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The Clinical Efficacy of Mindfulness-Based Treatments for Alcohol and Drugs Use Disorders: A Meta-Analytic Review of Randomized and Nonrandomized Controlled Trials

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Keywords
Alcohol use disorder · Drugs use disorders · Mindfulness · Incremental effectiveness · Primary and secondary outcomes · Meta-analysis

Abstract
Introduction: The current study aims to evaluate if and to what extent mindfulness-based interventions (MBIs) could promote an incremental effectiveness compared to interventions usually provided in clinical practice to treat Alcohol and Drugs Use Disorders. In line with this aim, we accomplished a meta-analytic review of randomized and nonrandomized controlled trials, considering primary and secondary outcomes that comprehensively operationalize treatment efficacy. ***Methods:*** We conducted the online research up to August 31st 2017. Adequate procedures for Cohen's *d* computation were applied. Heterogeneity indexes, moderators, bias of publication, and Orwin's fail-safe number were also estimated. ***Results:*** Thirty-seven studies were included (*n* = 3,531 patients). We observed null effect sizes for attrition rate and overall mental health. Small effect sizes were detected in abstinence, levels of perceived stress, and avoidance coping strategies. Moderate effect sizes were revealed in anxiety and depressive symptoms. Large effect sizes were associated to levels of perceived craving, negative affectivity, and post-traumatic symptoms. ***Conclusion:*** MBIs seemed to show clinically significant advantages compared to other clinical approaches in relation to specific primary and secondary outcomes. Conversely, treatment retention was independent of the therapeutic approach.

Introduction

Alcohol and Drugs Use Disorders (respectively AUD and DUD) are one of the most prevalent mental disorders worldwide [1–4]. Specially, a recent epidemiological study revealed that 12-month and lifetime prevalence respectively ranged from 13.9 to 29.1% for AUD and from 3.9 to 9.9% for DUD [1, 5]. They also add to global morbidity and mortality [6–8] as well as to severe deficiencies in productivity, interpersonal, social, and psychological functioning [9–10].

Currently, it is well known that there are several evidence-based interventions that demonstrated promising results for both AUD and DUDs. For instance, the U.S.

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Food and Drug Administration has permitted 3 medications to treat alcohol dependence – disulfiram, oral and injectable naltrexone, and acamprosate – and nalmefene were permitted by the European Medicines Agency [11–12]. Numerous studies also confirmed how pharmacotherapy might be beneficial in DUDs treatment (for overviews see: [13–15]). Furthermore, a variety of psychological and behavioral therapies also demonstrated to be effective (e.g., cognitive-behavioral therapy [CBT], motivational enhancement therapy, 12-step facilitation therapy [16–19]). Nevertheless, across substance use disorders (SUDs), relapse in dysfunctional substance use is considered the core clinical features of such population [20, 21]. Accordingly, in the last 2 decades, an increasing interest for alternative interventions that might yield better outcomes in treating SUDs has been observed. In this situation, some authors hypothesized how mindfulness-based interventions (MBIs) might positively integrate CBT to promote effective programs for addictive behaviors [22, 23].

The first western definition of mindfulness was given by Kabat-Zinn [24] who described it as "*paying attention in a particular way, on purpose, in the present moment, and non-judgmentally*" [24]. Consecutively, Bishop et al. [25] operationalized mindfulness as particular focus of attention categorized by 2 distinct features that are largely related to the self-regulation of attention toward the immediate present moment and an attitude marked by inquisitiveness, openness, and acceptance. Finally, Shapiro et al. [26] added a third component that underlines the intention or the personal motivation in engaging with mindfulness practice.

Numerous studies demonstrated how individuals learn their purposeful control of attention through training methods such as mindfulness meditation (e.g., [27–29]); also, it was postulated that the development of an observing and acceptance attitude toward present-moment experiences might permit "*the individual to more consciously choose thoughts, emotions, and sensations they will identify with, rather than habitually reacting to them*" ([30]; p. 569). Additionally, the development of this mental position can facilitate a skillful response to a given situation [22, 26] that contrast everyday habitual mental functioning or being on "autopilot."

Given the former evidences and assumptions, some authors proposed the rationale that sustains the integration of mindfulness practice into traditional treatments for SUDs individuals. For example, Groves and Farmer [31] confirmed "*In the context of addictions, mindfulness might mean becoming aware of triggers for craving…and choosing to do something else which might ameliorate or prevent craving, so weakening the habitual response*" (p. 189). Further, Witkiewitz et al. [32] continued how mindfulness meditation might disrupt the craving response system, which is considered by an association between environmental cues and rigid cognitive responding, by providing heightened awareness and acceptance of the initial craving response, without judging, analyzing, or reacting [32].

On the basis of previous deliberations, a manualized psychological treatment for addiction called "mindfulness based relapse prevention" (MBRP; [32–35]) has been developed. Likewise, during the last decade, other MBIs have been adapted for SUDs such as acceptance and commitment therapy (ACT; e.g., [36–38]), spiritual self-schema therapy (e.g., [39–41]), dialectical behavior therapy (e.g., [42–44]), mindfulness-based stress reduction (MBSR; e.g., [45]), and Vipassana Meditation (e.g., [46–48]).

The increasing body of empirical research on mindfulness-based programs use to treat SUDs led Zgierska et al. [49] and Chiesa and Serretti [50] to conduct 2 systematic reviews on this topic in order to draw some decisions about their efficacy in this clinical population. Even though the authors concluded in favor of hopeful results in using MBIs for addiction treatment, they underlined substantial methodological restrictions in most studies published and unclear evidences about which persons with addictive disorders might benefit most from these programs. Furthermore, Li et al. [51] recently published a quantitative meta-analytic review on the same field of research, concluding that MBIs could be beneficial in reducing substance use, craving, and perceived stress as well as in improving mindfulness skills.

However, this work has some relevant limitations regarding its informative value on incremental effectiveness of MBIs, compared to other standard programs, in treating AUD and DUDs. First of all, they included several studies carried out among nonclinical populations. Second, they separately considered results from randomized and nonrandomized trials (respectively RCTs and NRCTs), an aspect that might significantly influence studies outcomes [52], and they also included studies that compared MBIs with no active control conditions. Third, they did not present results related to an essential treatment outcome in SUDs that refer to the attrition rate (AR) [53]; also, they did not take into consideration several other secondary outcomes that are robustly associated with relapse in substance use among clinical populations (i.e., negative affectivity, depressive/anxiety and post-traumatic symptoms and avoidance coping strate-

gies; e.g., [20, 54–57]). Furthermore, they did not evaluate the effect of clinical setting (i.e., group, group + individual, individual) that is considered a core aspect in SUDs treatment efficacy [58]. Finally, they did not compare pooled effect sizes associated with different treatment outcomes so as to clarify if MBIs could have specific or generalized therapeutic effects; also, they did not report quantitative robustness indexes of their conclusions.

Consequently, our aim is to accomplish a meta-analytic review of the literature in order to demonstrate if and to what extent MBIs could promote an incremental effectiveness compared to other active programs usually provided in clinical practice for AUD and DUDs treatment. Consistent with this possibility, we considered RCTs and NRCTs that compared MBIs with other active programs, examining primary and secondary outcomes, which comprehensively operationalize treatment efficacy. In line with previous considerations regarding Li et al. [51] work, we chose to take into consideration AR, abstinence (e.g., any substance use vs. no substance use; duration of abstinence) and levels of perceived craving as primary outcomes of treatments. Levels of perceived stress, negative affectivity, overall mental health and specific (i.e., depressive, anxiety, post-traumatic) psychiatric symptomatology, and the use of avoidance coping strategies were evaluated as secondary outcomes. Furthermore, we investigated the role of core clinical features (i.e., research design, length of intervention/follow-up, short and long-term effects, types of MBIs, types of control conditions, clinical settings, sample characteristics, intervention developed for treating the co-occurrence of SUDs with other psychiatric conditions) that might explain the heterogeneity of findings, reporting quantitative indexes for the robustness of our conclusions. Eventually, we explored if MBIs could produce similar effects on such outcomes, or their therapeutic effects might be related to specific clinical domains relevant for SUDs treatment.

Methods

Criteria for Selecting Studies

In order to be included in this work, studies had to be published in scientific peer-reviewed journals. Consistently with Zeng et al. [169] suggestions, we referred to the Cochrane Collaboration's tool for assessing the risk of bias [170] in order to evaluate the quality of RCTs. Conversely, the quality of NRCTs was assessed by Methodological index for nonrandomized studies [171].

PsycINFO, PubMed, ISI Web of Knowledge, and Scopus were the primary sources of information. We conducted the on-line research up to August 31st 2017. The main search terms were "mindfulness", "mindfulness meditation," "MBI," "mindfulness training", "MBSR," "mindfulness-based cognitive therapy," "MBRP," "dialectical behavior therapy," "ACT," "spiritual self-schema therapy," "Vipassana meditation," and "Zen meditation" in combination with the name of each substance (i.e., substances, drugs, alcohol, marijuana, cocaine, opioid, heroin, methamphetamine). The references of reviews and meta-analyses were referred to as additional sources of information [49–51, 61–63].

Moreover, so as to assess the incremental effectiveness of MBIs in AUD and DUDs treatment, the studies included in this meta-analytic review had to feature an assessment of MBIs with other active interventions based on RCTs and NRCTs (e.g., [59, 60]). Particularly, studies had to compare MBIs with other psychological, psychoeducational, and/or pharmacological treatments usually provided in clinical practice. We considered studies that reported a clear description of the characteristics of interventions (e.g., protocol, setting, length of program/follow-up), especially referring to therapeutic strategies used to address AUD and DUDs clinical targets.

Finally, all studies had to refer to valid and reliable criteria for AUD and DUD diagnoses (Diagnostic and Statistical Manual of Mental Disorders) and all studies had to use valid and reliable instruments to assess treatment outcomes.

Figure 1 shows a detailed description of data extraction procedures and studies that met criteria for inclusion eligibility. Tables 2 and 3 summarize results of assessment procedures used to evaluate the quality of studies included in the current meta-analysis.

Data Analysis

Cohen's *d* [64] was calculated as a measure of effect size. The index was primarily calculated using descriptive statistics reported in the Results section of each study. In addition, *t* and χ^2 tests were used to evaluate Cohen's *d* when descriptive statistics was not available [66].

To consider primary and secondary outcomes pooled effect sizes comparable, we decided to estimate Cohen's *d* even in the case of binary data (i.e., AR; any substance use vs. no substance use). Accordingly, we computed OR and we converted them to Cohen's *d* [65].

Furthermore, we used adequate procedures proposed by Morris [172] to estimate Cohen's *d* when pre-post changes in outcomes measures were considered. Specifically, the Cohen's *d* computation was based on pre-post scores differences, the pooled pre- and posttest standard deviation and the application of a bias correction factor. In the case of multiple comparisons over time performed by the original authors, we computed *d* for each contrast and obtained a single pooled coefficient, consistently with procedures clarified by Borenstein et al. [65].

Values of Cohen's *d* less than or equal to 20, 50, and 80 were inferred as small, moderate, and large effect sizes respectively [64].

Overall the pooled effect size (*dw*) of each outcome measure was estimated using the weighted mean of the *d* value for each study [67]. The 95% CI was computed, as was its significance according to the ratio of *dw* to the standard error [67].

Heterogeneity in effect sizes was computed using the *Q* statistic [67] and I^2 index [68, 69]. Despite the small number of studies included in the current work, we used Begg and Mazumdar's rank correlation test ($r_{B\text{-}M}$) [70] and Egger's regression [71] to detect the publication bias. Given the small number of available studies, a bootstrap methodology (*bias corrected and accelerated*; [72]) was

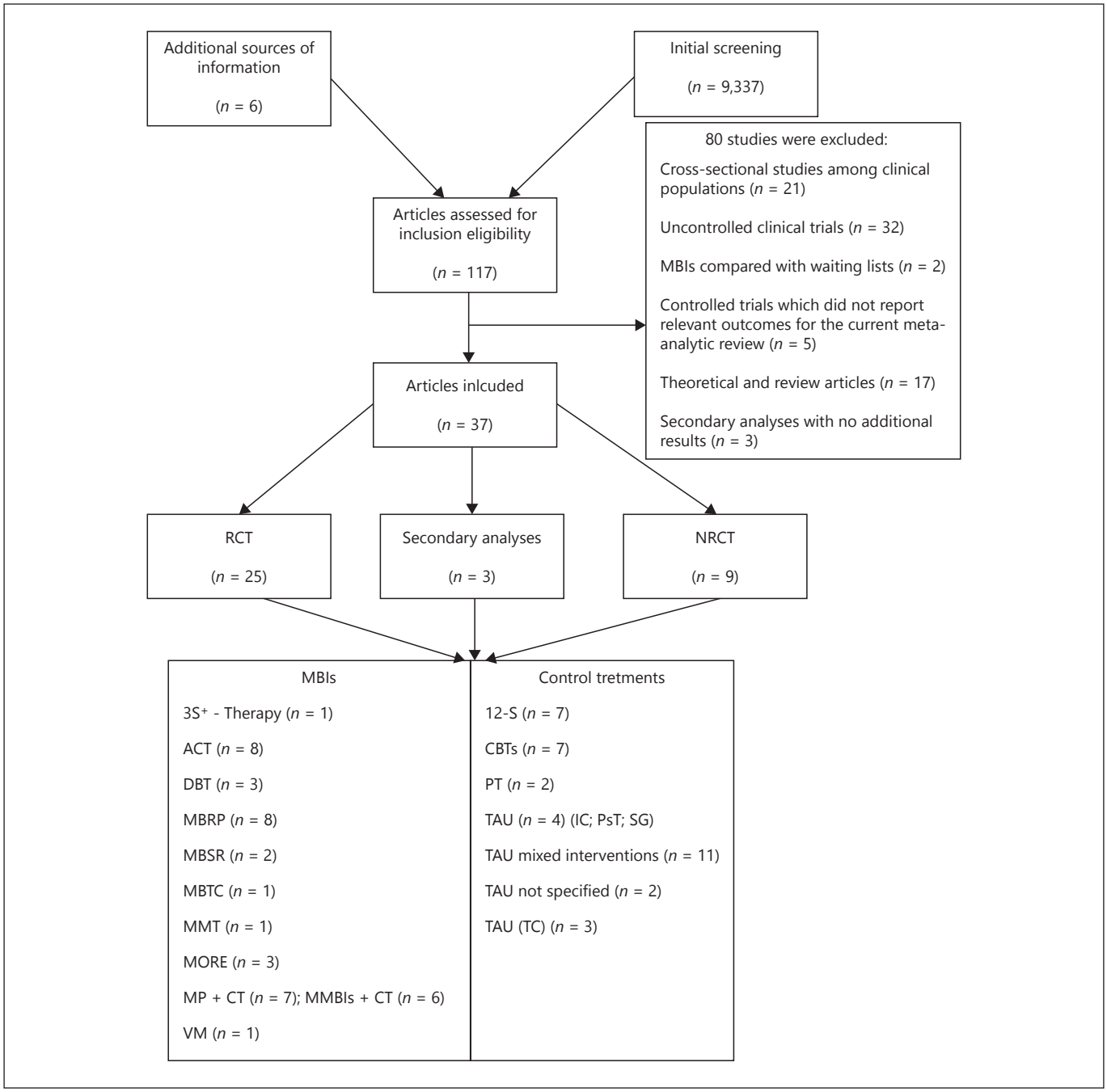

Fig. 1. Flowchart for literature search and screening results. 12-S, twelve steps focused; 3S+-therapy, spiritual self-schema therapy; ACT, acceptance and commitment therapy; CBTs, cognitive behavioral therapies; DBT, dialectical behavior therapy; IO, individual counseling; MBRP, mindfulness based relapse prevention; MBSR, mindfulness-based stress; MBTC, mindfulness based therapeutic community; MMBIs + CT, manualized mindfulness-based interventions + control treatment; MMT, mindfulness and modification therapy; MORE, mindfulness-oriented recovery enhancement; MP + CT, = mindfulness practices + control treatment; PsT, psychoeducational treatment; PT, pharmacological treatments; SG, supportive groups; TAU, treatment as usual; TC, therapeutic community; VM, vipassana meditation.

Table 1. Characteristics of studies

Study	Patients admitted	Gender	Research design	MBIs	Control condition	Setting	Type of substance	Treatment for comorbidity	Length of treatment	Follow-up	Abstinence assessment
Alfonso et al. [75], 2011	34	M + W	NRCT	GMT + MM GMT + twice weekly 90 min mindfulness session based on MBSR exercises	GMT Clinical neuropsychology-based rehabilitation of executive skills, including failure to stop prepotent responses, inadequate forethought and poor planning or decision-making skills	Individual	Alcohol; cocaine	No	7 weeks	–	Duration of abstinence (i.e., months) at the end of treatment. Methods for abstinence assessment ere not reported
Alterman et al. [76], 2004	31	M + W	RCT	12S + BM + MM 12S + BM + weekly 2 h-session of MM	12-S + BM 12-S and BM	Group	Alcohol, cocaine; heroin	No	8 weeks	22 weeks	–
Bowen et al. [47], 2006/Bowen et al. [46], 2007	305	M + W	NRCT	TAU + VM: TAU + 10-day course of VM	TAU (PT + PsT): Pharmacological and psychoeducational intervention	Group	Alcohol; cocaine; crack; marijuana	No	10 days	24 weeks	Quantity and frequency of alcohol and drugs use in the past 90 days. It was assessed at the end of the follow-up period
Bowen et al. [34], 2009/Witkiewitz and Bowen [77], 2010/Witkiewitz et al. [78], 2013	168	M + W	RCT	MBRP	12-S + RP 12-S and relapse prevention skills	Group	Alcohol, cocaine/crack, methamphetamines, opiates/heroin, marijuana	No	8 weeks	16 weeks	Daily use of alcohol and other drugs in the past 60 days. It was assessed at the end of treatment and follow-up
Bowen et al. [79], 2014	286	M + W	RCT	MBRP	RP; 12-S 2 control conditions: standard RP program; 12-S	Group	Alcohol, drugs (specific substances were not declared)	No	8 weeks	48 weeks	Daily use of alcohol and other drugs in the past 30 days. It was assessed at the end of treatment and follow-up
Brewer et al. [80], 2009	36	M + W	RCT	MBRP	CBT	Group	Alcohol, cocaine	No	12 weeks	–	Alcohol and drugs use in the past 28 days at the end of treatment. Random urine toxicology screens every 2 weeks
Chenet al. [81], 2010	207	M + W	NRCT	TAU + MM: TAU + daily qigong meditation	TAU: motivational Enhancement; CBT techniques, 12-S	Individual + group	Alcohol, drugs (specific substances were not declared)	No	4 weeks	–	–
Courbasson et al. [82], 2012	25	W	RCT	DBT	TAU motivational interviewing, CBT techniques, RP skills	Individual + group	Alcohol, cocaine, benzodiazepines	Yes eating disorders	48 weeks	24 weeks	–
Garland et al. [83], 2010	53	M + W	RCT	MORE	TAU (ASG): SG based on matrix model for SUDs outpatient programs	Group	Alcohol	No	10 weeks	–	–
Garland et al. [84], 2016	180	M + W	RCT	MORE	CBT; TAU 2 control conditions: CBT; psychoeducational + client-centered, supportive-expressive group	Group	Alcohol, amphetamine, cocaine, cannabis, opioid, sedative	Yes anxiety disorders, mood disorders, TSD	10 weeks	–	It was not mentioned how abstinence was assessed. Authors reported the number of relapsed patients

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Table 1 (continued)

Study	Patients admitted	Gender	Research design	MBIs	Control condition	Setting	Type of substance	Treatment for comorbidity	Length of treatment	Follow-up	Abstinence assessment
Garland et al. [85], 2014	115	M + W	RCT	MORE	TAU (SG)	Group	Opioid	Yes chronic pain	8 weeks	12 weeks	Frequency of opioid misuse in the past 30 days. It was assessed at the end of treatment and follow-up
Glasner et al. [86], 2017	63	M + W	RCT	CM + MBRP	TAU (CM + PsT) CM and psychoeducational intervention	Group	Stimulant	No	12 weeks	4 weeks	Random weekly urine analysis during the treatment and follow-up
González-Menéndeza et al. [87], 2014	37	W	RCT	ACT	CBT	Group	Alcohol, cannabis cocaine, heroin	No		72 weeks	Random urinal analysis. The frequency was not reported
Hayes et al. [36], 2004	124	M + W	RCT	ACT + PT(MMP)	12S + PT (MMP); PT (MMP) 2 control conditions: 12-S + pharmacological treatment based on MMP; only pharmacological treatment	Individual + group	Opioid	No	16 weeks	24 weeks	Random twice-weekly urine analysis during the treatment and follow-up
Himelstein et al. [88], 2015	35	M	RCT	IC + MM IC + weekly 5/25- min mindfulness training	TAU (IC) IC based on motivational interviewing, goal planning, and successful reentry back into the community	Individual	SUDs specific substances were not declared	No	12 weeks	–	–
Lanza et al. [89], 2014	50	W	RCT	ACT	CBT	Group	Alcohol, cocaine, cannabis, heroin,	No	16 weeks	24 weeks	Random twice-weekly urine analysis during the treatment and follow-up
Lee et al. [90], 2011	24	M	RCT	MBRP	TAU (PsT) psychoeducational intervention	Group	Amphetamine, cocaine, cannabis, glue, heroin, etamine, LSD, MDMA	No	8 weeks	–	–
Liheret al. [91], 2010	393	M + W	NRCT	MBTC	TAU (TC)	Group	SUDs specific substances were not declared	No	36 weeks	–	–
Linehan et. al. [43], 2002	23	W	RCT	DBT + MMP	CVT+ 12-S CVT for substance abusers	Individual + group	Opioid; cocaine, amphetamines, barbiturates, sedatives	Yes borderline personality disorder	52 weeks	16 weeks	Self-report quantity and frequency of opiate and other drugs use in the past 90 days during the treatment and follow-up. Thrice-week ly urine analysis of opiate and other drug use during the treatment and follow-up

Table 1 (continued)

Study	Patients admitted	Gender	Research design	MBIs	Control condition	Setting	Type of substance	Treatment for comorbidity	Length of treatment	Follow-up	Abstinence assessment
Linehan et al. [44], 1999	27	M + W	RCT	DBT + MMP	TAU not specified	Individual + group	Cocaine, opiates, marijuana, ethamphetamines	Yes borderline personality disorder	52 weeks	16 weeks	Self-report quantity and frequency of opiate and other drugs use in the past 90 days during the treatment and follow-up. Random urine analysis was collected. The screening frequency was not reported
Luoma et al. [38], 2012	133	M + W	RCT	ACT + TAU	TAU life skills, RP skills, parenting, physical health issues, recreational therapy, anger management; 12-S individual therapy	Individual + Group	Alcohol, methamphetamines; marijuana, hallucinogens; inhalants; heroin; opiates;	No	4 weeks	16 weeks	Self-report quantity of alcohol and other drugs use in the past 90 days during the treatment and follow-up. Saliva samples were collected during the treatment and follow-up. The screening frequency was not reported.
Marcus et al. [92], 2001	36	M + W	NRCT	MBSR + TC	TAU (TC)	Group	Alcohol, cocaine, heroin, marijuana, inhalants	No	8 weeks	–	–
Marcus et al. [93], 2009	459	M + W	NRCT	MBSR + TC	TAU (TC)	Group	Alcohol, cocaine, marijuana	No	72 weeks	–	–
Margolin t al. [94], 2007	38	M + W	NRCT	$3S^{+}$- therapy	PT (MMP) pharmacological treatment based on MMP	Individual	Alcohol, cocaine, heroin	Yes HIV risk behaviors	12 weeks	–	Self-report quantity of alcohol and drugs use in the past 30 days during the treatment. Twice-weekly urine analysis during the treatment.
Nakamura et al. [95], 2015	38	W	RCT	TAU + MM TAU + 20-session mind–body bridging program	TAU Life skills; RP skills; behaviormanagement	Individual + group	SUDs specific substances were not declared	Yes PTSD	10 weeks	–	–
Petersen and Zettle [96], 2009	24	M + W	RCT	12S + ACT	12S	Individual + group	Alcohol	Yes depressive disorder	4 weeks	–	–
Price et al. [97], 2012	46	W	RCT	TAU + MABT TAU + 1.5-h weekly mindfulness awareness body-oriented therapy	TAU 12-S, psychoeducational intervention; CBT techniques	Individual + Group	Alcohol, narcotic, opiates, stimulants	Yes PTSD	8 weeks	36 weeks	Self-report quantity and frequency of alcohol and drugs use in the past 90 days during the treatment and follow-up. Urine analysis and breathalyzer data were collected. The screening frequency was not reported
Silpakit et al. [98], 2016	60	M	NRCT	MBRP	TAU not specified	Group	Alcohol	No	2 weeks	16 weeks	Self- report of any alcohol use during the treatment and follow-up. Authors did not report assessment procedures.

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Table 1 (continued)

Study	Patients admitted	Gender	Research design	MBIs	Control condition	Setting	Type of substance	Treatment for comorbidity	Length of treatment	Follow-up	Abstinence assessment
Shorey et al. [99], 2017	117	M + W	RCT	TAU + MBRP +ACT TAU + twice weekly, 1.5-h session based on MBRP and ACT meditation practices and techniques	TAU (12S) 12-focused + coping skills groups, family therapy, exercise groups	Group	Alcohol, opioid, sedative, cocaine, cannabis, amphetamine, hallucinogen	No	4 weeks	–	–
Smout et al. [100], 2010	104	M + W	RCT	ACT	CBT	Individual	Methamphetamine	No	12 weeks	12 weeks	Self-report average amount of drugs use in the past 30 days. Hair analysis supported self-report drugs use. The assessment rocedures were administe-red at the end of treatment and follow-up
Stotts et al. [101], 2012	56	M + W	RCT	ACT + PT	TAU (DC + PT) Manualized approach based on DC and pharmacological intervention based on methadone dose reduction schedule	Individual + group	Opioid	No	24 weeks	–	Urine analysis twice-weekly during the treatment
Witkiewitz et al. [102], 2014	105	W	RCT	MBRP	RP	Group	Alcohol, cocaine, marijuana, methamphetamine opioid	No	8 weeks	15 weeks	Self-report quantity and frequency of alcohol and drugs use in the past 30 days during the treatment (every month) and at the end of follow-up
Wupperman et al. [103], 2015	25	W	NRCT	MMT	TAU multimodal program which includes techniques from CBT, DBT, interpersonal psychotherapy and ST	Individual+ Group	Alcohol, benzodiazepines; cannabis, cocaine, opioid	Yes aggressive behaviors	20 weeks	8 weeks	Self-report quantity and frequency of alcohol and other drugs use in the past 30 days at the end of treatment and follow-up
Zemestani and Ottaviani [104], 2016	74	M + W	RCT	MBRP	TAU psychoeducational intervention, 12-S, rational thinking skills and RP skills	Group	Cocaine, heroin, marijuana, methamphetamine	Yes depressive disorder	8 weeks	8 weeks	–

12-S, 12-steps focused; $3S^{+}$-therapy, spiritual self-schema therapy; ASG, alcohol dependence support group; BM, behavioral modification; CBT, cognitive behavioral therapy; CM, contingency management; CVT + 12-S, comprehensive validation therapy with 12 step; DBT, dialectical behavior therapy; DC, drug counseling; GMT, goal management training; IC, individual counseling; IT, interpersonal therapy; ITSF, intensive twelve step facilitation; M, men; MBIs, mindfulness based intervention; MBRP, mindfulness based relapse prevention; MBSR, mindfulness based stress; MBTC, mindfulness based therapeutic community; MM, mindfulness meditation; MMP, methadone maintenance program; MMT, mindfulness and modification therapy; MORE, mindfulness-oriented recovery enhancement; R, relapse prevention; SG, supportive group; ST, supportive therapy; TAU, treatment-as-usual; TC, therapeutic community; VM, vipassana meditation; W, women.

Table 2. Quality of randomized controlled trials: Cochrane collaboration's tool for assessing risk of bias

Items	Yes (low risk of bias)		Unclear		No (high risk of bias)	
	n	%	*n*	%	*n*	%
Adequate sequence generation?	14	56	10	40	1	4
Allocation concealment?	12	48	12	48	1	4
Blinding? (patient reported outcomes)	7	28	14	56	4	16
Incomplete outcome data addressed? (short-term outcomes [2–6 weeks])	25	100	0	0	0	0
Incomplete outcome data addressed? (long-term outcomes [>6 weeks])	25	100	0	0	0	0
Free of selective reporting?	25	100	0	0	0	0
Free of other bias?	21	84	2	8	2	8
Mean (SD)	18.43 (7.39)	73.71 (29.56)	5.42 (6.29)	21.71 (25.17)	1.14 (1.46)	4.57 (5.85)

applied in calculating the significance of the previous parameters. A total of 1,000 bootstrap independent samples were used with $p < 0.05$ (2-tailed). Spearman's *rho* was used to evaluate the significance of the correlation between effect size, sample size, year of publication, and length of intervention/follow-up. Subgroup analyses (i.e., RCTs vs. NRCTs; short- vs. long-term effects; MBIs + control condition vs. manualized MBIs; MBIs vs. CBTs/TAU; group vs. group + individual/individual settings; several SUDs vs. specific SUDs; SUDs-other psychiatric disorders vs. SUDs) were conducted using methodologies described by Borenstein et al. [65] based on the *Z*-test. *Z*-test was also used to compare pooled effect sizes within primary and secondary outcomes. Adequate Bonferroni correction was applied when we performed multiple comparisons.

Orwin's fail-safe procedure [73] was assessed in order to measure the number of studies with null results needed to overturn our conclusions. For Orwin's fail-safe *N*, the critical level was set at 20. Moreover, using the procedures proposed by Rosenthal [74], we computed the critical value ($5k + 10$; k = number of studies) of Orwin's fail-safe *N* to evaluate the power of our conclusions.

Results

Thirty-seven studies [34, 36, 38, 43, 44, 46, 47, 75–104] were eligible for a total of 3,531 AUD and DUDs patients admitted to the therapeutic programs.

Table 1 shows a comprehensive description of characteristics of each study. Seven studies implemented mindfulness practices into usually provided programs, 6 studies combined manualized MBIs (i.e., ACT, MBRP, MBSR) with other standard interventions. Twenty-one studies compared manualized MBIs adapted for SUDs with other active interventions.

Control treatments were represented by 12-steps focused programs (7 studies), CBTs (7 studies), individual counseling, or psychoeducational treatments or supportive groups (4 studies), mixed interventions which combined the previous treatment approaches (11 studies), and therapeutic community (3 studies). Figure 1 shows a detailed description of the distribution of clinical approaches.

As previously mentioned, we aggregated results for *AR* (28 studies), *abstinence* (21 studies), *levels of perceived craving* (7 studies) and *stress* (5 studies), *negative affectivity* (3 studies), *overall mental health* (6 studies), the severity of *depressive* (9 studies), *anxiety* (5 studies) and *posttraumatic* (3 studies) *symptoms*, and several forms of *avoidance coping strategies* (8 studies).

Tables 4–13 discretely summarize the effect sizes and show the forest plots for each outcome previously presented. Tables 4–13 also show detailed results related to Spearman's correlations, subgroup analyses, publication bias, and Orwin's fail-safe number of each outcome.

In the followings sections, we report main findings for primary and secondary outcomes. Figure 2 and 3 exhibit results related to multiple comparisons within the previous categories of treatment outcomes.

Attrition Rate

We observed a null pooled effect size in AR when MBIs were compared with other treatments. However, we detected a significant and high heterogeneity in effect sizes. Accordingly, we explored some possible source of heterogeneity. First of all, we excluded from analysis Marcus et al. [92] research because it represents a distribution outlier. Results displayed a decrease in extent of heterogeneity ($I^2 = 55.85\%$), albeit it remained moderate and significant ($Q_{[26]} = 58.90$, $p < 0.001$), and null pooled effect size (d_w = –0.06 [–0.02 to 0.14]; n*s*). The research design

Table 3. Quality of nonrandomized controlled trials: methodological index for non-randomized studies

Items	Reported and adequate		Reported but inadequate		Not reported	
	n	%	*n*	%	*n*	%
A clearly stated aim	9	100	0	0	0	0
Inclusion of consecutive patients	9	100	0	0	0	0
Prospective collection of data	9	100	0	0	0	0
Endpoints appropriate to the aim of the study	8	88.9	1	11.1	0	0
Unbiased assessment of the study endpoint	2	22.2	0	0	7	77.8
Follow-up period appropriate to the aim of the study	5	55.5	0	0	4	44.5
Loss to follow-up less than 5%	0	0	2	22.2	7	77.8
Prospective calculation of the study size	0	0	0	0	9	100
An adequate control group	9	100	0	0	0	0
Contemporary groups	9	100	0	0	1	11.1
Baseline equivalence of groups	9	100	0	0	0	0
Adequate statistical analyses	9	100	0	0	0	0
Mean (SD)	6.5 (3.73)	72.22 (41.44)	0.25 (0.62)	2.77 (6.90)	2.33 (3.44)	25.93 (38.30)

(RCTs: $d_w = 0.00$ [–0.10 to 0.10]; $Q_{[19]} = 29.80$, *ns*; NRCTs: $d_w = -0.18$ [–0.33 to –0.05], $p < 0.05$; $Q_{[6]} = 23.50$, $p < 0.001$, $I^2 = 74.47\%$; $Z = -2.16$; $p < 0.05$), the type of MBIs (manualized MBIs: $d_w = 0.01$ [–0.09 to 0.10], *ns*; $Q_{[18]} = 29.58$, $p < 0.05$, $I^2 = 39.16\%$; MBIs + control condition: $d_w = -0.22$ [–0.37 to –0.07], $p < 0.01$; $Q_{[7]} = 28.57$, $p < 0.01$, $I^2 = 68.98\%$; $Z = 2.59$; $p < 0.05$) and sample characteristics (several SUDs: $d_w = -0.15$ (–0.25 to –0.06); $p < 0.01$; $Q_{[20]} = 41.72$, $p < 0.01$; $I^2 = 52.06\%$; specific SUDs: $d_w = 0.18$ [0.03–0.33], $p < 0.05$ $Q_{[6]} = 3.52$, *ns*; $Z = -2.16$; $p < 0.05$) moderated the extent of pooled effect sizes and partially explained results variability. Publication bias was not detected.

Abstinence

Table 1 provides a detailed description of abstinence assessment procedures administered within each study. Even though we observed a large variability in methods of evaluation (e.g., self-report vs. objective measures; maximum duration of assessed abstinence), abstinence was generally operationalized both as a binary (e.g., any substance use vs. no substance use) or continuous (e.g., days of any substance use) outcome.

A significant small pooled effect size was found in abstinence, in association with significant and moderate heterogeneity across the results. Specifically, MBIs seemed to promote abstinence maintenance better than other conditions. Excluding the study of Wupperman et al. [103], which represented an outlier, we confirmed the previous MBIs advantages ($d_w = 0.37$ [0.30–0.45], $p < 0.001$) and this effect was consistent across studies ($Q_{[19]} = 29.59$, *ns*; $I^2 = 35.80\%$). We did not reveal bias of publication. As indicated by the value of Orwin's fail-safe number, the beneficial effect previously reported is so far considered to be conclusive.

Levels of Perceived Craving

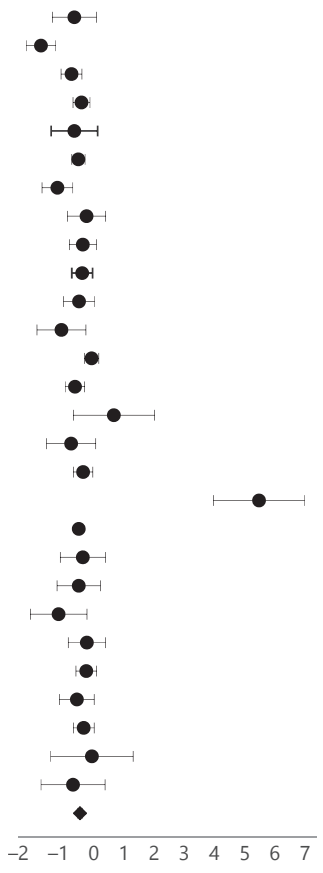
A large pooled effect size was found in relation to the levels of perceived craving during the interventions. Specifically, MBIs seemed to significantly decrease the levels of craving if they were compared with other approaches. We revealed a large heterogeneity across the results. However, MBIs seemed to be more effective than other active programs in reducing levels of craving when they were specifically carried out to treat the co-occurrence of SUDs and other psychiatric disorders ($d_w = -2.36$ [–2.61 to 2.11], $p < 0.001$; $Q_{[2]} = 6.37$, $p < 0.05$; $I^2 = 68.62$; only SUDs: $d_w = -0.10$ (–0.28 to 0.08), *ns*; $Q_{[3]} = 5.43$, *ns*; $Z = -14.47$, $p < 0.001$). The Orwin's fail-safe number ($n = 32.4$; critical value = 25) associated to this finding was robust enough to draw definitive conclusion in favor of MBIs, specifically in the case of the co-occurrence between SUDs and other psychiatric disorders.

Comparisons between Primary Treatment Outcomes

The improvement in levels of perceived craving was significantly different to abstinence ($Z = 6.03$, $p < 0.001$) and AR ($Z = 10.03$, $p < 0.001$). Additionally, the abstinence pooled effect size was significantly larger than AR ($Z = 6.02$, $p < 0.001$; Bonferroni correction: $\alpha = 0.0167$).

Table 4. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias and subgroups analysis for attrition rate

AR			
Studies	*d* (95% CI)	OR; 95% CI	Forest plot
Alterman et al. [76], 2004	–0.22 (–0.92 to 0.48)	0.67; 0.19 to 2.41	
Bowen et al. [47], 2006	–1.28 (–1.75 to –0.81)	0.10; 0.04 to 0.23	
Bowen et al. [34], 2009	–0.31 (–0.64 to 0.02)	0.57; 0.19 to 2.41	
Bowen et al. [79], 2014	0.01 (–0.26 to 0.28)	1.02; 0.62 to 1.67	
Brewer et al. [80], 2009	–0.22 (–0.96 to 0.52)	0.67; 0.17 to 2.59	
Chen et al. [81], 2010	–0.09 (–0.30 to 0.12)	0.85; 0.57 to 1.25	
Courbasson et al. [82], 2012	–0.76 (–1.25 to –0.27)	0.25; 0.57 to 1.25	
Garland et al. [83], 2010	0.17 (–0.43 to 0.78)	1.36; 0.45 to 4.09	
Garland et al. [84], 2016	0.05 (–0.38 to 0.48)	1.09; 0.50 to 2.39	
Garland et al. [85], 2014	0.03 (–0.30 to 0.36)	1.05; 0.58 to 1.93	
Glasner et al. [86], 2017	–0.07 (–0.56 to 0.42)	0.88; 0.36 to 2.14	
González–Menéndeza et al. [87], 2014	–0.63 (–1.41 to 0.15)	0.32; 0.08 to 1.32	
Hayes et al. [36], 2004	0.33 (0.09 to 0.56)	1.81; 1.19 to 2.78	
Liher et al. [91], 2010	–0.20 (–0.51 to 0.11)	0.70; 0.39 to 1.23	
Linehan et al. [43], 2002	1.04 (–0.25 to 2.33)	6.56; 0.63 to 68.63	
Linehan et al. [44], 1999	–0.32 (–1.10 to 0.46)	0.56; 0.13 to 2.32	
Luoma et al. [38], 2012	0.06 (–0.25 to 0.37)	1.11; 0.63 to 1.96	
Marcus et al. [92], 2001	5.66 (4.21 to 7.11)		
Marcus et al. [93], 2009	–0.08 (–0.14 to –0.02)	0.86; 0.78 to 0.96	
Margolin et al. [94], 2007	0.05 (–0.67 to 0.77)	1.09; 0.29 to 4.07	
Price et al. [97], 2012	–0.08 (–0.77 to 0.61)	0.86; 0.77 to 0.96	
Silpakit et al. [98], 2015	0.18 (–0.41 to 0.77)	1.38; 0.47 to 4.02	
Shorey et al. [99] 2017	–0.72 (–1.62 to 0.18)	0.27; 0.05 to 1.39	
Smout et al. [100], 2010	0.16 (–0.17 to 0.49)	1.33; 0.73 to 2.44	
Stotts et al. [101], 2010	–0.14 (–0.69 to 0.41)	0.77; 0.29 to 2.10	
Witkiewitz et al. [102], 2014	0.08 (–0.25 to 0.41)	1.15; 0.63 to 2.11	
Wupperman et al. [103], 2015	0.34 (–0.97 to 1.65)	1.85; 0.17 to 20.03	
Zemestani and Ottaviani [104], 2016	–0.26 (–1.28 to 0.76)	0.63; 0.10 to 3.96	
Summary	–0.04 (–0.11 to 0.03)		



– $Q_{(27)} = 118.20$, $p < 0.001$; $I^2 = 77.16\%$.
– $\rho_{\textit{d-year of publication}} = 0.05$ (bootstrap 95% CI –0.45 to 0.44) $p = 0.82$.
– $\rho_{\textit{d-sample size}} = 0.13$ (bootstrap 95% CI –0.28 to 0.53) $p = 0.51$.
– $\rho_{\textit{d-length of treatment}} = 0.01$ (bootstrap 95% CI: –0.43 to 0.44) $p = 0.96$.
– Consistent with the d_w value to Orwin's fail-safe number was not computed.
– $r_{B\text{-}M} = 0.05$ (bootstrap 95% CI –0.27 to 0.38) $p = 0.72$.
– Egger's coefficient = 0.32 (bootstrap 95% CI –2.70 to 1.88) $p = 0.82$.
– $Z_{\textit{RCTs vs. NRCTs}} = 2.16$ to $p = 0.04$.
– $Z_{\textit{MBIs + control condition vs. manualized MBIs}} = 2.59$, $p = 0.01$.
– $Z_{\textit{several SUDs vs. specific SUD}} = 3.69$, $p < 0.001$.

We did not find significant differences between pooled effect sizes when we evaluated effects of different control conditions (i.e., 12-S; CBTs; TAU) to clinical settings (i.e., group; group + individual) and type MBIs (i.e., MBIs for co-occurrence between SUDs and other psychiatric disorder vs. MBIs for SUDs).

Marcus et al. [92] represented an outlier. It was excluded from subgroup analyses.

AR, attrition rate; 12-S, 12-steps focused; CBT, cognitive behavioral therapy; MBIs, mindfulness-based interventions; MP, mindfulness practices; NRCTs, nonrandomized controlled trial; RCTs, randomized controlled trial; SUDs, substance use disorders; TAU, treatment as usual.

Table 5. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for abstinence

Abstinence				
Studies	Measure	*d* (95% CI)	OR; 95% CI	Forest plot
Alfonso et al. [75], 2011	DA	0.63 (–0.06 to 1.31)		
Bowen et al. [47], 2006	DDQ; DDTQ	0.44 (0.16 to 0.71)		
Bowen et al. [34], 2009	TLFB	0.21 (–0.02 to 0.44)		
Bowen et al. [79], 2014	TLFB	0.38 (0.26 to 0.50)		
Brewer et al. [80], 2009	TLFB; UA	–0.95 (–0.1.73 to –0.17)		
Garland et al. [84], 2016	NM	0.25 (–0.75 to 1.25)	1.57; 0.08 to 31.72	
Garland et al. [85], 2014	COMM	0.42 (0.14 to 0.70)		
Glasner et al. [86], 2017	UA	0.04 (–0.36 to 0.44)	1.08; 0.10 to 11.80	
González–Menéndeza et al. [87], 2014	UA	0.68 (0.21 to 1.15)	3.42; 0.28 to 41.23	
Hayes et al. [36], 2004	UA	0.55 (0.27 to 0.82)	2.70; 0.31 to 23.81	
Lanza et al. [89], 2014	UA	0.30 (–0.22 to 0.82)	1.70; 0.13 to 22.03	
Linehan et al. [43], 2002	TLFB; UA	0.88 (0.37 to 1.39)	4.91; 0.39 to 62.26	
Linehan et al. [44], 1999	TLFB; UA	0.30 (–0.09 to 0.69)		
Luoma et al. [38], 2012	TLFB; SS	0.46 (–0.24 to 1.16)	2.30; 0.15 to 36.10	
Margolin et al. [94], 2007	UA	0.28 (–0.48 to 1.04)	1.65; 0.10 to 27.55	
Price et al. [97], 2012	TLFB; Br; UA	0.63 (0.16 to 1.10)	3.13; 0.26 to 27.66	
Silpakit et al. [98], 2015	SR	0.65 (–0.13 to 1.43)	3.24; 0.19 to 54.80	
Smout et al. [100], 2010	HA	0.36 (–0.64 to 1.36)	1.91; 0.09 to 38.70	
Stotts et al. [101], 2010	UA	–0.29 (–0.94 to 0.35)	0.59; 0.04 to 8.75	
Witkiewitz et al. [102], 2014	TLFB	0.85 (–0.35 to 2.07)	4.72; 0.20 to 110.47	
Wupperman et al. [103], 2015	TLFB	3.52 (2.15 to 4.89)		
Summary		0.38 (0.31 to 0.46)***		
				–2 –1 0 1 2 3 4 5

*** $p < 0.001$.
– $Q_{(20)} = 49.71$, $p < 0.001$; $I^2 = 59.76\%$.
– $\rho_{d\text{-year of publication}} = 0.08$ (bootstrap 95% CI –0.45 to 0.56) $p = 0.72$.
– $\rho_{d\text{-sample size}} = -0.22$ (bootstrap 95% CI –0.64 to 0.24) $p = 0.33$.
– $\rho_{d\text{-length of treatment}} = 0.01$ (bootstrap 95% CI –0.43 to 0.44) $p = 0.96$.
– $\rho_{d\text{-length of follow up period}} = 0.14$ (bootstrap 95% CI –0.50 to 0.69) $p = 0.61$.
– Orwin's fail-safe number = 19.51 (critical value = 115).
– $r_{B\text{-}M} = 0.13$ (bootstrap 95% CI –0.32 to 0.55) $p = 0.58$.
– Egger's coefficient = 0.39 (bootstrap 95% CI –0.93 to 1.96) $p = 0.55$.

We did not find significant differences in pooled effect sizes when we evaluated type of assessment procedures (i.e., self-report vs. objective) short and long-term effects (i.e., follow up studies vs. no follow-up), different research designs (i.e., NRCTs vs. RCTs), type of MBI (i.e., MBIs + control condition vs. manualized MBIs) control conditions (i.e., 12-S; CBT; TAU), clinical settings (i.e., group; group + individual) and type of MBIs (i.e., MBIs for co-occurrence between SUDs and other psychiatric disorder vs. MBIs for SUDs) and SUDs heterogeneity (several SUDs vs. specific substance).

Wupperman et al. [103] represented an outlier. Excluding this study, we found the following indexes: $d_w = 0.37$ (0.30 to 0.45), $p < 0.001$; $Q_{(19)} = 29.59$, *ns*; $I^2 = 35.80\%$.

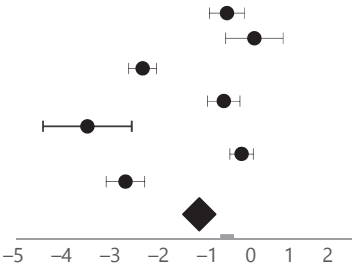
12-S, 12-steps focused; Br, breathalyzer; DA, duration of abstinence; COMM, current opioid misuse measure; DDQ, daily drinking questionnaire; DDTQ, daily drug-taking questionnaire; HA, hair analysis; MBIs, mindfulness-based interventions; NM, not mentioned; NRCTs, nonrandomized controlled trials; RCTs, randomized controlled trials; SR, self-report relapse; SS, saliva sample; SUDs, substance use sisorders; TLFB, timeline follow-back; UA, urinal analysis.

Levels of Perceived Stress

Considering levels of perceived stress during the programs, we found a consistent and small-to-moderate pooled effect size. MBIs seemed to reduce the levels of perceived stress if they were compared with other treatments. Nonetheless, we found a significant relationship between *d* and the sample size. Specifically, clinical trials characterized by larger samples showed smaller difference in this outcome. Bias of publication was not revealed. As indicated by Orwin's

Table 6. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for levels of perceived craving

Levels of perceived craving			
Studies	Measure	*d* (95% CI)	Forest plot
Bowen et al. [34], 2009^	PACS	−0.28 (−0.68 to 0.12)	
Garland et al. [83], 2010	PACS	0.33 (−0.31 to 0.98)	
Garland et al. [84], 2016	PACS	−2.16 (−2.48 to −1.84)	
Garland et al. [85], 2014	Cr	−0.35 (−0.72 to 0.02)	
Nakamura et al. [95], 2015	PACS	−3.97 (−4.39 to −2.40)	
Shorey et al. [99], 2017	PACS	0.05 (−0.22 to 0.31)	
Zemestani and Ottaviani [104], 2016	PACS	−2.54 (−2.97 to −2.11)	
Summary		−0.90 (−1.04 to −.75)***	



*** $p < 0.001$.
^ Secondary analyses: Witkiewitz et al. [78].
– $Q_{(6)} = 221.18$, $p < 0.001$; $I^2 = 97.28\%$.
– $\rho_{d\text{-year of publication}} = -0.27$ (bootstrap 95% CI −1.00 to 0.97) $p = 0.56$.
– $\rho_{d\text{-sample size}} = -0.29$ (bootstrap 95% CI −1.00 to 1.00) $p = 0.53$.
– $\rho_{d\text{-length of treatment}} = -0.27$ (bootstrap 95% CI −0.97 to 0.61) $p = 0.56$.
– $\rho_{d\text{-length of follow up period}}$ was not computed because only 3 studies reported follow-up results.
– Orwin's fail safe number = 24.5 (critical value = 45).
– $r_{B\text{-}M} = -0.05$ (bootstrap 95% CI −0.65 to 0.65) $p = 0.88$.
– Egger's coefficient = −4.75 (bootstrap 95% CI −23.58 to 12.92) $p = 0.45$.
– $Z_{SUDs\text{-other psychiatric disorders vs. SUDs}} = -14.47$, $p < 0.001$.
– All studies were carried out as RCTs.
– 5 studies reported results from manualized MBIs; 2 studies from MBIs + control condition.
– 5 studies compared MBIs with TAU, 1 study with CBT and 1 with 12-S.
– 6 studies were conducted in a group setting, 1 study in individual + group setting.
– 5 clinical trials were carried out to simultaneously treat several SUDs.
– No significant difference was found comparing short and long-term effects of MBIs.

12-S, 12-steps focused; CBT, cognitive behavioral therapy; Cr, craving evaluated by single item; MBIs, mindfulness-based intervention; MP, mindfulness practices; PACS, penn alcohol craving scale; RCTs, randomized controlled trials; SUDs, substance use disorders; TAU, treatment as usual.

fail-safe number, the beneficial effect of MBIs on reduction of perceived stress was not robust enough in order to definitely conclude in favor of such treatments.

Negative Affectivity

We observed a large pooled effect size for negative affectivity. When compared to other programs, MBIs seemed to significantly reduce negative emotional experiences. However, large heterogeneity was detected across the results. Specifically, only one study [84] demonstrated large differences between MBI and control condition in reducing negative affectivity. Conversely, the remaining 2 studies [91, 97] showed no differences between treatment approaches.

The paucity of studies did not permit in exploring possible sources of heterogeneity. Additionally, for the same reason, it was not possible to compute bias of publication.

The Orwin's fail-safe number showed that the beneficial effects of MBIs on this outcome are not conclusive.

Overall Mental Health

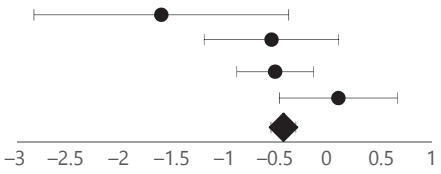
The null pooled effect size was observed in overall mental health. Results were consistent across studies. We did not detect bias of publication.

Depressive Symptoms

A moderate-to-large pooled effect size was observed, even though it was associated with high heterogeneity. MBIs seemed to support greater decrease of depressive symptomatology than other programs. Comparing pooled effect sizes, we found a significant difference when MBIs were specifically carried out to treat the co-occur-

Table 7. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for levels of perceived stress

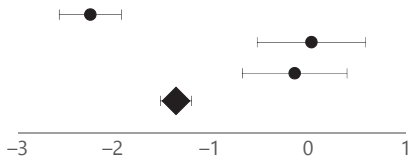
Levels of perceived stress			
Studies	Measure	*d* (95% CI)	Forest plot
Brewer et al. [80], 2009	VAS	–1.61 (–2.84 to –0.37)	
Garland et al. [83], 2010	VAS	–0.55 (–1.20 to 0.11)	
Garland et al. [85], 2014	C-SOSI	–0.51 (–0.88 to –0.14)	
Marcus et al. [93], 2009	C-SOSI	0.10 (–0.47 to 0.67)	
Summary		–0.43 (–0.70 to –0.16)**	



** $p < 0.01$.
– $Q_{(3)} = 7.04$, $p = 0.07$; $I^2 = 57.44\%$.
– $\rho_{d\text{-year of publication}} = 0.10$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.89$.
– $\rho_{d\text{-sample size}} = 1.00$ (bootstrap 95% CI 1.00 to 1.00) $p = 0.01$.
– $\rho_{d\text{-length of treatment}} = 0.20$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.80$.
– $\rho_{d\text{-length of follow up period}}$ was not computed because only 1 study reported follow-up results.
– Orwin's fail safe number = 4.6 (critical value = 30).
– $r_{B\text{-}M} = -0.40$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.60$.
– Egger's coefficient = –1.48 (bootstrap 95% CI –4.77 to 0.86) $p = 0.55$.
The consistency of results excluded other sources of heterogeneity.
C-SOSI, calgary symptoms of stress inventory; VAS, visual analogue scale.

Table 8. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for negative affectivity

Negative affectivity			
Studies	Measure	*d* (95% CI)	Forest plot
Garland et al. [84], 2016	PANAS	–2.25 (–2.57 to –1.93)	
Liher et al. [91], 2010	LIWC-NE	0.03 (–0.54 to 0.59)	
Price et al. [97], 2012	PANAS	–0.14 (–0.69 to 0.40)	
Summary		–1.37 (–0.84 to –0.52)***	

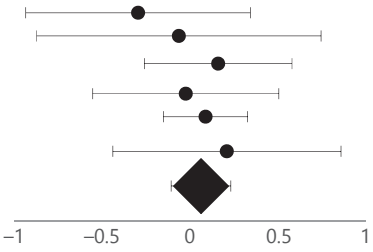


*** $p < 0.001$.
– $Q_{(2)} = 72.01$, $p < 0.001$; $I^2 = 97.22\%$.
– The paucity of studies did not permit to compute correlation between effect sizes and year of publication, sample size, and length of treatment/follow-up period. For the same reason, we did not compute publication bias and subgroups analyses.
– Orwin's fail-safe number = 17.55 (critical value = 25).
LIWC-NE, Linguistic Inquiry and Word Count Negative Emotions subscale; PANAS, positive and negative affect scale.

rence of SUDs and other psychiatric disorders ($d_w = -0.91$ [–1.07 to –0.74], $p < 0.001$; $Q_{[5]} = 48.03$, $p < 0.001$; $I^2 = 89.59\%$; only SUDs: $d_w = -0.04$ [–0.27 to 0.19], ns; $Q_{[2]} = 3.64$, ns; $I^2 = 45.11\%$; $Z = -6.03$, $p < 0.001$); also, when we took into consideration the sample characteristics (several SUDs: $d_w = -0.93$ [–1.09 to –0.76], $p < 0.001$; $Q_{[5]} = 43.50$, $p < 0.001$; $I^2 = 88.50\%$; specific SUD: $d_w = 0.04$ [–0.19 to 0.27], ns; $Q_{[2]} = .38$, ns; $I^2 = 0.00\%$; $Z = -6.64$, $p < 0.001$). Further significant difference in pooled effect sizes was observed when it was considered the effect of clinical setting (Group: $d_w = -1.09$ [–1.28 to –0.90], $p < 0.001$; $Q_{[4]} = 39.21$, $p < 0.001$; $I^2 = 89.80\%$; Group + Individual: $d_w = -0.03$ [–0.26 to 0.20], *ns*; $Q_{[2]} = 5.12$, *ns*; $I^2 = 60.93\%$).

Table 9. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for overall mental health

Overall mental health			
Studies	Measure	*d* (95% CI)	Forest plot
Garland et al., 2010 [83]	BSI	–0.29 (–0.94 to 0.35)	
González-Menéndeza et al. [87], 2014	ASI Psy	–0.06 (–0.87 to 0.75)	
Hayes et al. [36], 2004	ASI Psy	0.16 (–0.26 to 0.58)	
Luoma et al. [38], 2012	GHQ	0.09 (–0.15 to 0.33)	
Lanza et al. [89], 2014	ASI Psy	–0.02 (–0.55 to 0.51)	
Marcus et al. [92], 2001	SCL-90 GSI	0.21 (–0.44 to 0.87)	
Summary		0.06 (–0.11 to 0.23)	



– $Q_{(5)} = 1.81$, $p = 0.87$; $I^2 = 0.00\%$.
– In line with the d_w value, Orwin's fail safe number was not computed.
– $r_{B\text{-}M} = -0.20$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.57$.
– Egger's coefficient = –0.56 (bootstrap 95% CI –2.05 to 0.32) $p = 0.33$.
The consistency of results excluded possible source of heterogeneity.
ASI Psy, addiction severity index psychiatric; BSI, brief symptom inventory; GHQ, general health questionnaire-12; SCL-90 GSI, symptoms checklist-90 global severity index.

We did not detect bias of publication. However, the Orwin's fail-safe number demonstrated that the improvement in depressive symptomatology associated to MBIs is not robust enough.

Anxiety Symptoms

We found a moderate-to-large pooled effect size and large heterogeneity across the results. In detail, MBIs seemed to support greater decrease of anxious symptomatology than other approaches. We revealed significant differences between short- ($d_w = -0.37$ [–0.60 to –0.13], $p < 0.001$ [$n = 2$]) and long-term ($d_w = -1.50$ [–1.90 to –1.10], $p < 0.001$; $Q_{[3]} = 13.71$, $p < 0.001$; $I^2 = 85.42\%$; $Z = -4.85$, $p < 0.001$) effects of MBIs. Additionally, MBIs demonstrated significant different outcomes when we separately considered specific control conditions (CBTs: $d_w = -0.57$ [–0.81 to –0.35], $p < 0.001$ [$n = 2$]; TAU: $d_w = -1.00$ [–1.26 to –0.73], $p < 0.001$; $Q_{[2]} = 53.19$, $p < 0.001$; $I^2 = 96.24\%$). Nevertheless, the previous clinical aspects did not explain the large variability observed in studies results. On the other hand, we found a robust positive relationship between effect sizes and the length of treatment.

Publication bias was not revealed. The Orwin's fail-safe number did not permit to definitely support an advantage of MBIs on anxious symptomatology.

Post-traumatic Symptoms

We found a large pooled effect size in decrease of post-traumatic symptomatology when MBIs were compared to other approaches, although the variability across results was significant. The paucity of studies did not permit to investigate possible sources of heterogeneity and to compute bias of publication. Nevertheless, this finding was robust enough in order to conclude in favor of MBIs in reducing these specific symptoms.

Form of Avoidance Coping Strategies

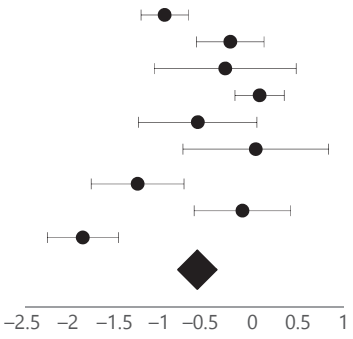
A small pooled effect size was observed. Findings were consistent across studies. MBIs seemed to reduce the use of avoidance coping strategies compared to other clinical approaches. We did not find bias of publication. The Orwin's fail-safe number revealed that the pooled effect size was not robust so as to conclude in favor of a therapeutic effect specifically related to MBIs.

Comparisons between Secondary Treatment Outcomes

The improvement in post-traumatic symptomatology was significantly larger than the other secondary outcomes considered in the current meta-analytic review ($4.55 \leq Z \leq 13.37$; $p < 0.001$; Bonferroni correction: $\alpha = 0.002$). The decreases of negative affectivity and anxious symptoms were significantly greater than outcomes re-

Table 10. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for depressive symptoms

Depressive symptoms			
Studies	Measure	*d* (95% CI)	Forest plot
Garland et al. [84], 2016	BSI Dep	−0.96 (−1.23 to −0.69)	
Garland et al. [85], 2014	C-SOSI Dep	−0.24 (−0.61 to 0.12)	
Glasner et al. [86], 2017	BDI-II	−0.30 (−1.09 to 0.49)	
Hayes et al. [36], 2004	BDI	0.08 (−0.19 to 0.35)	
Nakamura et al. [95], 2015	CES-D	−0.60 (−1.25 to 0.05)	
Petersen and Zettle [96], 2009	BDI-II	0.04 (−0.76 to 0.84)	
Price et al. [97], 2012	BSI Dep	−1.26 (−1.81 to −0.71)	
Smout et al. [100], 2010	BDI-II	−0.11 (−0.64 to 0.42)	
Zemestani and Ottaviani [104], 2016	BDI-II	−1.86 (−2.25 to −1.48)	
Summary		−0.61 (−0.74 to −0.47)***	



*** $p < 0.001$.
– $Q_{(8)} = 88.10$, $p < 0.001$; $I^2 = 90.92\%$.
– $\rho_{d\text{-year of publication}} = -0.71$ (bootstrap 95% CI −1.00 to 0.23) $p = 0.11$.
– $\rho_{d\text{-sample size}} = 0.77$ (bootstrap 95% CI −0.09 to 1.00) $p = 0.07$.
– $\rho_{d\text{-length of treatment}} = 0.33$ (bootstrap 95% CI −0.80 to 0.99) $p = 0.38$.
– $\rho_{d\text{-length of follow up period}} = 0.29$ (bootstrap 95% CI −0.79 to 1.00) $p = 0.58$.
– Orwin's fail safe number = 18.45 (critical value = 55).
– $r_{B\text{-}M} = -0.08$ (bootstrap 95% CI −0.85 to 0.64) $p = 0.83$.
– Egger's coefficient = −1.03 (bootstrap 95% CI −7.45 to 9.28) $p = 0.73$.
– All studies were carried out as RCTs.
– $Z_{\text{group vs. individual + group}} = -5.69$; $p < 0.001$.
– $Z_{\text{SUDs-other psychiatric disorders vs. SUDs}} = -6.03$; $p < 0.001$.
– $Z_{\text{several SUDs vs. specific SUDs}} = -6.64$; $p < 0.001$.
– We did not observe significant differences in pooled effect sizes comparing short to long-term effects of MBIs, type of MBIs (i.e., MBIs + control condition vs manualized MBIs), as well as when it was considered different control conditions (i.e., CBT and TAU).

BSI Dep, brief symptom inventory depression subscale; BDI, beck depression inventory; BDI-II, beck depression inventory-II; CBT, cognitive behavioral therapy; CES-D, center for epidemiologic studies depression scale; C-SOSI Dep, calgary symptoms of stress inventory depression subscale; MBIs, mindfulness-based interventions; MP, mindfulness practices; TAU, treatment as usual.

lated to overall mental health and the use of avoidance coping strategies ($3.72 \leq Z \leq 6.99$; $p < 0.001$), but they did not significantly differ from each other and from other depressive symptoms.

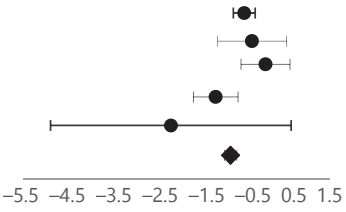
Discussion

The current meta-analytic review sought to demonstrate the incremental effectiveness of MBIs in AUD and DUDs treatment. In line with this objective, we included RCTs and NRCTs in order to draw conclusions about if and to what extent MBIs could promote additional benefits compared to other treatments usually provided in clinical practice. Additionally, we operationalized the efficacy in relation to primary (i.e., AR, abstinence maintenance, levels of perceived craving) and secondary outcomes (i.e., levels of perceived stress, negative affectivity, overall mental health, the severity of depressive, anxious and post-traumatic symptomatology and the use of avoidance coping strategies) for which there is a large consensus to consider them good indexes of therapeutic success. Eventually, we proposed multiple comparisons among primary and secondary outcomes so as to clarify if MBIs have a generalized effect on the previous dimensions, or they could be more effective for specific domains that are relevant for SUDs treatment.

We observed no difference between treatment conditions when we considered AR an outcome measure, especially when we tested the effect of RCTs. These findings

Table 11. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for anxiety symptoms

Anxiety symptoms			
Studies	Measure	*d* (95% CI)	Forest plot
Garland et al. [84], 2016	BSI Anx	–0.45 (–0.70 to –0.19)	
Glasner et al. [86], 2017	BAI	–0.27 (–1.06 to 0.52)	
Liher et al. [91], 2010	LIWC-AN	0.04 (–0.52 to 0.60)	
Price et al. [97], 2012	BSI Anx	–1.10 (–1.62 to –0.58)	
Zemestani and Ottaviani [104], 2016	BAI	–2.12 (–4.87 to 0.63)	
Summary		–0.76 (–0.93 to –0.58)***	



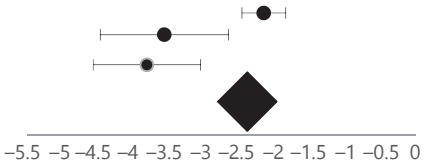
*** $p < 0.001$.
– $Q_{(4)} = 63.63$, $p < 0.001$; $I^2 = 93.71\%$.
– $\rho_{d\text{-year of publication}} = -0.21$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.74$.
– $\rho_{d\text{-sample size}} = 0.50$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.40$.
– $\rho_{d\text{-length of treatment}} = 0.97$ (bootstrap 95% CI –0.87 to 1.00) $p < 0.01$.
– $\rho_{d\text{-length of follow up period}}$ was not estimated because only 3 studies reported follow-up results.
– Orwin's fail-safe number = 14 (critical value = 35).
– $r_{B\text{-}M} = 0.00$ (bootstrap 95% CI –1.00 to 1.00) $p = 1.00$.
– Egger's coefficient = –0.62 (bootstrap 95% CI –3.30 to 6.55) $p = 0.40$.
– $Z_{short\text{-}term\ vs.\ long\text{-}term} = -4.85$; $p < 0.001$.
– $Z_{CBT\ vs.\ TAU} = -2.36$; $p < 0.05$.
– 4 studies were carried out as RCTs and 1 study as NRCT.
– 3 studies reported results from MBIs + control condition; 2 studies from manualized MBIs.
– 4 studies were provided in a group setting, 1 study in individual setting.
– 4 studies were specifically carried out to treat SUDs in comorbidity with other psychiatric disorders.
– All studies were carried out to simultaneously treat several SUDs.

BAI, beck anxiety inventory; BSI Anx, brief symptom inventory anxiety subscale; CBT, cognitive behavior therapy; LIWC-AN, Linguistic Inquiry and Word Count Anxiety subscale; MBIs, mindfulness-based intervention; MP, mindfulness practices; NRCT, nonrandomized controlled trial; RCTs, randomized controlled trials; SUDs, substance use sisorders; TAU, treatment as usual.

might be in line with the literature that has shown how the dropout factor is the norm rather than the exception in treating SUDs (e.g. [105–108]). This evidence might be ascribed to some patient characteristics such as age and cognitive deficits that represented robust risk factors across several clinical trials with different orientations (for a meta-analytic review see: [53]). Interestingly, we found a significant difference in pooled effect sizes when RCTs and NRCTs were compared. Specifically, when MBIs were carried out as an NRCT, they seemed to exhibit a benefit, albeit modest, in reducing the dropout phenomenon. This result may reflect the lack of control of a crucial variable, which has been related to treatment retention in SUDs and it has also been involved in engaging in mindfulness practices that refer to motivation. To explain in detail, lower motivation was related to a higher dropout rate [109–111]; it was also demonstrated how the personal intention in meditation practice is a core aspect in order to identify one of the potential mechanisms to explain how mindfulness affects positive change [112–115]. Further, Mascaro et al. [116] showed how preexisting brain functioning predicts the consequent practice of mindfulness during a Cognitively-Based Compassion Training. Taken the previous considerations together, we might conclude that patients assigned to MBIs in NRCTs could be characterized by preexisting conditions, both neural and psychological, that facilitate the learning and practice of mindfulness abilities and sustain their engagement in treatment retention.

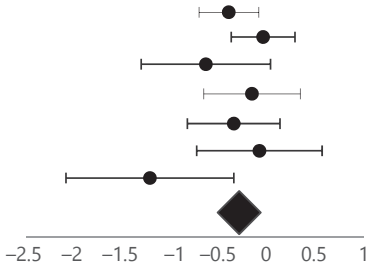
Additional variables that significantly influenced the AR referred to sample characteristics and type of MBIs. Particularly, MBIs seemed to show a slightly better treatment retention than other programs when they were carried out to treat mixed SUDs samples. Conversely, other approaches demonstrated less attrition, although nonsignificant, than MBIs in treating homogeneous

Table 12. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for posttraumatic symptoms

Posttraumatic symptoms			
Studies	Measure	*d* (95% CI)	Forest plot
Garland et al. [84], 2016	PCL-C	–2.14 (–5.30 to –1.83)	
Nakamura et al. [95], 2015	IES-R	–3.55 (–4.57 to –2.53)	
Price et al. [97], 2012	MPSS	–3.80 (–4.87 to –2.72)	
Summary		–2.38 (–2.67 to –2.08)***	

*** $p < 0.001$.
– $Q_{(2)} = 13.94$, $p < 0.001$; $I^2 = 85.65\%$.
– Given the paucity of studies, Spearman's correlations between effect sizes with year of publication, sample size and length of treatment were not estimated. For the same reason, we did not compute subgroups analyses and publication bias.
– Orwin's fail-safe number = 32.70 (critical value = 25).
IES-R, impact of event scale-revised; MPSS, modified posttraumatic stress disorder scale; PCL-C, PTSD Checklist-Civilian version.

Table 13. Effect sizes, forest plots, heterogeneity indexes, Spearman's correlation between effect sizes and clinical sources of heterogeneity, Orwin's fail-safe number, publication bias, and subgroups analysis for avoidance coping strategies

Avoidance coping strategies			
Studies	Measure	*d* (95% CI)	Forest plot
Bowen et al. [46], 2007^	WBSI	–0.40 (–0.72 to –0.08)	
Witkiewitz et al. [78], 2013^^	AAQ	–0.04 (–0.37 to 0.28)	
Garland et al. [83], 2010	WBSI	–0.64 (–1.31 to 0.03)	
González-Menéndeza et al. [87], 2014	AAQ-II	–0.16 (–0.66 to 0.34)	
Lanza et al. [89], 2014	AAQ-II	–0.35 (–0.83 to 0.13)	
Marcus et al. [92], 2001	WCCL-Es	–0.08 (–0.74 to 0.57)	
Petersen and Zettle [96], 2009	AAQ	–1.21 (–2.09 to –0.35)	
Summary		–0.29 (–0.47 to –0.12)**	

** $p < 0.01$.
^ secondary analyses from Bowen et al. [47].
^^ secondary analyses from Bowen et al. [34].
– $Q_{(6)} = 8.67$, $p = 0.19$; $I^2 = 30.86\%$.
– $\rho_{\textit{d-year of publication}} = -0.23$ (bootstrap 95% CI –1.00 to 0.95) $p = 0.50$.
– $\rho_{\textit{d-sample size}} = -0.44$ (bootstrap 95% CI –1.00 to 0.58) $p = 0.38$.
– $\rho_{\textit{d-length of treatment}} = -0.06$ (bootstrap 95% CI –1.00 to 1.00) $p = 0.91$.
– Orwin's fail safe number = 2.7 (critical value = 45).
– $r_{B\text{-}M} = 0.33$ (bootstrap 95% CI –1.00 to 0.59) $p = 0.29$.
– Egger's coefficient = –1.83 (bootstrap 95% CI –4.10 to 0.71) $p = 0.30$.
The consistency of results excluded possible sources of heterogeneity.
AAQ, acceptance and action questionnaire; AAQ-II, acceptance and action questionnaire-II; WBSI, white bear suppression inventory; WCCL, ways of coping checklist escape-avoidance subscale.

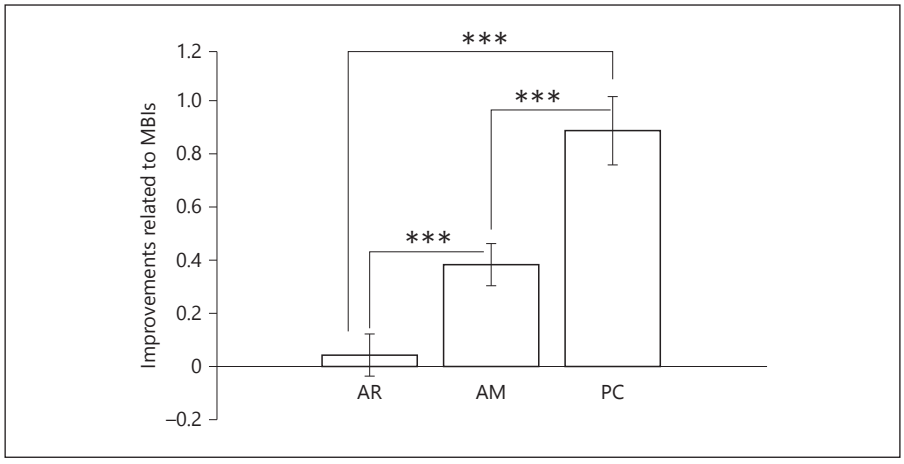


Fig. 2. Pooled effect sizes comparisons within primary outcomes. *** $p < 0.001$. AM, abstinence maintenance; AR, attrition rate; PC, perceived craving ($\alpha = 0.0167$).

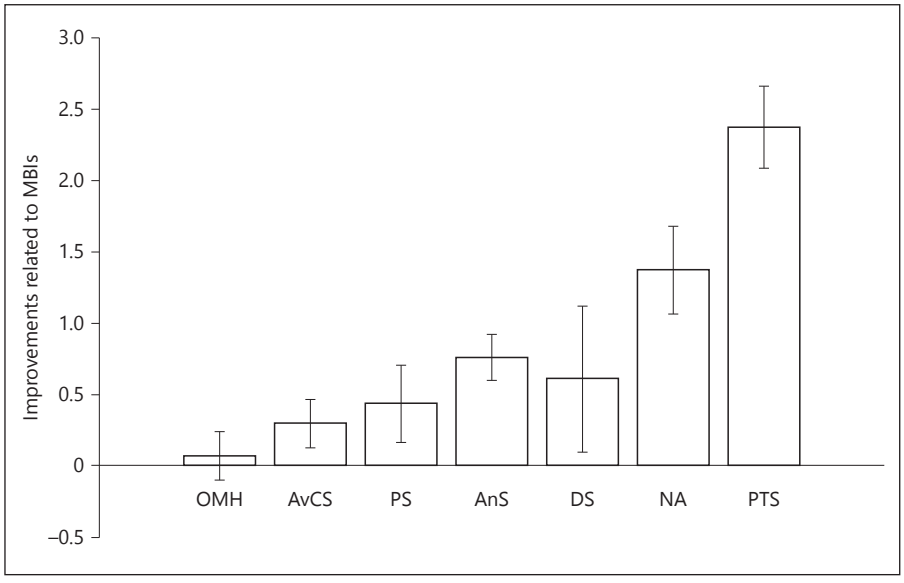


Fig. 3. Pooled effect sizes comparisons within secondary outcomes. Given the huge amount of comparisons, significant differences between pooled effect sizes are reported in results section ($\alpha = 0.002$). AnS, anxious symptoms; AvCS, avoidance coping strategies; DS, depressive symptoms; OMH, overall mental health; NA, negative affectivity; PS, perceived stress; PTS, post-traumatic symptoms.

SUDs samples. Although we might conclude that MBIs seemed to show preliminary advantages in sustain treatment retention when they were carried out to simultaneously treat several SUDs, future studies are needed in order to clarify which therapeutic strategies related to mindfulness approaches might be implicated in explaining this result. We might also extend the previous considerations regarding the relevance of studying therapeutic strategies in treatment retention to the difference observed between types of MBIs. To explain in detail, it seems that when MBIs are combined with standard programs show slightly less AR than manualized MBIs. Taking into consideration this finding, we might postulate that the combination of standard therapeutic strategies (e.g., relapse prevention skills, motivational enhancement interventions) with mindfulness principles (e.g., acceptance attitude) could reinforce the motivation to stay in treatment and reduce relevant interference factors (e.g., Abstinent Violation Effect) to treatment retention. Nevertheless, empirical process-outcome studies are necessary to demonstrate the previous clinical consideration.

As a whole, even though treatment retention seemed to be independent of clinical orientations and settings, considering the small benefit of MBIs in reducing AR in relation to specific conditions, we support a detailed pretreatment assessment of SUDs co-diagnoses, motivational processes, and cognitive functioning in order to recognize subjects who would be the best candidates for these types of intervention [49].

MBIs seemed to consistently promote a slightly better abstinence. It is well established that several neurocognitive aspects related to impulsivity explain the ability to successfully achieve and maintain abstinence during and following addiction treatments [117]. Several empirical studies also demonstrated the existence of a large relationship between dispositional mindfulness and traits related to impulsivity (e.g., [118–120]). An overlap between some mindfulness abilities and impulsivity in explaining the levels of alcohol consumption [121] and alcohol use motivations was also found [122, 123]. Furthermore, it was observed how MBIs have an effect in reducing levels of impulsivity in several clinical and nonclinical samples (e.g., [124–127]). Consequently, we might hypothesize how the slight advantages of MBIs in supporting abstinence in SUDs treatment could be ascribed to the reduction of several forms of impulsivity that are related to lapse and relapse in addictive behaviors. Even though this conclusion is in line with mindfulness theoretical assumptions in addiction treatment (e.g.. [31–32]), these considerations were not robust enough as indicated by the Orwin's fail-safe number. Consequently, future research in MBIs efficacy should focus on process-outcome studies that are needed to prove this hypothesis.

MBIs seemed to show large therapeutic effects in reducing levels of perceived craving in comparison with other approaches. During MBIs, patients are encouraged to bring consciousness to experience of craving and to learn to observe it without judgment and without expression any reaction [78], thereby reducing the activation of neural correlates of craving [128]. However, the heterogeneity of results was large. This variability was partially explained considering whether clinical trials were carried out to specifically treat the co-occurrence of SUDs and psychiatric disorders. Referring to the Orwin's fail-safe number, we can conclude that MBIs are effective programs in reducing levels of craving when they were provided to treat SUDs in comorbidity with other psychiatric disorders. Conversely, no significant differences between treatment orientations were found in craving changes when interventions aimed to exclusively treat SUDs. Given the well-documented therapeutic effects of mindfulness in reducing specific psychiatric symptoms (i.e., depressive, anxious, post-traumatic experiences) [156, 161, 162], these results could be ascribed to secondary effects of MBIs on such symptoms, which were related to craving episodes [129–134], especially in individuals with co-occurring psychiatric disorders and SUDs [135, 136]. This assumption is also corroborated by our results concerning the comparison between MBIs and other treatment approaches in reducing depressive symptoms among SUDs individuals. Particularly, we exclusively found large advantages in favor of MBIs when they were specifically carried out to treat the co-occurrence of SUDs and other psychiatric disorders. Although MBI's therapeutic effects on the decrease of levels of perceived craving seem to be limited to individuals who are affected by SUDs and other psychiatric disorders, such clinical target represents the best primary outcome when MBIs were compared with other active programs.

In light of all the previous considerations, we might preliminarily conclude that formal mindfulness practices, which represent the core feature that differentiate MBIs from treatments usually provided in clinical practice, could be considered effective craving-related coping skills, especially when craving episodes are functionally associated with other psychiatric symptoms. However, future research on MBIs in SUDs should systematically investigate the levels of perceived craving as an outcome measure so as to empirically clarify the role of mindfulness practice, and clarify in detail which mindfulness abilities are implicated, in reducing and/or managing this aspect that it is considered with a large consensus as one of the strongest predictors of relapse in addiction treatment (e.g., [137–139]).

Consistent with a large amount of literature (e.g., for a meta-analysis see: [140]), MBIs seemed to show consistent and small-to-moderate advantages in reducing levels of perceived stress. It was postulated how the ability to observe situations and thoughts nonjudgmentally without reacting to them impulsively, helps people to develop a more reflexive awareness of inner and outer experiences, and it could represent an efficacious tool for the reduction of stress [24, 141]. Even though this dimension might represent a promising treatment outcome, particularly in relation to the well-established role of stress in inducing craving and relapse (e.g., [142–144]), the difference between clinical conditions in reducing the level of perceived stress is not robust enough to definitively conclude in favor of MBIs. One possible explanation of the small difference between MBIs and other treatments might be related to a primary effect of detoxification itself (e.g., reduction of withdrawal symptoms) rather than a specific psychotherapeutic effect. As a consequence, future research should investigate which psychological processes could be exclusively improved by MBIs in response to discomfort and stress and how they are implicated in craving management and relapse prevention.

We observed great advantages in reducing the negative affectivity associated with MBIs, even though only one

study [84] explained the pooled effect size. Generally speaking, this finding is principally consistent with the results from the empirical literature that demonstrated how mindfulness programs produced their benefits in clinical and nonclinical samples by decreasing the negative affect and by improving the positive affect (e.g., [26, 145]), as well as by enhancing emotion regulation [146–148]. It is well known, how one of the most prominent risk factors for craving and relapse in SUDs is a negative factor (e.g., [149–151]). Consistently, it is possible to assume how MBIs could work on several processes, both psychological and neural [146–148], that might prevent relapse reducing levels of negative emotionality. Nonetheless, the large variability of results, the paucity of studies that specifically investigate the previous aspect, and the extent of pooled effect size did not permit to draw definitive conclusions. Consequently, given the central role of negative affect in relapse prevention, future clinical research in SUDs treatment should systematically include the evaluation of this dimension as a secondary outcome, especially assessing its temporal stability after the end of interventions.

We observed no significant differences between MBIs and other approaches in improving the overall mental health. We might assume how this finding could reflect the consequence of abstinence. It is well established how a wide range of psychiatric symptoms presented by SUDs individuals at admission to treatment are associated with substance intoxication and show a quick remission during and after the treatment (e.g., [152–154]). Therefore, we may conclude that it is needed to demonstrate if mindfulness practice could really represent a long-term protective factor for relapse in psychopathology among SUDs subjects, as showed in other clinical populations (e.g., [155]) that represented an antecedent of relapse in substance use (e.g., [136]).

However, when we considered specific psychopathological symptoms, we found significant dissimilar findings. Considering depressive symptomatology, we observed moderate-to-large improvements when MBIs were compared to other treatments. However, we revealed the existence of a large variability across studies, several sources of heterogeneity, and pooled effect size was not large enough to consider it as definitely robust. In detail, MBIs showed significant larger benefits in reducing depressive symptoms when it was considered specific clinical features: (a) MBIs seemed to be more effective when they were carried out to treat the co-occurrence of SUDs and other psychiatric disorders; (b) MBIs supported larger improvements in mixed SUDs samples than in homogeneous populations; (c) MBIs sustained a larger decrease in depressive symptomatology when they were provided in a group setting than in a combined setting (i.e., group + individual).

The efficacy of MBIs is well supported by several RCTs in treating depression [158]. Taking into consideration such evidences and our results, we might preliminarily conclude that MBIs are also effective in reducing depressive symptoms among AUD and DUDs populations, especially when they co-occur with other psychiatric disorders. Additionally, given the controversial results regarding the effects of clinical settings in treating depression [157] and the well-established efficacy of peer-based groups in SUDs [158, 159], future research should explore possible therapeutic factors that sustain the efficacy of MBIs in reducing depressive symptoms when they are exclusively carried out in a group setting, and which interference processes could be associated to the patient-therapist relationship [160].

Consistent with data regarding the efficacy of MBIs in treating anxiety disorders [161], we might partially extend similar considerations to the decrease of anxious symptoms among SUDs individuals. Particularly, even though we observed large variability in studies results and not conclusive findings, we observed large differences between MBIs and TAU control conditions, as well as when long-term effects of MBIs were evaluated. Specifically, as demonstrated in other clinical populations [163], MBIs seemed to promote better long-term therapeutic effects than short-term ones in reducing anxious symptoms. Moreover, the significant difference observed in pooled effect sizes when we separately considered TAU and CBT control conditions might reflect the demonstrated efficacy of CBT interventions in treating anxiety disorders, even when they co-occur with SUDs [168].

Eventually, robust findings in favor of MBIs were found when we took into consideration the severity of post-traumatic symptoms. In line with the therapeutic efficacy of MBIs in treating post-traumatic stress disorder (PTSD) [162] and values of effect sizes found in the current meta-analytic review, we can conclude that such interventions might be considered an effective alternative in treating the co-occurrence of SUDs and PTSD.

In relation to the decrease of avoidance coping strategies, we found a consistent and small benefit associated with MBIs compared to other treatment approaches. Even though it was demonstrated that MBIs were more effective programs than other interventions in reducing

avoidance coping strategies among several clinical populations [163–166], we cannot support the same conclusion among SUDs. This finding might be in line with Arch and Craske [167] who argued that both cognitive restructuring (CBT process) and cognitive defusion (e.g., ACT process) aim to decrease avoidance and enhance exposure to previously avoided and suppressed internal experiences. Consequently, we might consider the reduction of avoidance coping strategies as common therapeutic dimension that different therapeutic orientations seem to equally address with dissimilar techniques.

Eventually, taking into consideration results from multiple comparisons within secondary outcomes, we conclude that the most robust therapeutic effect of MBIs refers to the decrease of post-traumatic symptoms. Considering comparable pooled effect sizes of depressive/anxious symptoms and negative affectivity, we might also assume that MBIs improve several aspects related to the emotional well-being of patients.

In conclusion, MBIs seemed to show clinically significant, albeit preliminary, advantages compared to other clinical approaches when it was considered specific relapse factors that refer to anxious and depressive symptoms, especially when SUDs co-occur with other psychiatric disorders. Furthermore, we might assume that MBIs are valid and effective therapeutic alternatives when SUDs individuals are affected by PTSD. Formal mindfulness practices could be considered additional craving-related coping strategies, particularly for dual-diagnosis individuals. Modest, although significant, benefits in favor of MBIs were detected in relation to abstinence. Treatment retention was independent of the therapeutic approach. Eventually, taking into consideration null differences regarding AR between MBIs and other active programs, we also conclude that the benefits described above should be exclusively applied to patients who go through the complete course of treatment.

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