and answering some questions about their weekly alcohol consumption.

After reading the opening page's instructions, participants will then complete the alcohol consumption questions, before completing the pre-training VAS, the AAT, and the post-training VAS. The VAS is included so that cravings can be monitored before and after completing the AAT, where participants can access additional support if they indicate that their cravings are extreme (i.e., through links to Counselling Online and the National Alcohol and Other Drug Hotline). At the end of week 1 (i.e., 7 days post-baseline) participants will receive a notification reminder to complete the weekly alcohol consumption questions, followed by the pre-training VAS, AAT and post-training VAS. This process is repeated at the end of each week throughout the intervention period (i.e., 14-, 21- and 28-days post-baseline).

Procedure: Staff at participating services will briefly describe the study to clients who they believe may meet eligibility criteria. To allow for blinding, no specific details will be provided regarding approach bias modification, and participants will merely be informed that the study tests "a new smartphone 'brain-training app'" that "involves doing brief game-like tasks on your phone each week for 4 weeks". Clients who are interested will be asked to sign a form providing consent for the treatment service to provide their phone number to research staff. In the event they are unable to sign the form (e.g., if not present in person due to a telehealth appointment), clients can give verbal consent for the clinician to sign the form on their behalf. Clinicians can also complete the form online via Qualtrics Plus, by scanning a QR code on the paper form which directs them to an online

survey that collects information on the client's first name, mobile number, treatment site, and contains a tick box to indicate the client's verbal consent. Clinicians can also provide clients with the research team's details (study email address and contact number) if the client prefers to approach the researchers themselves. These forms are to be stored by the service, and treatment service staff will send the client's name and phone number to the research team email address.

Research staff will phone clients who have provided consent to be contacted to confirm eligibility (administering the AUDIT, checking age and phone operating system, confirming that they have no plans to enter residential/inpatient treatment in the next month, confirming absence of past-month residential rehabilitation and any past-week inpatient treatment (e.g., hospitalisation or residential withdrawal), as well as asking about number of days spent in inpatient treatment in the past month if the person underwent any inpatient treatment prior to the previous week.). After confirming eligibility, the researcher will explain the study, including requirement to complete baseline and follow-up questionnaires, duration of the study, nature of confidentiality, and payments participants can receive for completing assessments. If the researcher who conducts this recruitment phone call believes the participant is too impaired to understand the information they were presented with, they will not proceed with recruitment. If the client remains interested, they will be sent (via SMS and/or email) a link to a Qualtrics page that displays the participant information sheet (the information sheet will also be sent as a pdf attachment so participants can store and access it without re-visiting the Qualtrics page). They will also be advised to enable automatic updates on their smartphone to ensure that updates to AAT-App will not disrupt functionality.

Participants will be required to indicate that they have read and understood the information and consent to participate. This will result in the remaining baseline questionnaires being displayed including items assessing gender, which AOD treatment service the participant is attending, type(s) of treatment being accessed, drugs of concern, date of commencement of the current episode of treatment, treatment goal (abstinence or moderation), SDS, CEQ-F, and ATOP quality of life items. They will also be required to enter their smartphone number, and are encouraged to enter additional contact details (e.g., name, email, other phone numbers, and postal address) to assist with ensuring follow-ups are completed, although this is not required.

Completing the Qualtrics survey will result in an email being automatically sent to researchers, who will access the list of access codes, select the first unused code, and send the download link and access code to the participant via SMS. The researcher will record which access code was sent to which phone number. Once participants have downloaded the app, they will be prompted to enter the access code, thus resulting in either the ApBM or minimal version of the app being installed on their phone. Participants in the active condition will view a short introductory animation explaining how the ApBM intervention works, while participants in the minimal condition will be onboarded through written text that ensures blinding is maintained (see details provided above). Participants will then be required to complete the baseline alcohol consumption questions, before completing the pre-training VAS craving measure, the AAT, and the post-training VAS craving measure. Participants in the active condition will then proceed to the image selection feature, where they will be prompted to upload or select 6 alcohol-related images and 6 positive images to be used in the ApBM training task. These participants will then complete the pre-training VAS craving measure, their first session of the ApBM task, and the post-training VAS craving measure.

Participants in the active condition will be instructed to complete at least 2 sessions of the ApBM training task (approximately 3-5 minutes in duration) each week for the duration of the 4-week intervention period, though they can complete more sessions if they wish (via a "more training" option in the app's homepage). Participants in the minimal condition will not complete any ApBM sessions. At the end of each week throughout the intervention period (i.e., 7-, 14-, 21- and 28-days post-baseline) participants will complete the weekly alcohol consumption questions. Participants in

the minimal condition will also complete the AAT (preceded and followed by the VAS craving measure) immediately after the alcohol consumption questions at each 7-day timepoint (which they will be told is an "attention training task", to maintain blinding), while participants in the active condition will only complete the AAT again at the 28-day post-baseline timepoint. There will be no limitation on concomitant care/interventions that participants can commence during the intervention period (or the following follow-up period).

After completing the 28-day post-baseline alcohol consumption questions and AAT, participants in both conditions will be provided with an in-app link to a post-test Qualtrics survey which includes SDS, CEQ-F, ATOP items, and ratings of the app's acceptability. The questionnaire will also ask if they have undergone any residential/inpatient treatment (e.g., residential rehabilitation, withdrawal treatment, or hospitalisation) in the past 28 days and, if so, will ask how many days they spent entirely within residential treatment (i.e., with no opportunity to drink alcohol), whether any of these days were in the past week, and, if so, how many. Participants will be reimbursed with a $20 supermarket voucher for completing the post-test Qualtrics survey within 1 week (the link will expire after this point).

Twenty-eight days later (i.e., 56 days post-baseline), participants will be prompted with an app notification reminder to report their past-month alcohol consumption via the in-app calendar (this link will expire if it is not completed within 14 days). They will then receive an in-app link to a 1-month follow-up Qualtrics survey measuring SDS, CEQ-F and ATOP and asking about past-month residential/inpatient treatment. They will be reimbursed with a $20 supermarket voucher for completing this follow-up within this 2-week data collection window (i.e., 56-70 days post-baseline).

Finally, 56 days later (i.e., 112 days post-baseline) participants will be prompted with another app notification reminder to report their past-month alcohol consumption via the in-app calendar (this link will expire if the survey is not completed within 28 days). They will then receive an in-app link to a 3-month follow-up Qualtrics survey measuring SDS, CEQ-F, ATOP and AUDIT scores, and asking about past-month residential/inpatient treatment. They will receive a $20 supermarket voucher if they complete this survey within the 4-week data collection window (112-140 days post-baseline).

Participants who have not completed post-test/follow-up surveys within 24 hours will be sent an SMS reminder by a researcher. If they still fail to complete the survey within another 24 hours, a researcher who is blind to their randomised condition will attempt to contact them (using provided contact details) to remind them to complete these questionnaires. Participants will be asked to provide their mobile phone number in the post-intervention, 1-month, and 3-month follow-up surveys to allow their gift card link to be sent by SMS. The phone number will also function as the identifier used to link responses across different time points. However, in case participants' phone number has changed, items will be included in these follow-up surveys asking whether the phone number entered for reimbursement is the same as the phone number used to originally receive an app download link. If their phone number has changed, participants will be asked to also enter the phone number used at baseline to allow data linkage across time points. Completing these Qualtrics follow-up surveys will result in an email being automatically sent to the research team to ensure prompt sending of gift voucher links. However, participants will be informed that sending of gift cards may not be immediate (e.g., in case participants complete surveys at times of reduced monitoring of the trial email account, such as late at night, weekends, or holidays).

Additionally, the 1-month follow-up survey will have an item at the end stating: "We are interested in interviewing some participants about their experiences using AAT-App. If you would be willing to participate in a 30-minute interview, please indicate below. We pay participants $40 for participating in the interview. Please note, we may not be able to invite everyone who is interested to participate in the interview." We will aim to recruit a representative sample of 20 participants. Initially, we will invite anyone who indicates their willingness to participate to be interviewed. However, after the

first 10 interviews are completed, we will review the representativeness of the sample, in terms of gender, age and phone type (iOS or Android), and may attempt to target further recruitment more specifically (e.g., by only inviting participants of certain age groups or gender to participate) if the sample appears unrepresentative. An unblinded researcher (not involved in follow-ups) will phone participants to briefly explain the qualitative study, including the study's purpose, the approximate duration of the interview, the opportunity to receive $40 reimbursement, that the interview is audio-recorded, and the measures taken to preserve participants' confidentiality. If participants remain interested in participating, the researcher will schedule a time to complete the interview and send the participant information sheet as an attachment by SMS or email. At the agreed interview time, the researcher will phone the participant, remind them that the interview will be recorded, and obtain audio-recorded verbal consent to participate. Once consented, the researcher will conduct the interview according to the interview schedule detailed in Appendix 1. Upon completion of the interview, participants will be reimbursed with a $40 supermarket voucher.

Data management

Questionnaire data will be stored in Qualtrics databases, all located within a Monash University-hosted, password-protected Qualtrics account with access limited to members of the research team. These databases will include:

- Client referral data (first name, phone number, treatment site, verbal consent to provide research staff with contact details), entered into Qualtrics by clinicians who complete the client referral and verbal consent form online.
- Researcher-collected screening data (AUDIT, age, phone operating system), entered into Qualtrics by the researcher who conducts the screening questionnaire, along with the participant's phone number (used to link these data with data collected in other questionnaires).
- Baseline, post-intervention, 1-month, and 3-month follow-up questionnaire databases, with data entered by participants via the online surveys. As noted above, participants also enter their smartphone number in the baseline survey to receive an app access code, and are asked to enter their phone number at follow-ups to receive their gift card, and this will allow linking of data across separate time-points.

Data will be exported from Qualtrics in excel and/or csv file formats for storage and analysis on Turning Point's Clinical Research shared drive. Access to the project folder will be restricted to project team members, such that the folder can only be opened on a computer where a designated team member is logged in using their password-protected Eastern Health login. In-app alcohol use data and back-end user metrics (number of sessions commenced; number completed; session duration and total score; AAT trial reaction time, trial type, and error data; weekly and monthly alcohol consumption data; pre- and post-AAT VAS craving data; and pre- and post-ApBM VAS craving data) will be stored on a secure Google Firebase server, with the database only accessible to project personnel and the app developers (ANT Development Studios). These data will be exported in csv format for storage in the restricted-access project folder located on Turning Point's Clinical Research shared drive at the end of the study.

Data will be merged into single files, as necessary, for statistical analyses. Google Firebase datasheets will list participants' access codes, not their phone numbers, while Qualtrics datasheets will include phone numbers but not access codes. Thus, a separate spreadsheet will be stored on a password-protected Google drive hosted by Monash University, and shared only with research team members, in which the correspondence between phone numbers and access codes will be recorded. This sheet will allow Google Firebase and Qualtrics data to be linked at the individual level. Merged datasheets may be uploaded to team member's personal, password-protected Monash University

online drives where analyses require access to statistical software available through Monash University that is not available on Turning Point computers. However, statistical analysis files will need to be exported for storage on the Turning Point Clinical Research drive and deleted from team member's Monash drives once statistical analyses are complete, such that long-term storage of data following completion of the project will only be on the Turning Point drive. As such, data stored on Qualtrics, Google Firebase, and Google drives will also be deleted from these locations after publication of findings are complete and all data has been exported and stored on the Turning Point drive.

Participating services will be asked to retain signed "permission to share contact details" forms in secure filing cabinets at least as long as recruitment and data collection is proceeding, and then to dispose of these according to their data management policies. Following completion of the study, researchers will delete phone numbers and any other identifying information from data files stored on the Turning Point Clinical Research Drive (i.e., these data will only be labelled with access codes). The spreadsheet detailing the correspondence between access codes and phone numbers will be deleted. Additionally, all emails from participating services containing participants' names and phone numbers will be deleted from the project email account once data collection is complete. As such, data stored after completion of the project will be permanently and irreversibly deidentified. These deidentified data will be stored on the Turning Point Clinical Research drive for at least 7 years following publication of the last paper arising from this study, or 7 years after the final report to the ethics committee, or 7 years after final reporting of outcomes on the clinical trials registry, whichever occurs latest.

Audio-recorded qualitative interviews and verbal consent will be stored as .mp4 files on a secure Google drive hosted by Monash University, access to which will be restricted to project personnel (but which will not be made accessible to blinded quantitative data collectors until data collection is complete). The .mp4 files will be securely transferred to Pacific Transcription, a trusted transcription service provider that is frequently used by Monash University and Turning Point. To preserve participant anonymity the recording of verbal consent (where the participant states their full name and is also asked about their phone number) will be separated from the rest of the file and stored separately, while the main interview file will be labelled with a participant number (this number will be the same as the participant access code used to access the app, allowing baseline demographic data to be matched to qualitative interview data), not their name. Transcripts returned by Pacific Transcription will be stored as .docx files on the secure Google drive until data collection is complete. Once data collection is complete and blinding no longer required, these files will be stored in the project folder on the Turning Point Clinical Research Drive. They will be deleted from the Google Drive once analysis and publication is complete, and stored for at least 7 years following publication of the last paper arising from this study, or 7 years after the final report to the ethics committee, or 7 years after final reporting of outcomes on the clinical trials registry, whichever occurs latest.

Data Analysis

Statistical significance will be ascertained using α=.05. Any participants who commenced at least 1 session of ApBM (if in the ApBM condition) or AAT (if in the minimal control condition) will be included in the analysis population.

Primary outcome: A linear mixed-effects model (LMM) will be used to compare change in mean standard drinks consumed per week between groups across 4 time points (baseline, post-intervention, 1-month follow-up, and 3-month follow-up). This model will test the main effects of time and group and (most crucially for determining efficacy) the group x time interaction. Planned follow-up comparisons between groups at post-intervention, 1-month follow-up, and 3-month

follow-up time-points will be conducted using t-tests, with post-intervention being the primary endpoint. A secondary sensitivity analysis will be conducted excluding a participant's data from any time-point where they had been in residential/inpatient treatment in the past week (i.e., restricting analyses to time-points where a participant's opportunity to drink had not been limited by hospitalisation, rehabilitation, etc.). If a difference between groups is found post-intervention, a secondary LMM analysis of difference between groups in change in weekly standard drinks during the intervention period (i.e., 5 levels of time: Baseline, week 1, week 2, week 3, post-intervention) will be conducted to examine how quickly differences between groups emerge, with t-tests used to compare groups at week 1, 2, 3, and post-intervention time-points. This secondary analysis will be conducted excluding participants who had engaged in any residential/inpatient treatment within the intervention period.

Secondary outcomes: Continuous outcome variables (CEQ, SDS, AUDIT, past-week HDDs, past-month drinking days, ATOP items, and approach bias) will be analysed in a similar manner to the primary analysis described above. In analyses of CEQ, SDS, past-week HDDs, past-month drinking days, and the 3 ATOP items, there will be 4 levels of time (baseline, post-intervention, 1-month, and 3-month follow-ups). Sensitivity analysis of past-week drinking days to control for the possible effect of past-week residential/inpatient treatment will be conducted as described for the primary outcome. Past-month drinking days will be expressed as a percentage of the total number of days on which a participant had the opportunity to drink (i.e., if a participant was in residential/inpatient treatment for 10 days at a certain time point, then for that time point, their past-month drinking days will be expressed as a proportion of the remaining 18 days on which they had the opportunity to drink), although data will be excluded at any time point where the participant did not have at least 14 days on which they had the opportunity to drink alcohol (i.e., if they were within residential/inpatient treatment on 15 or more days). For CEQ, secondary analyses will be conducted for each of its 3 subscales. Analyses of AUDIT scores will use 2 levels of time (baseline, 3-month follow-up). Approach bias analyses will also use 2 levels of time (baseline, post-intervention) and approach bias scores will be analysed separately for alcohol and positive images. As past-month HDDs can only be calculated at 1 time point (post-intervention), they will simply be compared between groups using a t-test post-intervention after converting scores to a proportion of days on which the participant had an opportunity to drink (as described for past-month drinking days). Proportions of groups reporting complete past-week and past-month abstinence will be compared between groups at post-intervention, 1-month follow-up, and 3-month follow-up using Pearson's chi-squared. uMARS "functionality", "aesthetics", and " subjective quality" scores, and participants' subjective ratings regarding AAT-App's effect on drinking and cravings will be explored within each group separately using descriptive data (e.g., mean, median, quartile cut-offs, percentages scoring above 3) to quantify typical ratings and proportions of participants providing favourable ratings. Where relevant, exploratory analyses will also compare mean scores of uMARS scales between groups using t-tests.

Psychometric properties of AAT: The internal consistency of the AAT will be calculated by separately calculating Cronbach's α for the alcohol approach bias items and the positive approach bias items, following the method reported by Kersbergen, Woud and Field (2015). As such, we will calculate difference scores between each nth "swipe-up alcohol" trial and each nth "swipe-down alcohol" trial, deriving 20 difference scores for alcohol images. The same process will be used to derive difference scores for the 20 neutral images. Bootstrapping will be used to calculate 95% confidence intervals for Cronbach's α values. Test-retest reliability of alcohol approach bias and positive approach bias scores will be assessed in the control group by testing Pearson's correlations between scores from their first 2 AAT assessments (baseline and week 1). Exploratory analyses will also test Pearson's correlations between baseline alcohol approach bias scores and scores on measures of alcohol craving (CEQ-F scores; pre-session VAS craving scores), dependence severity (SDS; AUDIT),

and consumption (drinking days, heavy drinking days and standard drinks, using the in-app alcohol calendar).

Qualitative data: Interview transcripts will be subjected to a thematic qualitative analysis in order to identify underlying themes and patterns within each respondent's discourse. Thematic analysis will proceed according to the six stage process described by Braun and Clark (2006):

1 Familiarisation with the data: Reading and re-reading transcripts, noting initial ideas.
2 Coding: Deriving codes which label important features of the data that might be relevant to answering research questions. Then systematically attributing meaning throughout the dataset by identifying chunks of text with similar meanings and labelling them with corresponding codes.
3 Generating initial themes: Examining codes and collated data for broader patterns of meaning, using codes as building blocks to construct candidate themes (and promoting a code to a theme where appropriate), then collating data for each candidate theme to be "tested" in relation to research question or overall dataset.
4 Reviewing themes, checking them against the dataset to determine whether they tell a convincing story of the data that addresses the research questions; splitting, combining, and/or discarding themes as appropriate.
5 Defining and naming themes: Developing a detailed analysis of each theme, determining the 'story' of each.
6 Writing the manuscript: Weaving analytic narrative and data extracts, contextualising the analysis in relation to existing literature, remaining open to revising themes even at this stage.

The coding process will be primarily conducted by two researchers, and a third researcher will oversee and verify coding decisions in order to ensure agreement and consistency throughout the process. To avoid possible conflicts of interest, neither Victoria Manning nor Hugh Piercy will be involved in qualitative data collection, coding or analysis. The digital qualitative data analysis software NVivo 11.4.0 will be used to facilitate qualitative data analysis.

Free-text responses to app acceptability questions in the post-intervention survey will be reviewed primarily to identify reports of functionality issues (e.g., "bugs" in the app) and safety issues (e.g., reports of triggering). Any such issues will be catalogued to inform further improvements to the app (if necessary) and its delivery/implementation in future research and/or treatment contexts. As we do not expect these data to be as thematically rich as data derived from interviews, and they are therefore less likely to contribute to publications, we do not anticipate applying an analysis protocol as formal as that applied to interview transcripts.

Interim analyses: There are no planned interim analyses of either quantitative or qualitative data. The pre-planned analyses are intended to be conducted after all data has been collected. Nevertheless, interim analyses will be permitted if necessary for student projects (e.g., an honours project where data analysis and thesis writing is required to be completed prior to the project end date). In this case, the unblinded research officer or statistician will provide the student with the randomisation sequence and the student will be instructed not to share this with anyone else.

Dissemination

We intend to submit at least one manuscript describing quantitative outcomes and at least one describing qualitative findings to peer-reviewed academic journals. All principal investigators, as well as Hugh Piercy and Joshua Garfield, will be eligible for authorship of the manuscript describing the primary outcome, along with anyone else deemed by the coordinating principal investigator to have

contributed significantly to data analysis and/or writing of the manuscript. All authors of this version of this protocol (i.e., Victoria Manning, Hugh Piercy, Joshua Garfield, and Adam Rubenis) are eligible for authorship of the qualitative manuscript, along with anyone else substantively involved in analysing data or writing the manuscript. Authorship of additional manuscripts (e.g., if secondary outcomes are published separately) will be determined by the coordinating principal investigator, noting that the role of Victoria Manning, Hugh Piercy, and Joshua Garfield in developing AAT-App and this protocol's quantitative methodology, and all protocol authors' involvement in developing the qualitative methodology would typically make them eligible for authorship.

We also intend to present the findings to addiction researchers and clinicians through conference presentations (particularly the Victorian Alcohol and Drug Association (VAADA), Australasian Professional Society on Alcohol and other Drugs (APSAD), and International Society of Addiction Medicine (ISAM) conferences) within a year of completing the trial. We intend to publish a lay summary of the findings on the Monash Addiction Research Centre, Turning Point, and ADRIA websites. If the findings support the efficacy of AAT-App, we will also promote the findings to a much wider audience to encourage the implementation of AAT-App in clinical practise and among members of the general community who wish to reduce their alcohol use. This will include workshops and webinars for the AOD service sector (e.g., Connect & Learn, Talking Point) explaining ApBM and how to implement it. We will also aim to disseminate any positive findings in media outlets such as the Conversation, social media and radio interviews. Victoria Manning and Hugh Piercy's financial interests in the possible commercialisation of a related app that includes ApBM as part of its suite will be disclosed in any publications or presentations of research findings. Quantitative findings will be reported on the clinical trials registry regardless of outcomes and regardless of whether or not findings are published.

To preserve blinding, this protocol will not be made publicly-available until the completion of data collection. There is no specific plan for granting public access to the dataset. However, researchers interested in accessing deidentified data may contact the coordinating principal investigator. Granting access to other researchers to use deidentified data will require additional approval by the Saint Vincent's Hospital Melbourne HREC and possibly other HRECs/institutional review boards, and seeking these approvals will be the responsibility of the researchers seeking access to the dataset.

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Appendix – qualitative interview schedule

SECTION A: INTRODUCTION, SCREENING, AND CONSENT

Introduction

Thanks for agreeing to be involved in the project we are conducting about your experiences using "AAT-App".

This interview is expected to take about 30 minutes. I'll ask a number of questions about your experiences using the app and what you thought of it, but the interview is meant to be pretty informal, and you can consider it like a conversation. The interview will be recorded. At the end of the interview, I'll send you a $40 eVoucher for participating. If you would like to take a break just let me know and we can take one part-way through the interview.

Before we begin, could I please confirm that you've had a chance to read and understand the information about the study in the online survey that you completed?

☐ No (either read the PICF to the participant or arrange to call back another time)

☐ Yes.

Do you have any questions before we go on?

Screening

We check in with everyone before we start the interview, so I just wanted to know whether you are feeling up to conducting the interview today?

☐ No (direct to Counselling Online/Directline details listed on PICF if participant indicates distress)

☐ Yes.

[**IF NO**] Would you like to conduct the interview at another time?

☐ No ☐ Yes, arrange another interview time.

Consent

Ok, so before we start the interview, I will need to turn on the recorder and begin by recording your consent to participate. Is that ok with you if I start recording now?

RECORDER ON

I'll now record your consent to participate in the interview. Can you please state your full name first. [participant states name]

I will now read out a list of questions, if you could answer either 'yes' or 'no' at the end of each.

- I have read the Participant Information Sheet, or someone has read it to me, and I understand the purposes, procedures, and risks of the research. ☐ No ☐ Yes

- I have had an opportunity to ask questions and I am satisfied with the answers I have received. ☐ No ☐ Yes
- I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the interview. ☐ No ☐ Yes
- I give consent for the interview to be audio-recorded ☐ No ☐ Yes

I also need to confirm some details about the mobile phone number that you used for this study.

- Is the mobile number I'm phoning you on the same as the phone number you originally used to sign up to AAT-App?
- [**if no to previous question**] What was your old mobile number (the one you originally used when signing up to the study)?

RECORDER OFF

RECORDER ON

SECTION B: INTERVIEW

[Main dot-points represent the primary interview questions, sub-dot-points represent suggested prompts or follow-up questions that may be used as appropriate]

- To start off, I'm interested in knowing about what kind of treatment you were getting for alcohol use when you decided to try AAT-App. Can you tell me about that?
    - How long had you been involved in that treatment?
    - How were those treatments going for you?
- And what made you want to try AAT-App?
    - Can you describe the concerns you had about your alcohol use when you decided to use AAT-App?
    - Can you describe what was going on in your treatment when you decided to try AAT-App?
- Tell me about your experience using AAT-App. How'd you find it?
    - What were the positives/negatives?
    - Any bugs or glitches that came up?
- How (or in what contexts) did you use the brain-training app?
    - Did you use it at any particular times or places?
    - Did you try using it for immediate craving relief/support when urges to drink arose and, if so, how did that go?
- Can you tell me about any effects that AAT-App had on your alcohol cravings or drinking?
    - [*If they felt it was helpful*] When did you notice it helping?
- Do you have any thoughts about how AAT-App combined with the treatment you were receiving?
- What was your understanding of how the brain-training is supposed to work?
    - What do you think about the information provided in the app about how the brain-training works (if you can remember it)?
    - What influence, if any, do you think that knowing the theory behind the brain-training has on how the app worked (or didn't work) for you?
- What images did you choose to use for the brain-training?
    - [prompt for information regarding both positive and alcohol images if they only describe one category]
    - Did you use your own photos, or the ones provided in the app?
    - [*If they used photos provided in the app*] What did you think of the photo options provided in the app? (Do you have any suggestions about changes to the options?)

    - What guided your decision about which photos to use?
- Do you have any suggestions for how the app could be improved?
- Do you have any other thoughts or opinions about the app that you would like to share?

Conclusion

Thanks, we've covered a lot today and I appreciate you sharing your thoughts about your experiences with the app. We really value hearing people's feedback, so your input is a huge help!

RECORDER OFF

End of interview wellbeing check:

Finally, after everything we've discussed, I just wanted to make sure that you're ok and don't have any concerns by anything we've talked about today?

☐ No concerns ☐ Requires support – proceed to support option (see Lifeline, DirectLine, and Counselling Online details on participant information sheet)

Arrange eVoucher to be texted or emailed to participant

And I'd just like to check whether you'd prefer your $40 voucher be texted or emailed to you?

☐ Text ☐ Email

Brilliant. I'll arrange to get that sent to you ASAP, and thanks again for participating in the study and doing the interview with me today. Take care!

Labelling of interview file
Check participant's phone number and determine corresponding access code. Label the interview file with this access code.