European Addiction Research

Research Article

Eur Addict Res
DOI: 10.1159/000537811

Received: August 28, 2023
Accepted: February 2, 2024
Published online: March 19, 2024

Implementing Approach-Bias Modification as Add-On to Varieties of Clinical Treatment for Alcohol Use Disorders: Results of a Multicenter RCT

Edwin J. Schenkel[a, b, c] Mike Rinck[c] Reinout W. Wiers[d] Eni S. Becker[c]
Stephan Muehlig[e] Robert Schoeneck[b] Johannes Lindenmeyer[a, b]

[a]Department of Psychology, Medizinische Hochschule Brandenburg Theodor Fontane, Neuruppin, Germany; [b]Salus Clinic Lindow, Lindow, Germany; [c]Behavioural Science Institute, Radboud University, Nijmegen, The Netherlands; [d]Department of Psychology, Addiction Development and Psychopathology (ADAPT) Lab, ABC and Yield Research Priority Areas, University of Amsterdam, Amsterdam, The Netherlands; [e]Department of Psychology, Chemnitz University of Technology, Chemnitz, Germany

Keywords
Cognitive bias modification · Alcohol-approach bias · Alcohol dependence · Relapse prevention

Abstract
Introduction: Abstinence rates after inpatient treatment for alcohol use disorder (AUD) are modest (1-year rate around 50%). One promising approach is to re-train the automatically activated action tendency to approach alcohol-related stimuli (alcohol-approach bias) in AUD patients, as add-on to regular treatment. As efficacy has been demonstrated in well-controlled randomized controlled trials, the important next step is to add alcohol-approach-bias modification (alcohol-ApBM) to varieties of existing treatments for AUD. Therefore, this prospective, multicenter implementation-RCT examined whether adding alcohol-ApBM to regular treatments (various abstinence-oriented treatments including both individual and group-based interventions) would significantly increase abstinence rates compared to receiving regular treatment only, in a variety of naturalistic settings with different therapeutic approaches. ***Methods:*** A total of 1,586 AUD inpatients from 9 German rehabilitation clinics were randomly assigned to receive either ApBM in addition to regular treatment or not. Training satisfaction of patients and therapists was measured after training. Success rates were determined at 3, 6, and 12 months post-treatment. ***Results:*** Return rates of the post-treatment assessments varied greatly between clinics, often being low (18–76%). Nevertheless, ApBM significantly increased success rates after 3 months. After 6 and 12 months, the differences were not significant. ApBM was evaluated mostly positively by patients and therapists. ***Discussion/Conclusion:*** ApBM was an effective add-on to regular treatment of AUD at 3 months follow-up, across a variety of AUD treatment settings. However, low return rates for the clinical outcomes reduced the effect size of ApBM considerably. The application of ApBM proved feasible in varying clinical settings, offering the opportunity to modify automatic processes and to promote abstinence.

karger@karger.com
www.karger.com/ear

Karger
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Correspondence to:
Edwin J. Schenkel, edwin.schenkel@ru.nl

Introduction

Alcohol use disorder (AUD) is a significant health burden [1], causing a wide range of medical, psychological, interpersonal, and economic problems [2]. These problems threaten health, life expectancy, and participation in the workplace [3]. To reduce the detrimental consequences of AUD while aiming for long-term abstinence and reintegration into the work force, most treatments in Europe involve a combination of cognitive-behavioral therapy (CBT) [4] and motivational interviewing [5], sometimes supplemented with community reinforcement [6]. Also, psychodynamic therapy is sometimes still applied [7]. Nevertheless, relapse after treatment remains frequent [8].

Arguably, this has been sustained by insufficient implementation of new techniques, based on evidence from recent clinical RCTs [9, 10]. During the past decades, research in AUD has highlighted the role of automatically activated processes in the development and maintenance of AUD [11] as well as in the maintenance of abstinence after treatment [12]. Prominent examples of such processes are selective attention for and attentional capture by substance-related stimuli (attentional bias) [13] and the action tendency to approach alcohol cues (approach bias) ([14, 15]; for an in-depth discussion of the role of automatically activated processes in AUD, see [16]). In clinical practice, however, these processes are rarely targeted, and treatments focus on the modification of cognitively controlled cognitive-motivational processes (e.g., "It is important for me to remain abstinent in order to prevent divorce"). More generally, there is a gap between the existence of evidence-based treatments and their implementation into clinical practice [10, 17].

The interplay between controlled and automatic processes in addiction was emphasized by translational etiological models [11]. According to them, addictive behaviors are characterized by an imbalance between strong impulsive reactions to drug-related cues versus relatively weak control over these impulses [18, 19]. These processes may then give rise to the tendency to approach alcohol cues in the environment (the approach bias; [16, 20, 21]). The approach bias toward alcohol was found to be related to the consumption of alcohol [16, 21], and it likely contributes to the maintenance of AUD and to relapse after treatment [12]. Although there is a theoretical debate about the nature of the processes involved (e.g., [22–24]), there is little doubt that automatic processes play an important role in the etiology and maintenance of addictions [11, 25].

To reduce the influence of the alcohol-approach bias on patients with AUD, a specific form of cognitive bias modification was developed, called alcohol-approach-bias modification or alcohol-ApBM [16], in the remainder here referred to as ApBM. A first clinical randomized-controlled trial (RCT) showed that ApBM in abstinent AUD patients lead to increased abstinence rates 1 year after treatment discharge with 13% [20]. Therefore, patients completed 4 sessions of ApBM (4 × 15–20 min), in addition to their regular abstinence-oriented treatment. In the training, they were to push pictures of alcoholic beverages away with a joystick and pull nonalcoholic beverages closer. The beneficial relapse-prevention effect of ApBM was replicated in three additional phase-III-RCTs in the same clinic in Germany [26–28]. In addition, two Australian studies successfully applied a slightly different variety of ApBM during alcohol withdrawal treatment [29, 30].

Despite the promising effects of ApBM, its implementation is still limited. Therefore, it is important to test the implementation potential of this new add-on to AUD treatment in everyday practice as promising effects in well-controlled clinical RCTs do not always generalize to efficacy in clinical practice [10, 31]. ApBM offers a cheap and easily administrated addition to the existing treatments for AUD, and it addresses automatically activated processes that are not easily changed by existing treatment protocols.

Therefore, this multicenter-clinical RCT examined whether ApBM training as an add-on to treatment-as-usual (TAU) would significantly increase success rates compared to receiving TAU-only, across various inpatient clinics in naturalistic settings. In all of these clinics, individualized treatment packages consisted of 3 months of abstinence-oriented therapy, including both individual and group therapy based on CBT or psychodynamic therapy, complemented by adjunct treatments based on the patients' needs. All treatments followed the standards and guidelines of the German Addiction Society. Our main goal was to test if adding ApBM to different German varieties of TAU would increase abstinence rates. Success was assessed after 3, 6, and 12 months after discharge from treatment (see the definition of success and relapse below in the Assessment and Outcome Measures section). Following the results of previous studies, we preregistered to expect higher success rates for patients after TAU + ApBM than after TAU-only. Further, we explored the acceptance of ApBM by patients and therapists because novel treatments are often accepted as part of research projects but less so in daily practice when they require additional resources from therapists and patients [8, 9, 10].

Methods

Participants

Participants were 1,586 currently abstinent alcohol-dependent patients from 9 participating clinics. All clinics were certified medical rehabilitation clinics specialized in the treatment of addictions, with each clinic treating at least 160 patients per year. The clinics applied different therapeutic approaches (CBT, psychodynamic therapy). Treatment duration ranged from 8 to 16 weeks. To participate in the study, all clinics affirmed that they had follow-up questionnaire return rates of at least 65%, in compliance with the guidelines of the German Addiction Society.

Patients were informed about the study and their possibility to withdraw from it without incurring any disadvantages in their treatment. We included every patient with a primary diagnosis of AUD (F10.2 in ICD-10) [32], as assessed during the clinics' standard intake procedure. Exclusion criteria were additional addiction diagnoses except for tobacco dependence, insufficient command of the German language, neurocognitive health impairments, and use of anti-craving drugs. Included patients signed written informed consent and were randomly assigned to receive TAU + ApBM or TAU-only. The study protocol was reviewed and approved by the Ethics Committee of the Department of Human and Social Sciences of the Technical University Chemnitz, Germany (#02022011). This clinical trial was registered in the ISRCTN Registry (ID: ISRCTN18432640), with the only deviation being that we had aimed for 10 clinics, but only 9 could be included. Figure 1 shows a CONSORT diagram of the participant flow. The TAU + ApBM group and the TAU-only group did not differ in any of the variables shown in Table 1.

Procedure Overview

After the first 4 weeks of treatment, patients assigned to TAU + ApBM started with ApBM as part of their treatment, whereas patients in the control group received TAU-only. The naturalistic setting of the present study prevented blinding of the therapists and patients. Patients assigned to TAU + ApBM were scheduled to complete 6 sessions of training within the next 2 weeks (15–20 min each). TAU consisted of various forms of abstinence-oriented therapy, including both individual and group therapy. After finishing ApBM, both patients and therapists completed questionnaires to evaluate ease, feasibility, and practicability of the ApBM.

Three, 6, and 12 months after discharge, participants received a standard follow-up questionnaire, asking whether they had continuously been abstinent during the past 3, 6, or 12 months, respectively. If they denied, they were asked additional questions regarding the type of drugs used (e.g., alcohol, hypnotics, sedatives, stimulants), the number and duration of relapse(s), and the way they ended the last relapse. At all follow-up timepoints, 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. When patients were contacted by phone, this was done by therapists or interns blind to treatment condition. At 3 months, 831 were reached (441 TAU + ApBM, 390 TAU-only), after 6 months 716 (379 and 337, respectively), and after 12 months 752 (385 and 367, respectively). Note that there were big differences between clinics, ranging from 21% to 66% at 1-year follow-up, for example (Table 2). However, the retention of the two groups never differed [all $\chi^2(1) < 3.74$, all $p > 0.05$]. For a detailed overview per clinic, see Table 2.

Assessment and Outcome Measures

Before admittance to one of the participating clinics, the German Pension Fund that finances rehabilitation treatment for AUD in Germany verified the presence of an AUD according to ICD-10 criteria [32]. Then, at each participating clinic, the presence of a clinical diagnosis of AUD was confirmed for each patient, with the same criteria.

Previous studies have repeatedly shown a small, but clinically and statistically significant, effect of alcohol-ApBM training on relapse rates 1 year after treatment discharge, by approximately 10% [20, 26, 27]. We therefore aimed for a minimal sample size of 1,260 patients to yield conventional power of $1-\beta = 0.80$ with $p = 0.05$ for the detection of a small effect on relative frequencies ($w = 0.10$). The achieved sample size of 1,586 patients exceeded the minimal sample size, yielding excellent statistical power of $1-\beta = 0.94$, at least for the previously achieved return rates of about 80%.

The preregistered, main outcome variables of this RCT were measured after 3, 6, and 12 months. They were coded as a binary outcome variable (successful outcome or not), using conservative intention-to-treat (ITT) principles. Following the DGSS-4 standard defined by the German Addiction Society ("Deutsche Gesellschaft für Suchtforschung, Standard" DGSS-4 [33]), successful outcome was defined as no relapse or a single lapse (shorter than 3 days, ended by the patient without further negative consequences, followed by at least 4 weeks of abstinence until the assessment). Failure was defined as everything else: relapse, death, no contact, or refusal to provide information (as in [26–28]). For comparison, we added an explorative, more liberal definition of treatment success, namely, DGSS-1. By DGSS-1 standards, only the patients who were reached at follow-up are included in the analyses. For each follow-up timepoint, the success rates were analyzed for both DGSS-4 and DGSS-1 standards, using the multilevel general linear mixed-model approach described in detail in the online supplementary materials (for all online suppl. material, see https://doi.org/10.1159/000537811). The multilevel analysis controls for the fact that patients were randomized in different treatment settings (middle level). Given the nature of the generalized linear mixed-model approach, we report odds ratios indicating the probability that patients who received TAU + ApBM will be more likely to be successful at each follow-up than those who received TAU-only. Complementarily, we also report the success rates of the two groups. Our secondary outcomes were the patients' and therapists' evaluations of the ApBM, which we report descriptively below.

Training Evaluation Questionnaires

After training, the TAU + ApBM group answered 12 questions addressing the subjective evaluation of acceptance, ease, feasibility, and practicability of the ApBM. Their therapists received a comparable, slightly reformulated version of the same questions. English translations of the questionnaires can be found in the online supplementary materials.

Experimental Groups and Alcohol-ApBM Training

In the present RCT, permuted block randomization [34] was used per clinic to randomly assign patients to TAU + ApBM or TAU-only. Patients assigned to the TAU + ApBM group ($n = 805$) were scheduled to receive 6 sessions of active ApBM next to regular

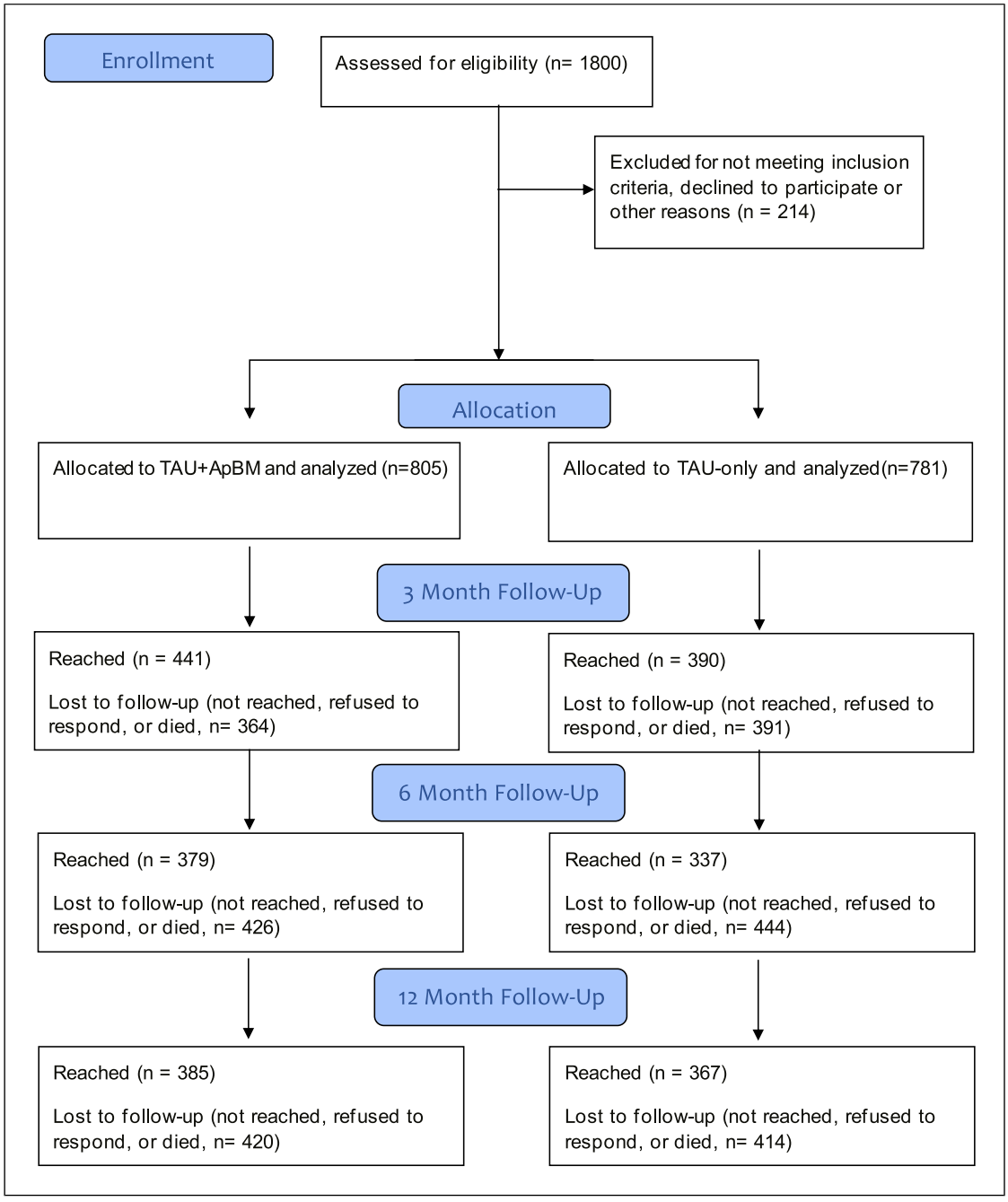

Fig. 1. CONSORT diagram. The sample sizes shown here relate to analyses of the primary outcome variables "success at 3-, 6-, and 12-month FU." ITT is the intention-to-treat analysis using DGSS-4 rules (includes all 1,586 randomized patients, at each follow-up). The DGSS-1 analysis includes only the patients reached at follow-up.

treatment. Patients in the control condition received TAU-only (n = 781). For ApBM, we used the joystick-based alcohol-avoidance training employed in previous studies (see [26–28]). The picture materials were adapted by using pictures of 20 well-known beverages sold in all of Germany (10 alcoholic, 10 non-alcoholic). In each of the 15-min sessions, participants used a joystick to push away 100 pictures of alcohol beverages and pull closer 100 pictures of non-alcoholic beverages. Each training session started with 40 assessment trials during which both drink types were approached and avoided ten times each.

Table 1. Mean characteristics of the sample: means (with SDs) and significance of group differences

Characteristic	All patients (N = 1,586)	TAU + ApBM (n = 805)	TAU-only (n = 781)	p value
Duration of treatment, days	89.60 (27.32)	90.15 (26.65)	89.06 (27.97)	0.49
Age, years	47.10 (10.02)	47.33 (10.11)	46.87 (9.93)	0.40
Age (range)	19–76	19–76	20–76	
Gender, % female	37	35	38	0.46
Education level[a]	2.91 (1.57)	2.84 (1.54)	2.99 (1.59)	0.14
Unemployment, %	38	37	38	0.84
Psychiatric comorbidity[b], %	46	46	47	0.72

Age was analyzed with a two-group ANOVA. The remaining variables were analyzed with χ^2 tests. Standard deviations are presented in parentheses. For all analyses, p values are two tailed, and alpha is set at 0.05. [a]Education level was scored on a scale from 1 (only 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]Comorbidities included a wide range of psychiatric disorders ranging from other substance use disorders to affective disorders and personality disorders.

Table 2. Overview of return rates at follow-ups after 3, 6, and 12 months and numbers of subjects at baseline: absolute numbers and percentages

Clinic	FU-3				FU-6				FU-12			
	TAU plus ApBM		TAU-only		TAU plus ApBM		TAU-only		TAU plus ApBM		TAU-only	
	n (%)	base	n (%)	base	n (%)	base	n (%)	base	n (%)	base	n (%	base
1	42 (48)	86	44 (43)	101	31 (36)	86	35 (34)	101	34 (39)	86	33 (32)	101
2	56 (69)	81	48 (62)	77	57 (70)	81	47 (61)	77	56 (69)	81	48 (62)	77
3	36 (44)	81	20 (33)	61	30 (37)	81	15 (24)	61	37 (46)	81	33 (45)	61
4	32 (28)	113	28 (25)	112	28 (25)	113	20 (18)	112	23 (20)	113	25 (22)	112
5	40 (59)	68	31 (42)	74	29 (42)	68	37 (50)	74	37 (54)	68	45 (60)	74
6	57 (69)	83	59 (69)	86	30 (36)	83	37 (44)	85	45 (54)	83	54 (63)	85
7	34 (38)	90	35 (39)	89	31 (34)	90	31 (35)	89	39 (43)	90	36 (40)	89
8	74 (73)	102	57 (76)	75	74 (73)	102	50 (67)	75	67 (65)	102	46 (61)	75
9	70 (69)	101	68 (64)	106	69 (68)	101	65 (61)	106	47 (46)	101	47 (44)	106

Results

We report the effect of ApBM on the success rates at the three follow-ups regarding our main preregistered outcome variable DGSS-4, involving all 1,586 randomized patients. On average, the 805 patients in the TAU + ApBM group finished 5.84 sessions of ApBM, with 750 of them completing all 6 sessions. For success rates per clinic and assessment point, see Table 3. Because of the low return rates, the corresponding analyses involving completers only did not yield any significant effects. Their results are reported in the online supplementary materials.

Treatment Outcome: Effects of ApBM on Success Rates at 3-, 6-, and 12-Month Follow-Up

Three-Month Follow-Up

Clinical outcomes were obtained from 52% of the patients, with an overall success rate of 44.9%. The ITT analyses of the success rates yielded a significant difference between the success rates of the TAU + ApBM group and the TAU-only group according to DGSS-4 criteria, $\chi^2(1) = 4.61$, $p = 0.035$. The TAU + ApBM group was more likely to be abstinent after 3 months, OR = 1.12, CI [1.01, 1.24]. Their success rate (43.0%, CI [33.8%, 51.7%]) was higher than the rate for the TAU-only group (37.1%, CI [28.9%, 46.1%]).

Table 3. Success rates at follow-ups after 3, 6, and 12 months: absolute numbers and percentages

Clinic	FU-3		FU-6		FU-12	
	TAU + ApBM *n* (%)	TAU-only *n* (%)	TAU+ ApBM *n* (%)	TAU-only *n* (%)	TAU + ApBM *n* (%)	TAU-only *n* (%)
Clinic 1	33 (38)	33 (32)	26 (30)	28 (28)	29 (34)	24 (24)
Clinic 2	42 (52)	36 (47)	46 (57)	32 (42)	66 (57)	34 (44)
Clinic 3	33 (41)	16 (26)	27 (33)	13 (21)	34 (42)	25 (41)
Clinic 4	31 (27)	22 (20)	25 (22)	17 (16)	19 (17)	17 (15)
Clinic 5	35 (52)	28 (38)	25 (37)	33 (45)	25 (37)	35 (47)
Clinic 6	52 (63)	51 (60)	25 (30)	34 (40)	38 (46)	43 (51)
Clinic 7	30 (33)	34 (38)	28 (31)	29 (33)	34 (38)	31 (35)
Clinic 8	65 (74)	48 (64)	58 (57)	42 (56)	59 (58)	37 (49)
Clinic 9	65 (64)	59 (55)	57 (57)	58 (54)	35 (35)	41 (38)

Six-Month Follow-Up

Outcomes were obtained from 45% of the patients, with an overall success rate of 32.5%. Here, the ITT analysis according to DGSS-4 criteria of the success rates did not show a significant difference between the two groups, $\chi^2(1) = 2.47$, $p = 0.103$, CI [0.98, 1.21], OR = 1.09. The success rate of the TAU + ApBM group (33.8%, CI [26.8%, 41.5%]) was not significantly higher than the rate of the TAU-only group (30.0%, CI [23.5%, 37.5%]).

Twelve-Month Follow-Up

Outcomes were obtained from 47% of the patients, with an overall success rate of 38.2%. Again, the ITT analysis according to DGSS-4 criteria of the success rates did not show a significant difference between the two groups, $\chi^2(1) = 0.82$, $p = 0.378$, CI [0.95,1.16], OR = 1.05. The TAU + ApBM group (39.6%, CI [31.5%, 48.3%]) did not show a significantly higher success rate than the TAU-only group (37.3%, CI [24.4%, 46.0%]).

Training Evaluations

In total, 695 patients (86.3% of the TAU + ApBM group) and 54 therapists evaluated the training (see Table 4). Overall, patients were highly satisfied with the ApBM training. Specifically, the training was perceived as clear and easy and as fitting into the program of the clinic. About 40% of the patients found the training beneficial to prevent relapse, and the majority of them recommended it for further use (85%). These positive evaluations were shared by the therapists. Most importantly, they found the training clear and easy to execute, about 45% saw it as beneficial to prevent relapse, and 73% recommended its future use.

Discussion

This multicenter implementation RCT examined whether adding alcohol-ApBM to regular treatment supports abstinence after treatment across various naturalistic settings. Treatment success was assessed 3, 6, and 12 months after treatment. Following previous monocenter RCTs [26–28], we expected increased success rates in patients who had received alcohol-ApBM next to TAU. Additionally, to assess the acceptance and feasibility of alcohol-ApBM, and to promote its dissemination, the participating patients and their therapists were asked to evaluate the training.

As predicted, success rates were increased by ApBM; however, this effect was statistically significant only after 3 months, when tested in the ITT analysis according to DGSS-4 criteria. Moreover, it was slightly smaller (5.9%) than the effects observed in previous studies after a year [26–28]. When adhering to DGSS-1 criteria, including only patients who were reached after 3 months, there was still a numerical advantage for TAU + ApBM compared to TAU-only, but this was not statistically significant. Similarly, at follow-ups after 6 and 12 months, neither the ITT analyses nor the DGSS-1 analyses yielded a significant advantage for TAU + ApBM, although the observed success rates always favored TAU + ApBM.

The evaluations of the training by patients and therapists were predominantly positive, with the majority of them recommending ApBM as regular treatment for AUD. These positive results notwithstanding, a significant proportion of patients (60%) and therapists (55%) did not believe that ApBM could reduce relapse rates,

Table 4. Evaluations of the Alcohol-ApBM training by patients and therapists: percent agreement to statements

The training ...	Patients (N = 695)	Therapists (n = 54)
... has a clear setup, %	98.3	95.8
... is easy to execute, %	95.5	100.0
... has perceivable positive effects, %	70.5	76.5
... fits into the clinic's program, %	91.2	79.6
... fits into the clinic's therapeutic approach, %	69.6	75.0
... shows progress in terms of reaction times, %	87.9	32.7
... is beneficial to prevent relapse, %	40.2	45.9
... transfers to daily behavior, %	29.1	8.2
... is easier than regular treatment, %	46.7	48.2
... is no alternative to regular treatment, %	71.0	87.7
... is difficult to participate in, %	10.5	18.4
... is recommended for further use in treatment, %	85.7	73.6

even though it did so significantly at 3-month follow-up. Therefore, we advise that the implementation of computerized cognitive trainings such as ApBM into clinical practice should be preceded by thorough information given to both therapists and patients. This should be supported by referring to the results of previous RCTs (e.g., the results reported in [26–28]). Similar recommendations were given by a recent study examining patients' perceptions of cognitive bias modification for anxiety [35].

The present study lends empirical support to ApBM as part of regular treatment for AUD by showing its effectiveness in everyday practice in clinics that vary in therapeutic approach, extending the results of previous monocentric RCTs [26–28, 36]. Furthermore, ApBM was easily implemented and positively evaluated by both patients and therapists. The positive evidence for ApBM found in earlier RCTs [26–28, 36] led to its inclusion in treatment guidelines in Germany [37] and Australia [38]. However, being included in treatment guidelines does not necessarily imply that a new treatment is implemented in daily practice. Showing that a new treatment like ApBM is not only evidence-based and effective, but also feasible, acceptable, and recommendable in daily practice, will hopefully foster its implementation, thereby giving more patients access to it.

These positive conclusions notwithstanding, it must be noted that the current study also has its limitations. The small effects observed in the success rates illustrate the most severe limitation: low return rates at all follow-ups. Unlike earlier RCTs, where 70–85% of patients could be reached after 12 months, and in contrast to the agreements made with the clinics before participation, only 52%, 45%, and 47% were reached after 3, 6, and 12 months, respectively. Moreover, these percentages represent the means; in some cases, not even 30% were reached. In general, low return rates have serious detrimental effects on the observed effect sizes and on the power of RCTs. The lower the return rates, the larger the number of patients for whom the effect of ApBM is artificially set to zero. Hence, the effect size of 6% observed here is likely to be an underestimate. In hindsight, we may have underestimated the extra time investment required by the follow-ups for clinics where these were not already implemented. A lesson we learned for future multicenter trials is to guide and accommodate the process of follow-up assessments more carefully.

The follow-up durations, return rates, and results of the present study are comparable to the ones reported by Manning and colleagues [29] who added ApBM to withdrawal treatment. Therefore, success rates were also increased by ApBM at 3 months after discharge from treatment but not at 6 or 12 months.

Another potential limitation might be seen in the control group chosen for this study. Strictly speaking, comparing TAU-only to TAU + ApBM only shows that the addition of any new treatment will be better than "sticking to the usual." However, the active ApBM used here has been compared to structurally similar sham trainings and TAU-only conditions before [26–29]. In all these studies, active training increased abstinence rates more than sham training, and sham training was no better than TAU-only. Second, the TAU-only control condition fits the current research question perfectly, since we aimed to determine the effects of

adding ApBM to TAU, compared to leaving TAU as it is.

Moreover, this multicenter trial focused solely on the clinical effectiveness of ApBM as an add-on to regular treatment across different therapeutic approaches. Hence, we did not require the participating clinics to share reaction times or error rates of the training sessions. Therefore, approach-bias scores and their change across sessions could not be computed (for the calculation, see [27]). As a result, we could not test whether the change of the approach bias into an avoidance bias mediates ApBM's relapse-preventing effect. So far, only one clinical monocenter RCT by Eberl et al. [26] established evidence for this, whereas others [20, 27, 28] did not, possibly because of suboptimal measurement properties of the assessment instrument used. Therefore, despite ApBM's value in promoting abstinence after inpatient treatment, future studies should apply stricter methodological standards to test the proposed underlying working mechanism of ApBM [39, 40].

This study also has multiple strengths. It is the first multicenter study in a naturalistic setting that examined the effects of adding alcohol-ApBM to regular inpatient treatment for AUD, in clinics varying in therapeutic approach. Further, to assess the time course of the ApBM effects in more detail than previously possible, treatment success was measured 3, 6, and 12 months after discharge (as in [29]). Finally, the acceptance and feasibility of ApBM was evaluated by both patients and therapists.

The results of our study highlight the effectiveness and feasibility of this evidence-based add-on treatment in clinical practice under realistic circumstances. Importantly, ApBM was positively evaluated by both patients and therapists and showed its effectiveness in reducing relapse rates after treatment. This effect, however, was significant only at 3 months after treatment, and the low return rates achieved under realistic clinical circumstances limited further insights into the long-term clinical value of the training. Note that although the effect is small (6% after 3 months, which translates into a number needed to treat of 17), it is still in the range of current medication of AUD (see [41]), and likely an underestimation, given the high dropout rates. This illustrates the need for more support of applied clinical research. With increased return rates at follow-up measurements, for instance, it will be possible to test the long-term effectiveness of novel treatments in real clinical settings.

Acknowledgments

The authors would like to thank all patients and therapists who participated in the study, as well as the collaborating clinics (in alphabetical order, not corresponding to the order 1–9 in the article): AHG Klinik Toenisstein, AHG Klinik Wilhelmsheim, Bernhard-Salzmann-Klinik, Fachklinik Fredeburg, Fachkrankenhaus Hansenbarg, Fontaneklinik Motzen, Paracelsus Wiehengebirgsklinik, salus klinik Friedrichsdorf, and salus klinik Huerth. We are also grateful to Natalie Becht and Silvia Hoffmann who supervised data collection in the collaborating clinics.

Statement of Ethics

This research was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Department of Human and Social Sciences of Technical University Chemnitz, Germany (#02022011). All patients provided informed consent.

Conflict of Interest Statement

E.S.B., M.R., R.W.W., S.M., R.S., and E.J.S. declare that they have nothing to disclose. At the time of data collection, J.L. was CEO of the Salus Clinic Lindow, which did not participate in the study, but served as the coordinating clinic of the current multicenter trial.

Funding Sources

The study was supported by a grant from the German Pension Fund (#8011-106-31/31.96.2), awarded to J.L.

Author Contributions

J.L., E.S.B., M.R., R.W.W., and S.M. designed the study and wrote the protocol. E.J.S. performed the statistical analyses and wrote the first draft of the manuscript. M.R., J.L., R.W.W., S.M., and R.S. provided critical feedback on the first version of the manuscript. All seven authors provided comments and edits on subsequent revisions of the manuscript and have approved the final manuscript for submission.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons (they are sensitive patient data) but are available from Mike Rinck (mike.rinck@ru.nl) upon reasonable request.

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