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**DOI**
10.1111/acer.15431

**Publication date**
2024

**Document Version**
Final published version

**Published in**
Alcohol, Clinical and Experimental Research

Received: 21 August 2023 | Accepted: 9 August 2024

DOI: 10.1111/acer.15431

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RESEARCH ARTICLE

# Long-term effects of alcohol-avoidance training: Do changes in approach bias predict who will remain abstinent?

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## Abstract

**Background:** Patients with alcohol use disorder (AUD) tend to selectively approach alcohol cues in the environment, demonstrating an alcohol-approach bias. Alcohol-approach-bias modification (Alcohol-ApBM) effectively increases abstinence rates in patients with AUD when added to abstinence-focused treatment, but the evidence for its proposed working mechanism (reduction of the alcohol-approach bias) is limited. Moreover, not all patients benefit from Alcohol-ApBM, and previous research did not identify reliable pretreatment predictors of Alcohol-ApBM effectiveness. Therefore, the current study focused on learning processes during the Alcohol-ApBM training itself. Specifically, we examined whether changes in approach-avoidance tendencies over the course of Alcohol-ApBM would predict abstinence after inpatient treatment.

**Methods:** The training data of 543 AUD patients in Germany (70% male, $M = 47.96$, $SD = 9.08$), receiving Alcohol-ApBM training during inpatient treatment, were used to examine whether various aspects of learning during training predicted abstinence 1 year after treatment discharge, both separately and in interaction with potential sociodemographic and clinical moderators of Alcohol-ApBM effectiveness.

**Results:** Overall, successful learning across six Alcohol-ApBM training sessions was observed; that is, the approach tendency toward alcoholic stimuli was reduced over time. However, none of the examined learning parameters were predictive of abstinence, neither separately nor in combination with clinical or sociodemographic variables.

**Conclusions:** Previous studies have shown that Alcohol-ApBM is an effective add-on to abstinence-focused treatment for AUD, and this study showed that learning took place during Alcohol-ApBM training. However, specific learning parameters during training did not predict abstinence 1 year after treatment discharge. Therefore, we cannot specify which patients are most likely to benefit from ApBM with regard to abstinence after 1 year.

KEYWORDS
alcohol-approach bias, cognitive bias modification, learning, relapse prevention

## INTRODUCTION

Despite continuous efforts to improve treatments, relapse rates are high in substance use disorders (e.g., Cutler & Fishbain, 2005; McKetin et al., 2018; Suter et al., 2011). Relapse can occur both during and after treatment, highlighting the cardinal role of relapse prevention as part of clinical treatment (e.g., see Cutler & Fishbain, 2005). This requires a continuous search for predictors of treatment success, along with adjustments of current treatments. In alcohol use disorder (AUD), relapse rates after treatment typically exceed 50% 1 year after treatment (e.g., Cutler & Fishbain, 2005; Sliedrecht et al., 2019). This contributes to high mortality rates (Schwarzinger et al., 2017), as well as to disability and societal costs (Carvalho et al., 2019).

In AUD and other addictions, automatically activated cognitive-motivational processes have been suggested to explain high relapse rates after treatment. Specifically, the tendency of heavy-drinkers and alcohol-dependent individuals, compared to healthy controls, to approach alcohol cues in the environment (the so-called alcohol-approach bias; Wiers et al., 2011, 2013; Wiers & Gladwin, 2017) was found to correlate positively with the consumption of alcohol (Wiers et al., 2009, 2013). The empirical evidence about the relationship between the approach bias and relapse rates after treatment, however, is mixed. While the results of one study suggest that an alcohol-avoidance bias might predict higher relapse rates (Spruyt et al., 2013) or no effect on relapse at all (Spruyt, A., Laporte, W., Boffo, M., Herremans, S., Impe, P., Vercruysse, I., Verdée, T., Verhelst, M., Wiers, R.W., De Raedt, R., unpublished data described by Wiers et al., 2023), the presence of an approach bias is frequently considered to contribute to maintenance of the addiction and to relapse after treatment (reviews: Kakoschke et al., 2017; Wiers et al., 2023). To counter the negative influences of cognitive biases, a new form of translational interventions was developed, collectively called Cognitive Bias Modification (CBM; Wiers et al., 2013, 2023).

In AUD, the most effective CBM training so far consists of modifying the patients' automatic alcohol-approach tendency. This so-called Approach Bias Modification (ApBM; for a detailed description, see the section on Alcohol-approach-bias modification training; alcohol-ApBM) can reduce the alcohol-approach tendency significantly and sometimes even reverse it into an avoidance bias (Manning et al., 2021; Wiers et al., 2011). Moreover, Alcohol-ApBM was repeatedly found to increase abstinence rates of abstinent alcohol-dependent patients by approximately 10 percent as late as 1 year after treatment when applied in addition to regular inpatient treatment in residential rehabilitation settings (Eberl et al., 2013; Loijen et al., 2020; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011). When applied during inpatient alcohol detoxification, Manning et al. (2016, 2021) found ApBM to reduce relapse rates at 2 weeks post-discharge. In the same patients as in Manning et al. (2021), a significant reduction was also found after 3 months, but not after 6 or 12 months (Manning et al., 2022). Given the promising effects of Alcohol-ApBM in clinical contexts (see Kakoschke et al., 2017; Wiers et al., 2023), it was added to the German (Kiefer et al., 2022) and Australian (Haber et al., 2021) treatment guidelines for AUD.

Although Alcohol-ApBM proved beneficial for preventing relapse in AUD, it is unclear who benefits (most) from Alcohol-ApBM. Knowing this, however, is crucial, as there are many different factors that contribute to relapse in AUD (e.g., Sliedrecht et al., 2019).

Following this line of thought, previous studies of Alcohol-ApBM (Eberl et al., 2013, 2014; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011) already examined potential patient-related and sociodemographic factors that might moderate the effectiveness of Alcohol-ApBM. Among these factors, age was identified as a patient characteristic that predicted the effects of Alcohol-ApBM, with older patients benefiting more from Alcohol-ApBM, particularly when they had a stronger approach bias before Alcohol-ApBM (Eberl et al., 2013). This finding, however, was not replicated in later studies (see, for instance, Rinck et al., 2018). Moreover, Salemink et al. (2022) found that Alcohol-ApBM was more effective when patients met criteria for a comorbid anxiety or affective disorder. Note, however, that these variables were identified as moderators in randomized controlled trials (RCTs) when active Alcohol-ApBM was compared to a control condition. As such, they suggest for whom it might make a difference whether Alcohol-ApBM or a control condition is applied. This, however, does not necessarily imply that they would also predict who benefits from a treatment that everyone receives, without a comparison to another treatment or control condition. This is currently the case in many clinics where ApBM is part of treatment-as-usual (TAU) for all AUD patients.

Nevertheless, moderator variables are likely to be predictive, and therefore age and presence of affective comorbidity were included in the current study. In current clinical practice, Alcohol-ApBM is recommended as an add-on to TAU for AUD. This situation, however, could be improved if we were able to predict who is likely to benefit from Alcohol-ApBM. Simply giving the training to all patients in a one-size-fits-all fashion does not tell us how it could be adjusted to the patients' needs, nor does it allow for strong conclusions regarding its working mechanisms.

In general, the potential role of changes in alcohol-approach bias may be investigated in different ways. First, in RCTs by testing whether patients who receive active Alcohol-ApBM show a greater reduction than patients in a control group (typically sham-training or no-training). Second, for each group separately, by testing retrospectively whether patients who remained abstinent had shown a larger reduction of their alcohol approach bias during training than patients who relapsed. Third, if a control group is not available, one could use the latter strategy in a large group of patients, all of whom received active Alcohol-ApBM as part of their treatment as usual. This is the approach taken here.

Regarding training effects in RCTs, only Eberl et al. (2013) found evidence that a reduction of the alcohol approach bias could be the proposed mechanism of change, which, in turn, reduced relapse rates (significant mediation). Similarly, Gladwin et al. (2015) showed that increased avoidance bias for alcohol stimuli as measured on the Implicit Association Task (IAT) partly mediated the improved clinical outcome of TAU, including Alcohol-ApBM. The studies by Wiers et al. (2011), Rinck et al. (2018), and Manning et al. (2021) found significantly reduced relapse rates after treatment, after add-on Alcohol-ApBM

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compared to sham- or no-training, but they did not find evidence for the aforementioned mediation. A limitation of all these studies is that the alcohol-approach bias was measured only twice, namely before and after training. The only study that measured the alcohol-approach tendency repeatedly across several training sessions was reported by Eberl et al. (2014). This rather small study ($N = 111$) found evidence that the quadratic component of the rate of change in approach bias across 12 training sessions predicted relapse. However, none of the 12 sessions yielded a significant difference between the alcohol-approach biases of patients who would later relapse and those who would stay abstinent. This may be due to the low statistical power of the study, caused by a small sample and a small effect size, with the latter being further reduced by including patients who could not be reached at follow-up and counting them as relapsed.

Therefore, the current study was designed in a way similar to the one reported by Eberl et al. (2014), with the following improvements: Testing a large sample of patients who receive Alcohol-ApBM as part of TAU, measuring the alcohol-approach bias at the start of each of six training sessions, and excluding patients whose status at follow-up was unclear.

Regarding the patients' learning during Alcohol-ApBM, we expected that the way the alcohol-approach bias changes across sessions would follow a typical learning curve. Although individual learning curves tend to vary greatly, the average curve for a group of individuals typically shows a negatively accelerated increase in learning (Gallistel et al., 2004). A large increase from Session 1 to Session 2, a somewhat smaller increase from Session 2 to 3, an even smaller increase from Session 3 to 4, and so on, until learning has reached a plateau. How stable the latter is and when it is reached varies greatly (Gallistel et al., 2004). Research with humans and with animals has identified numerous factors that influence the shape of learning curves (Speelman & Kirsner, 2005). However, little is known about how the shape of the learning curve predicts later outcomes. Research addressing this question tends to focus on later performance of the trained behavior itself, as in medical procedures (Tapking et al., 2020), or it uses near-transfer tasks (Sáiz Manzanares et al., 2017). In contrast, except for Eberl et al. (2014), we are not aware of any other study that used session-to-session changes in approach-avoidance tendencies during Alcohol-ApBM or another CBM training to predict later clinical outcomes. In our case, to predict relapse in currently abstinent AUD patients, we used indicators of learning derived from the suggestions by Pusic et al. (2017). These indicators reflect baseline performance (alcohol-approach bias before Session 1), the potential upper asymptote of learning (bias at Session 6), stability in learning performance (variance of scores across sessions), and various indicators of session-to-session bias change.

The purpose of the current study was twofold: First, from a more theoretical perspective, by examining whether better learning during Alcohol-ApBM predicts abstinence, we aim to test the proposed working mechanism of Alcohol-ApBM, namely, the reduction of the alcohol-approach bias. This would complement the findings of previous studies that tried to identify mediating factors of Alcohol-ApBM efficacy. Second, we also included variables that were found to be moderators in earlier studies (affective comorbidity and age) because this offers an opportunity to test whether these variables are also useful as predictive variables when moving from RCTs to regular clinical settings. The present study cannot answer whether it might be possible to predict which patient should receive Alcohol-ApBM as part of TAU versus who would not benefit from Alcohol-ApBM. This would require a moderation study in which there is a group who receives active Alcohol-ApBM and a control group who would not get the training.

As far as we know, the current study is the first sufficiently powered study to examine whether a change in the tendency to approach alcohol during Alcohol-ApBM is predictive of abstinence after treatment. Specifically, this nonexperimental, observational study explored whether and how various aspects of learning curves over the course of a 6-session ApBM training, when applied during regular treatment for alcohol addiction, are predictive of treatment success at 1-year follow-up. Previous studies either measured alcohol-approach bias only pre- and post-training (Eberl et al., 2013; Manning et al., 2021; Rinck et al., 2018; Wiers et al., 2011), or they were underpowered for the prediction of relapse (Eberl et al., 2014). It is important to note that, in contrast to the RCTs reviewed above, the current study did not involve a control group. Instead, Alcohol-ApBM was part of TAU, and it was offered to all AUD patients who received treatment during the period of data collection. Therefore, only learning performance in the active form of Alcohol-ApBM and its potential predictive value for treatment success were explored. Being explorative in nature, the current study also examined whether clinical and sociodemographic characteristics interacted with learning curves during Alcohol-ApBM to predict abstinence after treatment. Specifically, we tested the general predictive potential of several patient characteristics, including sociodemographic factors and two moderators identified in previous studies: age (Eberl et al., 2013) and presence of affective comorbidity (Salemink et al., 2022). The classification of the presence of affective comorbidity followed the criteria described by Salemink et al. (2022) (outlined in the Predictors of treatment success section).

## METHODS

### Participants

We aimed to analyze the data of 2200 currently abstinent alcohol-dependent patients who received a 3-month inpatient treatment at the salus clinic Lindow, Germany, between July 2013 and July 2016. The patients in the present study did not participate in any of the previous studies (Eberl et al., 2013, 2014; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011) conducted at this clinic. The current data were collected during regular treatment, and there is no overlap with other studies. All patients were diagnosed with a primary diagnosis of Alcohol Use Disorder (F10.2 in ICD-10; WHO, 1992), as assessed during the standard intake procedure of the clinic. From this sample, we included only patients for whom

complete training data and explicit information about abstinence status after 1 year were available. As a result, we excluded all patients who completed fewer than 6 sessions and all patients whose treatment outcome was different from abstinence, relapse, or lapse (i.e., death, refusal to answer, and not reached, all of which are usually counted as relapse). This deviates in several ways from approaches chosen in RCTs and was dictated by the current research question: Since we aimed to predict treatment outcome by learning during Alcohol-ApBM, we had to limit ourselves to patients who did indeed complete the Alcohol-ApBM and for whom we were able to measure the outcome. This yielded a total analytical sample of 543 patients (Figure 1 shows an overview of the participant flow). Therefore, the current sample and its abstinence rate cannot be directly compared to unselected groups of patients as they were included in previous RCTs. Table 1 shows an overview of sociodemographic factors, severity of alcohol dependence, nicotine dependence, depression, comorbidity, and mental burden in the analytical sample. Prior to the start of treatment, all patients gave consent that their clinical data, including Alcohol-ApBM training data, could be used for scientific analyses. All procedures were in accordance with the ethical standards of the ethics committee of the German Pension Fund and with the 1964 Helsinki declaration. The analysis plan was preregistered at https://aspredicted.org/ (https://aspredicted.org/blind.php?x=5JF_F6M). There were no deviations from the preregistered plan. Descriptive inspection of the data showed that the presence of comorbid anxiety disorders was significantly more frequent in abstinent patients than in those who relapsed (see Table 1). Therefore, we added nonregistered analyses in which we repeated the preregistered analyses (outlined in the Analyses section) including this moderator variable.

## Procedure overview

During the first 4 weeks of treatment, all patients started with the Alcohol-ApBM as part of TAU. TAU consisted of abstinence-oriented cognitive behavioral therapy, including both individual and group therapy. Next to TAU, patients were scheduled to complete 6 sessions of Alcohol-ApBM within the next 2 weeks (each session taking approximately 10 min, separated by 1 or 2 days with a total training duration of approximately 60 min). One year after discharge from treatment, participants received a standard follow-up questionnaire. In the questionnaire, they were asked whether they had continuously been abstinent during the past 12 months. If this was not the case, they were asked additional questions regarding the type of substances used, the number and duration of relapse(s), and the way they had ended the last relapse. Patients who did not return the questionnaire were reminded twice by mail, and if they did not answer, a final attempt was made to reach them by phone. Using this procedure, a total of 543 patients with complete training data could be reached and supplied information about treatment outcome at 1-year follow-up, whereas another 184 patients with complete training data had to be excluded from the analyses because they could not be reached, they refused to answer, or they were deceased (see Figure 1).

## Assessment and outcome measures

At intake, all patients were diagnosed using the Composite International Diagnostic Interview (CIDI; Kessler & Ustün, 2004), which was complemented by a diagnostic interview based on the "German Manual for Documentation in Addiction Help," as published by the German "Hauptstelle für Suchtfragen DHS." Both the CIDI and the clinical interview were conducted by clinical psychologists and formed the basis for the diagnoses. The German versions of the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993), the Beck Depression Inventory (BDI; Hautzinger et al., 1994), and the Symptom Checklist 90-R (SCL-90-R; Franke & Stacker, 1995) were also administered during intake (for an overview of the administered questionnaires, see the Data S1). The main outcome variable of TAU for AUD, including Alcohol-ApBM,

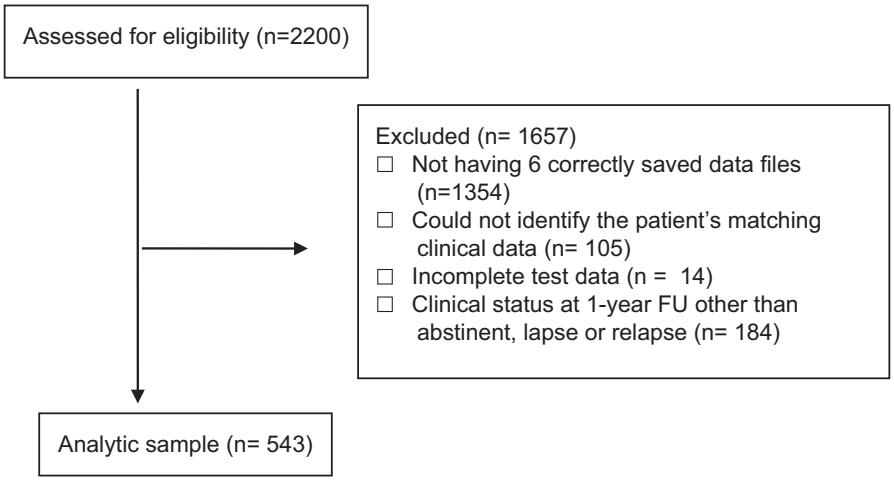


FIGURE 1 Overview of the participant flow.

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**TABLE 1** Characteristics of the sample: significance of group difference between patients with successful versus nonsuccessful clinical outcome at 1-year follow-up.

| Characteristics | All patients ($N = 543$) | Patients with success outcome ($n = 370$) | Patients with non success outcome ($n = 173$) | $p$ Value |
|---|---|---|---|---|
| Age (years), mean (SD), range | 47.96 (9.08), 19–72 | 48.04 (8.85), 19–72 | 47.80 (9.57), 23–71 | 0.77 |
| Gender (% female) | 30% | 27% | 39% | 0.10 |
| Education level[a], mean (SD), range | 3.06 (0.84), 1–5 | 3.09 (0.85), 1–5 | 2.90 (0.83), 1–5 | 0.72 |
| Smoking (% with nicotine dependence) | 73% | 73% | 72% | 0.90 |
| Beck Depression Inventory, mean (SD), range | 13.68 (10.55), 0–47 | 13.01 (10.60), 0–41 | 14.24 (9.14), 0–47 | 0.20 |
| Mental burden: SCL-90, mean (SD), range | 62.03 (12.82), 26–80 | 61.60 (11.94), 26–80 | 62.88 (11.57), 27–80 | 0.25 |
| AUDIT score, mean (SD), range | 25.58 (10.55), 0–40 | 25.54 (7.52), 3–40 | 26.26 (7.30), 0–40 | 0.15 |
| Anxiety (% comorbidity)[b] | 5% | 7% | 2% | 0.02* |
| Depression (% comorbidity)[c] | 27% | 25% | 29% | 0.33 |
| Affective psychopathology (% comorbidity)[c] | 30% | 29% | 31% | 0.75 |

*Note*: Continuous variables were analyzed with two-group ANOVAs, with $F(1,541)$. Categorical variables were analyzed with chi-square tests ($df = 1$). For all analyses, $p$-values were two-tailed at $p = 0.05$. Standard deviations are presented in parentheses.

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; SCL-90, Symptom Checklist-90.

[a]Education level was scored on a scale from 1 (primary school), 2 (lower secondary school), 3 ("Mittlere Reife," roughly comparable to the British General Certificate of Secondary Education), 4 ("Abitur," roughly comparable to the International Baccalaureate Diploma Programme or the British A-levels) to 5 (finished university).

[b]Anxiety disorders include panic disorder, agoraphobia, generalized anxiety disorder, social anxiety disorder, specific phobia, and unspecified anxiety disorder.

[c]Depression includes major depressive disorder (single episode moderate, severe, or reactive; or recurrent in nature).

[c]Affective psychopathology, includes the presence of an anxiety disorder and/or major depressive disorder, as specified in 'a' and 'b'. *$p < 0.05$.

is abstinence at one year after treatment discharge as assessed by a binary outcome variable (successful outcome or not). Following the guidelines of the German Addiction Society, successful outcome consisted of either no relapse at all or a single lapse shorter than 3 days in duration, ended by the patient without further negative consequences, and followed by at least 4 weeks of abstinence before the follow-up assessment. As explained above, all other outcomes (refusal, not reached, and deceased) were not re-coded as relapse but excluded from the analyses.

## Alcohol-approach bias modification training (alcohol-ApBM)

The Alcohol-ApBM used a similar setup as in previous studies (Eberl et al., 2013, 2014; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011; for an extensive description of Alcohol-ApBM see the Data S1): In each of 6 training sessions, patients used a joystick to push 100 pictures of alcoholic beverages away (avoidance) and to pull 100 pictures of nonalcoholic beverages closer (approach), based on an irrelevant stimulus feature (tilt of the picture). The task started with 13 practice trials showing neutral objects. To assess the alcohol-approach bias throughout Alcohol-ApBM, in each session, the 200 training trials were preceded by 40 assessment trials. In these, both drink types were approached and avoided (with 10 trials each in the four combinations). From these trials, separately for each patient and session, we computed mean reaction times (RTs) for each of the four combinations of "drink type (alcohol, nonalcohol)," and "movement (pull, push)." No trials were excluded for computation of RTs, as a trial during assessment and training parts could only be ended by providing the correct response. All patients fulfilled the minimum requirement of seven for each "drink-type"-by-"movement-direction" combination, with most providing 9–10 valid trials per combination. Prior to computation of mean RTs, we excluded extreme outliers from the RTs, which amounted to only 2% of the data (the fastest 1% and the slowest 1% of all responses).

To assess changes across sessions, we computed a difference score, which reflects how compatible all 4 mean RTs are with the training goal: Change of an alcohol-approach tendency at baseline to an alcohol-avoidance tendency at the end of training. To examine whether throughout Alcohol-ApBM, patients learn to simultaneously avoid alcohol and to approach nonalcoholic drinks or whether they solely learn to either avoid alcohol or approach nonalcoholic drinks, we calculated both compatibility scores and separate alcohol-approach and nonalcohol-approach tendencies (the calculation procedure is explained in Data S1).

## Predictors of treatment success

We explored whether and how several aspects of learning observed over the course of the 6-session Alcohol-ApBM were predictive of success at 1-year follow-up. Based on the expected, negatively accelerated shape of the learning curves, the tested predictors

included the size of the compatibility scores at each specific time point throughout training (scores at Sessions 1 to 6). Further, reflecting the change in the compatibility scores across training sessions, we included, first, the change in the compatibility score from Session 1 to 6. This is comparable to the pre- to postmeasurements of changes in approach bias from previous RCTs. Second, we included the change in the compatibility score from Session 1 to 3. This is based on a graphical inspection of Figure 2, showing both the largest change in approach bias during training and the change from an approach to an avoidance tendency. Third, we included the change in the approach bias from Session 1 to 4 to examine its predictive capacity after the first half of Alcohol-ApBM. Finally, we included the variance of the compatibility score from Session 4 to 6. This was based on a graphical inspection of Figure 2, showing that both groups show an avoidance tendency from Session 4 on. Though similar on group level, there might be variability at subgroup (i.e., abstinence vs. relapse) or individual level. Therefore, as for all types of learning, including Alcohol-ApBM predicting abstinence after treatment, it might be that if the variance of avoidance bias during training is less variable, the training effect of Alcohol-ApBM becomes more stable during and after training. As the aim of a training such as Alcohol-ApBM is to hold the variability of the learned avoidance bias during training as low as possible, it might be assumed that a lower variance of the avoidance bias during Alcohol-ApBM might lead to a higher probability of being abstinent after treatment. This way, we aimed to thoroughly represent a variety of potentially important aspects of changes in approach-avoidance tendencies during the 6-session Alcohol-ApBM.

Furthermore, previous studies suggested that receiving Alcohol-ApBM or not made a larger difference for patients with comorbid affective disorders (Salemink et al., 2022) and for older patients (Eberl et al., 2013). This suggests that in the current study, these variables might also predict who will remain abstinent and who will relapse if everyone receives Alcohol-ApBM. We therefore tested the predictive value of age and of the presence of comorbid affective disorders as well. The classification of patients regarding the presence of affective comorbidity followed the criteria described by Salemink et al. (2022) as outlined in the Data S1. Based on this, a dichotomous variable "Presence-of-affective-comorbidity (yes, no)" was computed and included in the analyses. Table 1 shows an overview of the presence of affective comorbidity as specified here.

## Analyses

We first determined the internal consistency of the compatibility scores described above to check if they could be used as predictors or dependent variables. This was done using the *cronbach.alpha* function of the *ltm* package in R (Rizopoulos, 2006). Second, to determine whether changes in these compatibility scores over the course of Alcohol-ApBM would predict treatment success, we conducted a mixed-factors ANOVA with the between-subjects factor "outcome status (success, relapse)" and the within-subjects factor "time (Session 1 to Session 6)" on the "Alcohol-ApBM compatibility scores," using the aov_ez function of the *afex* package

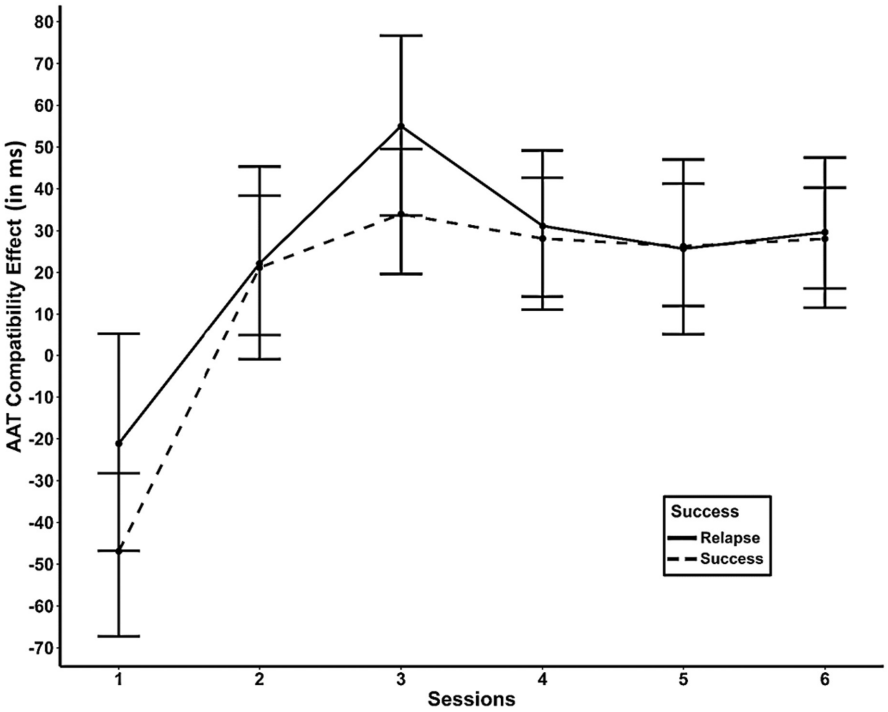


FIGURE 2 Change in approach-avoidance tendencies over the course of the 6 training sessions. Positive scores indicate a training-compatible, relative alcohol-avoidance tendency, and negative scores indicate a training-incompatible, relative alcohol-approach tendency, with larger scores implying stronger tendencies.

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in R (Singmann et al., 2016). The ANOVA was complemented by planned contrasts that tested the session-to-session changes in compatibility scores and by t-tests to check for baseline deviations from zero. To determine whether any effects observed in the compatibility scores were based on effects in the alcohol-approach tendencies, the nonalcohol-approach tendencies, or both, we repeated the ANOVAs with these tendency scores. Given the dichotomous nature of the dependent variable, we used logistic regressions to examine the predictive value of the learning indices for success at 1-year follow-up. For all preregistered and nonregistered logistic regressions, the primary outcome variable was the binary variable "outcome status (success, relapse)" at 1-year follow-up. The learning indices, as outlined above, constituted the independent variables. The previously found moderator variables "presence-of-comorbid-affective-disorders" and "age" and their interactions with the learning parameters were also added to the preregistered analyses. Specifically, for these analyses, we added all learning parameters as specified above with the following exception: We added only the compatibility scores at Session 1 and at Session 3 to examine the interaction with the moderator variables at the start of training and during the strongest depiction of an avoidance tendency during ApBM, respectively. Further, as comorbid anxiety disorders were significantly more frequent in abstinent patients than in those who relapsed (see Table 1), we repeated the preregistered analyses including the dichotomous moderator variable "presence-of-comorbid-anxiety-disorder." For all analyses, the required assumptions (for an overview, see the Data S1) were checked, and deviations with corresponding adjustments are reported in the text. All analyses used two-sided tests with $p = 0.05$, and they were performed in R (R Core Team, 2020).

## RESULTS

For all preregistered and nonregistered analyses, if not reported otherwise, there were no violations of the required assumptions.

### Reliability of approach bias measures

In order to predict relapse by means of approach bias scores, the latter have to be reliable enough. We therefore computed the reliability in the same way as in Rinck et al. (2018): For each of the 20 images used in the assessment phases, we computed the difference of each patient's reaction time for pushing it minus the reaction time for pulling it. Then, separately for the six sessions, we computed the internal consistency for these 20 difference scores. For Sessions 1 to 6, we found values of Cronbach's alpha of 0.603, 0.534, 0.499, 0.516, 0.504, and 0.627, respectively. As in Rinck et al. (2018), these values are low, but in the upper range of what is usually reported for RT tasks.

### Group differences between successful versus relapsed patients

#### Clinical and sociodemographic variables

Overall, of the 543 patients included in the analyses, 370 were classified as successful at 1-year follow-up, and 173 were classified as relapsed, yielding an overall success rate of 68.1%. Note that this percentage cannot be compared to earlier studies (Eberl et al., 2013, 2014; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011) because it excludes cases that were recoded as relapse due to lack of information. As Table 1 shows, both success groups did not statistically differ on relevant clinical and sociodemographic variables, except for the presence of a comorbid anxiety disorder. In other words, the likelihood of relapse 1 year after treatment discharge could not be predicted by age, gender, education level, smoking, depression scores, general psychopathology symptoms scores, or AUDIT scores of the patients. There was, however, a significantly higher proportion of patients with a comorbid anxiety disorder who were found to be abstinent after one year.

#### Baseline biases

Regarding their pretraining compatibility scores, the patients showed a significant alcohol-approach bias before treatment, as indicated by their negative mean compatibility score ($M = -38.65$, $SD = 197.81$), which deviated significantly from zero $t(542) = 4.55$, $p < 0.001$. There was no significant difference between participants who were successful at 1-year follow-up and patients who had relapsed $t(541) = 1.45$, $p = 0.15$, $d = 0.130$. Successful patients showed a significant alcohol-approach bias before treatment ($M = -46.10$, $SD = 207.10$), which deviated significantly from zero $t(369) = 4.35$, $p < 0.001$. Patients who would later relapse also showed a pretraining approach bias ($M = -21.12$, $SD = 175.35$), which, however, did not deviate significantly from zero $t(172) = 1.58$, $p = 0.11$.

#### Change of compatibility scores across Alcohol-ApBM

The compatibility scores of the patients across the 6 training sessions showed the negatively accelerated increase that is typical of learning curves (see Figure 2). There was a significant main effect of session, $F(4.38,2367.90) = 16.69$, $p < 0.001$, $\eta_p^2 = 0.030$, with significant increases of the scores from Session 1 to Session 2, $F(1,541) = 24.67$, $p < 0.001$, and from Session 2 to Session 3, $F(1,541) = 5.72$, $p = 0.017$. As expected, over the course of the six sessions, the patients' baseline alcohol-approach bias (see above) turned into an alcohol-avoidance bias, which was significantly different from zero (Session 6: $M = 28.54$, $SD = 118.62$, $t(542) = 3.09$, $p = 0.002$). However, this was true to a similar degree for successful

and relapsing patients: First, there was no significant main effect of outcome status, $F(1,541)=1.53$, $p=0.21$, $\eta_p^2=0.003$. Moreover, there was no difference between groups in how the compatibility score changed over time, yielding a nonsignificant interaction: $F(4.38,2367.82)=0.75$, $p=0.56$, $\eta_p^2=0.001$. As Figure 2 illustrates, the two groups showed highly similar changes in their compatibility scores, and for each session, the scores were very similar. In sum, the expected learning occurred, but to a similar degree in both groups.

## Change of approach tendencies across Alcohol-ApBM

Since the compatibility scores just described combine responses to both alcohol and nonalcohol stimuli, we also analyzed these stimuli separately with the same ANOVAs. The results yielded very similar results: The 2×6 ANOVA of the alcohol-approach tendencies showed a significant main effect of session, $F(4.56,2465.66)=22.70$, $p<0.001$, $\eta_p^2=0.040$, with the tendency to approach alcohol stimuli reducing over the course of sessions (Session 1: $M=-81.90$, $SD=168.50$ to Session 6: $M=-21.74$, $SD=101.77$). However, there was neither a significant main effect of outcome status, $F(1,541)=0.49$, $p=0.82$, $\eta_p^2<0.001$, nor a significant interaction, $F(4.56,2465.66)=0.39$, $p=0.84$, $\eta_p^2=0.001$. The same was true for the nonalcohol approach tendencies: We observed a significant main effect of session, $F(4.315,2334.61)=82.77$, $p<0.001$, $\eta_p^2=0.133$, with the tendency to approach nonalcoholic stimuli changing over training sessions from an approach tendency (Session 1: $M=-120.56$, $SD=163.36$) to a tendency to avoid nonalcoholic beverages (Session 1: $M=-6.80$, $SD=98.85$). Still, there was neither a significant main effect of outcome status $F(1,541)=1.22$, $p=0.27$, $\eta_p^2=0.002$, nor a significant interaction $F(4.315,2334.61)=0.71$, $p=0.59$, $\eta_p^2=0.001$. Again, the expected learning occurred, but to a similar degree in both groups. Table 2 shows an overview of the changes in compatibility scores and approach tendencies toward both alcohol and nonalcoholic stimuli.

## Success prediction by alcohol-ApBM behavior

To examine whether and how several aspects of learning observed over the course of the 6-session Alcohol-ApBM were predictive of success at 1-year follow-up, we conducted preregistered logistic regressions with predictors of learning as specified above in the Predictors of treatment success section. The results, however, did not reveal any significant predictors of later abstinence (1 year after treatment discharge, the standard long-term clinical outcome assessed in the clinic). More specifically, all regression models were nonsignificant, and this was accompanied by an absence of

**TABLE 2** Change of approach-avoidance tendencies throughout training sessions: Means (with SDs), overall and specified by outcome status after 1 year.

| | Training sessions, mean (SD) | | | | | |
|---|---|---|---|---|---|---|
| Characteristic | Session 1 | Session 2 | Session 3 | Session 4 | Session 5 | Session 6 |
| Compatibility score[a] | | | | | | |
| Overall | −38.65 (197.81) | 21.49 (162.22) | 40.64 (147.63) | 29.08 (132.34) | 26.05 (143.83) | 28.54 (118.62) |
| Per outcome status | | | | | | |
| Abstinence | −46.85 (207.10) | 21.18 (163.36) | 33.93 (147.78) | 28.13 (131.17) | 26.24 (147.56) | 28.05 (117.15) |
| Relapse | −21.12 (175.35) | 22.16 (160.21) | 54.99 (146.71) | 31.13 (135.16) | 25.64 (135.92) | 29.60 (122.05) |
| Alcohol-approach tendency[b] | | | | | | |
| Overall | −81.90 (168.50) | −68.05 (139.95) | −53.06 (126.02) | −29.95 (122.07) | −25.99 (125.38) | −21.74 (101.77) |
| Per outcome status | | | | | | |
| Abstinence | −77.64 (176.46) | −68.60 (144.51) | −53.34 (126.02) | −30.70 (122.97) | −27.53 (113.12) | −20.06 (99.70) |
| Relapse | −91.01 (150.14) | −67.31 (130.08) | −52.47 (126.41) | −28.34 (120.48) | −22.69 (125.38) | −25.32 (106.28) |
| Nonalcohol-approach tendency[b] | | | | | | |
| Overall | −120.56 (163.36) | −46.56 (142.28) | −12.42 (122.35) | −0.86 (108.20) | 0.07 (109.84) | 6.80 (98.85) |
| Per outcome status | | | | | | |
| Abstinence | −124.50 (168.84) | −47.22 (141.94) | −19.40 (123.90) | −2.57 (110.53) | −1.28 (110.01) | 7.98 (97.05) |
| Relapse | −112.13 (151.08) | −45.15 (143.42) | 2.53 (117.91) | 2.79 (103.27) | 2.98 (107.35) | 4.28 (102.84) |

*Note*: Changes in approach-avoidance tendencies through training sessions.

[a]Positive scores indicate a training-compatible, relative alcohol-avoidance tendency, and negative scores indicate a training-incompatible, relative alcohol-approach tendency, with larger scores implying stronger tendencies. A negative score at baseline would constitute the expected relative alcohol-approach tendency. Similarly, a positive score at the end of training would constitute the desired relative alcohol-avoidance tendency.

[b]The alcohol-approach tendency was computed as the mean RT of pushing alcohol minus the mean RT of pulling it. Similarly, the nonalcohol-approach tendency was computed as the mean RT of pushing nonalcohol minus the mean RT of pulling it. In both cases, a positive difference indicates an approach tendency (faster pulling than pushing).

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significance of all included learning parameters. A detailed overview of the preregistered logistic regressions can be found in the Data S1.

### Success prediction in relation to age and presence of comorbid psychopathology

To examine whether changes in approach-avoidance tendencies during ApBM might be related to the patients' age or the presence of comorbid affective psychopathology (following Eberl et al., 2013, and Salemink et al., 2022), we also computed regression analyses with these previously found moderators of abstinence, and regression analyses that combined them with the descriptors of learning as specified in the Analyses section. However, including these additional variables did not yield a significant prediction of abstinence, nor did the variables moderate the aforementioned null results. As the percentage of patients with a comorbid anxiety disorder was higher among the patients who stayed abstinent compared to the ones who relapsed (see Table 1), we added nonregistered regression analyses with the descriptors of learning (as specified in the Analyses section) interacting with the presence of a comorbid anxiety disorder. The results, however, did not yield a significant prediction of abstinence after 1 year. An overview of all aforementioned results can be found in the Data S1.

## DISCUSSION

The current study examined whether learning parameters during alcohol-approach bias modification (Alcohol-ApBM) would be predictive for abstinence after treatment. Specifically, we explored whether and how learning curves over the course of 6-session alcohol-avoidance training, when applied during regular abstinence-oriented treatment for alcohol use disorder (AUD), were predictive of abstinence at 1-year follow-up. Therefore, various parameters describing the learning trajectory during Alcohol-ApBM were extracted, including alcohol-approach tendencies using compatibility scores, separate approach tendencies for alcohol and nonalcoholic drinks at specific learning points during training, changes in tendencies across sessions, and variance across sessions. In addition, we included previously observed clinical and sociodemographic moderators of abstinence, aiming to achieve a comprehensive overview of changes in approach-avoidance tendencies during Alcohol-ApBM. Our results, however, did not reveal any significant predictors of later abstinence (1 year after treatment discharge, the standard long-term clinical outcome assessed in the clinic). More specifically, all regression models were nonsignificant, and this was accompanied by an absence of significance of all included learning parameters. Interestingly, however, descriptive analyses revealed a significantly higher proportion of patients with comorbid anxiety disorder to be abstinent after 1 year. The results of nonregistered analyses with the learning indices interacting with the presence of comorbid anxiety disorder, however, mirrored those of the preregistered analyses: All regression models were nonsignificant, which was accompanied by an absence of significance of all included learning parameters and their interactions with the presence of a comorbid anxiety disorder. Simultaneously, however, control analyses verified the presence of an overall alcohol-approach bias before treatment, which, however, did not statistically differ between the groups. Moreover, only the patients who would later be abstinent showed a statistically significant alcohol-approach bias before treatment. Patients who would later relapse did show an alcohol-approach bias which, however, was not statistically significant.

Likewise, we found an overall change of the alcohol-approach bias into an avoidance bias of alcohol, but again both in patients who would be abstinent 1 year later and in those who would not. In sum, although Alcohol-ApBM successfully modified alcohol-related approach-avoidance tendencies (as seen in the experimental conditions in previous clinical RCTs), we did not find any evidence for the hypothesis that learning during Alcohol-ApBM could serve as a predictor of abstinence 1 year later.

Although our finding of an overall training effect during Alcohol-ApBM is in accordance with earlier studies (Eberl et al., 2013, 2014; Manning et al., 2021; Rinck et al., 2018; Wiers et al., 2011), the current study could not unravel novel predictors of abstinence based on how learning progresses during Alcohol-ApBM. Given the fact that factors contributing to relapse in AUD encompass various areas (e.g., Sliedrecht et al., 2019), previous studies aimed to identify patient-related and sociodemographic moderators with potential predictive capacity. Promising moderators from previous studies were found by Eberl et al. (2013), showing that older patients benefitted more from Alcohol-ApBM, particularly when they had a stronger approach bias before Alcohol-ApBM. Similarly, Salemink et al. (2022) found that Alcohol-ApBM was more effective for patients who met criteria for a comorbid anxiety or affective disorder. However, as neither variable has been replicated, it cannot be used to select patients. Moreover, these findings do not tell us why and how ApBM works, neither in general nor in these sub-groups.

Changing the alcohol-approach bias is the frequently proposed working mechanism of Alcohol-ApBM, assumed to reduce consumption and prevent relapse (Eberl et al., 2013, 2014; Manning et al., 2022; Rinck et al., 2018; Wiers et al., 2011, 2013). Next to Eberl et al. (2013), who found support for this working mechanism of Alcohol-ApBM, Gladwin et al. (2015) found that increased avoidance bias for alcohol stimuli as measured by the IAT partly mediated the improved clinical outcome of TAU, including Alcohol-ApBM. Therefore, the current study concentrated on changes of the alcohol-approach tendency that occur during Alcohol-ApBM. If the quality of the changes determines later success, we should be able to find learning differences between patients who remain abstinent and those who relapse. We had also hoped to identify relevant individual differences in learning to later tailor the training to the patients' individual needs. Currently, patients who probably will not benefit from Alcohol-ApBM cannot be identified reliably; therefore, current guidelines recommend Alcohol-ApBM for all AUD patients.

A potential explanation for this might be the low reliability of the RT difference scores we used to compute the learning parameters.

In sum, the specific learning curves and patterns studied here did not predict abstinence or relapse. This seems to contradict the assumption that a change of the alcohol-approach bias into an avoidance bias is the crucial component of Alcohol-ApBM. This assumption is based, however, on comparing changes during active Alcohol-ApBM versus sham Alcohol-ApBM. Evidence for this assumption is limited in previous RCTs and nonexistent in this study. Moreover, in this study, contrary to previous RCTs, all patients received active Alcohol-ApBM as part of TAU. Within this group of patients, the indicators of learning performance that we measured may have been unable to predict relapse because the reasons for relapsing may be completely independent of what happened during training months before. Moreover, the current study's focus on learning during ApBM is based on the associative learning account of ApBM, while other forms of learning might better explain the effects of Alcohol-ApBM. Recently, the associative learning account has been challenged by an inferential learning account (Van Dessel et al., 2019) and by a devaluation account (Garfield et al., 2022). These definitely deserve further investigation.

It must also be kept in mind that the patients included in the current study may not be representative of all AUD patients, not even of the ones treated in the same clinic at the same time. In order to answer the current research question, we used data only from patients for whom we had both complete training data and information about their abstinence status at one-year follow-up. One might argue that we should have included patients with incomplete trainings to determine whether they are more likely to relapse. We decided against this because we could not safely determine whether data sets were incomplete because of missed training sessions or because of errors during data saving. Previous studies, however, because they were RCTs using intention-to-treat principles, have also included patients who dropped out of the training or who could not be reached at follow-up. Compared to the samples of those earlier studies, the current sample shows very similar values regarding the demographic and clinical variables (see Table 1). Nevertheless, the current study is based on a subset of patients who conform to an ideal research situation (full effect of the independent variable "training" and full information about the dependent variable "success"), which hardly reflects the typical clinical situation of patients.

Other limitations of the current study are also worth mentioning. First, we did not have information about the training sessions other than the saved responses with the joystick during training. Second, as alcohol-approach bias was measured at the beginning of each of the six sessions, we do not know how much the sixth session added to the first five sessions. Third, the lack of a control group prevents us from concluding whether the Alcohol-ApBM had the intended relapse-preventing effect in addition to the observed effect on alcohol-approach tendencies. However, we believe that previous studies have yielded sufficient evidence for this assumption (Eberl et al., 2013, 2014; Manning et al., 2016, 2021, 2022; Rinck et al., 2018; Salemink et al., 2022; Wiers et al., 2011). Fourth, the large standard deviations of the approach biases, based on RT data derived from the ApBM training, might have contributed to their low reliability. Similarly, the approach biases that served as predictors in this study were computed as difference scores, which might also have contributed to their low reliability. Future research should thoroughly examine these issues. Moreover, though there was a significantly higher proportion of patients with a comorbid anxiety disorder to be found abstinent than relapsed at one-year follow-up (see Table 2), this was based on a very small number of patients. Correspondingly, statistical power to examine moderation with the learning indices was very poor, calling for a replication in a well-powered sample.

Note that, though Salemink et al. (2022) found Alcohol-ApBM to be more effective to promote abstinence in patients with a comorbid anxiety or affective disorder, they employed an active Alcohol-ApBM and a Sham-ApBM training, whereas the patients in the present study solely received active Alcohol-ApBM as part of TAU. Therefore, contrary to the present study, the finding of Salemink et al. (2022) might have also been influenced by having the contrast of active versus control training. This was impossible in the present study as Alcohol-ApBM was part of TAU. Finally, time to follow-up might be associated with relapse, as we used abstinence data, which were assessed during standard procedures of clinical practice. These procedures followed the guidelines of the German Addiction Society, which leave some room around the requested 12-month follow-up. Hence, and combined with the fact that the present study included only patients who were reached during these procedures, we cannot make any inference about whether time to follow-up might have impacted relapse after discharge from treatment.

In sum, this study aimed to unravel whether and how learning performance during Alcohol-ApBM would be predictive for abstinence after treatment. Despite learning taking place during Alcohol-ApBM, we could not derive any predictors from the training itself that would predict who will remain abstinent and who will not 1 year after treatment. Therefore, given that previous studies showed the relapse-preventive effect of Alcohol-ApBM, we still advise giving Alcohol-ApBM to all patients, as a part of their standard inpatient treatment for AUD.

## ACKNOWLEDGMENTS

We would like to thank the reviewers for helpful comments and all patients who participated in the study.

## CONFLICT OF INTEREST STATEMENT

Johannes Lindenmeyer was Chief Executive Officer (CEO) of the clinic at the time the study was conducted. All other authors declare that they have no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

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

**How to cite this article:** Schenkel, E.J., Schöneck, R., Becker, E.S., Wiers, R.W., Lindenmeyer, J. & Rinck, M. (2024) Long-term effects of alcohol-avoidance training: Do changes in approach bias predict who will remain abstinent? *Alcohol: Clinical and Experimental Research*, 48, 1979–1990. Available from: https://doi.org/10.1111/acer.15431