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ORIGINAL PAPER

Mindfulness-Oriented Recovery Enhancement for Addictive Behavior, Psychiatric Distress, and Chronic Pain: A Multilevel Meta-Analysis of Randomized Controlled Trials

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Abstract

Objectives Mindfulness-Oriented Recovery Enhancement (MORE) is an integrative intervention designed to ameliorate addiction, chronic pain, and psychiatric symptoms. Although multiple randomized controlled trials (RCTs) have examined the clinical efficacy of MORE, no study has quantitatively synthesized this body of research. Thus, we conducted a meta-analysis of RCTs examining the effects of MORE on addictive behaviors, craving, opioid dose, pain, and psychiatric symptoms.

Methods Relevant manuscripts were identified through comprehensive searches of four bibliographic databases. Two- and three-level random-effects models were used to generate synthesized effect size estimates, and meta-regressions were performed to examine whether study and sample characteristics influenced the magnitude of aggregate effect sizes.

Results Our search identified 16 manuscripts reporting data from eight RCTs ($N = 816$). Moderate to small effects in favor of MORE were observed for addictive behaviors (SMC = −.54, $p = .007$), craving (SMC = −.42, $p = .010$), opioid dose (MC = −17.95, $p < .001$), chronic pain (SMC = −.60, $p < .001$), and psychiatric symptoms (SMC = −.34, $p < .001$). MORE's effects on psychiatric symptoms and craving were not moderated by participant race, gender, age, or income.

Conclusions Study findings provide empirical evidence of MORE's efficacy for a wide diversity of individuals, and as such, MORE should now be disseminated broadly throughout the healthcare system.

Meta-analysis Pre-registration: PROSPERO #CRD42022319006

Keywords Mindfulness · Addiction · Substance use disorders · Chronic pain · Mental health · Opioids

Approximately 275 million people worldwide use addictive substances each year, and of these, 36.3 million have a substance use disorder (SUD; UNODC, 2021). Since 1990, the global prevalence of drug and alcohol use has increased and is now the leading preventable cause of death worldwide (Murray et al., 2020; Ritchie & Roser, 2019). In the United States (US), over 91,000 Americans died from drug overdoses in 2020—the highest number ever recorded in a year (Hedegaard et al., 2021; Wilson, 2020). Millions more were impacted by the deleterious consequences of addiction on health, social well-being, and quality of life (Ignaszewski, 2021), which have only worsened under the coronavirus disease 2019 (COVID-19) pandemic (Czeisler et al., 2020). To curb this rapidly accelerating public health crisis, there is an urgent need for interventions that treat addiction and prevent overdose.

Nationally representative surveys estimate that 52.8% of individuals who experience an SUD in their lives will also experience chronic pain (Ilgen et al., 2010), and 37.9% will have a co-occurring psychiatric disorder (Han et al., 2017). Likewise, SUDs are not uncommon among individuals with psychiatric disorders, as well as among people with chronic pain—and particularly those patients prescribed long-term opioid therapy for analgesia (LTOT; Boscarino et al., 2010; Groenewald et al., 2018; Manchikanti et al., 2007; van Rijswijk et al., 2019; Vowles et al., 2015). When comorbid with SUDs, chronic pain and psychiatric

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disorders are associated with decreased functional impairment, a more chronic and protracted course of illness, and a higher risk of fatal overdose (Andersson et al., 2019; Ditre et al., 2019; Fernandez et al., 2019; Griffin et al., 2016; Jakubczyk et al., 2016; Larson et al., 2007; Morasco et al., 2011; Rogers et al., 2021; Sheu et al., 2008). Indeed, epidemiological research has linked increases in the prevalence of these intersecting "diseases of despair" to the declining health and rising mortality rates in the US (Case & Deaton, 2015, 2017; Glei & Preston, 2020; Woolf & Schoomaker, 2019).

Mounting evidence suggests that pain and mental health factors play a dynamic and reciprocal role in the initiation and maintenance of addictive behaviors. Psychoactive substances are often used to relieve physical pain and psychiatric distress (Khantzian, 1997). Such self-medication motives are commonly observed among chronic pain patients (Alford et al., 2016), as well as among individuals with mood and anxiety disorders (Turner et al., 2018). However, when substances are repeatedly used in the context of physical and/or emotional pain, these states may come to elicit craving that, in turn, motivates addictive behavior (Baker et al., 2004; Parisi et al., 2022b). As such, both interoceptive (e.g., physical or emotional pain) and exteroceptive cues (e.g., the sight of the drug) can activate the automatic habit of addiction even in the absence of the conscious intention to use drugs (Tiffany, 1990). Over time, addiction induces allostatic changes in the brain's stress and reward systems that decrease sensitivity to natural reinforcing stimuli while increasing sensitivity to negative emotions and physical pain (Edwards et al., 2011; Koob, 2021; Shurman et al., 2010). As natural rewards lose their value and aversive experiences intensify, individuals may increase their substance consumption—whether illicit or prescribed—as a means of counteracting a progressively worsening emotional state. For individuals with chronic pain and/or psychiatric comorbidities, this allostatic shift may exacerbate the affective dysregulation, anhedonia, and blunting of reward function already associated with both conditions (Borsook et al., 2016; Elvemo et al., 2015; Koob, 2021; Manchikanti et al., 2007; Trøstheim et al., 2020), propelling a downward spiral of addictive behavior (Garland et al., 2013b).

To reverse this trajectory, interventions are needed to target the pathogenic mechanisms undergirding addiction, chronic pain, and psychiatric symptoms. To this end, Mindfulness-Oriented Recovery Enhancement (MORE) is an intervention grounded in affective neuroscience that unites mindfulness training, cognitive-behavioral therapy (CBT), and positive psychological principles into a transdiagnostic approach designed to simultaneously address addictive behavior, physical pain, and psychiatric symptoms.

MORE is a manualized, group-based intervention that provides sequenced training in mindfulness, reappraisal, and savoring skills (Garland, 2013). The original MORE protocol included 10 weekly sessions; subsequently, an 8-session protocol was developed and tested in multiple clinical trials. Participants first receive training in mindfulness meditation techniques to strengthen meta-awareness and cognitive control as a means of regulating maladaptive automatic habits and decreasing affective bias during appraisals of pain and craving sensations. This enhanced cognitive control facilitates subsequent training in reappraisal—a technique aimed at reinterpreting stressful life events to reduce negative emotions and reevaluating the adverse consequences of substance misuse. Finally, mindfulness amplifies the practice of savoring naturally rewarding experiences, a technique intended to boost reward processing, positive emotions, and meaning in life (Garland, 2013). Ultimately, the MORE treatment sequence culminates in a focus on self-transcendence—the sense of being connected to something greater than the self (Garland & Fredrickson, 2019; Hanley et al., 2018). Unlike other mindfulness-based interventions, MORE leverages principles from social-behavioral learning theory to enhance the motivation to practice mindfulness, build therapeutic expectancy, and positively reinforce success experiences to increase engagement with the intervention. Through an integration of mindfulness, reappraisal, and savoring techniques, MORE aims to restructure reward processing from valuation of drug rewards back to valuation of natural rewards as a means of decreasing addictive behaviors and craving (Garland, 2021). At the same time, MORE applies these techniques in an effort to reduce physical pain and psychiatric symptoms while enhancing well-being (Garland, 2016).

Since its inception, multiple clinical trials have supported the clinical efficacy of MORE across a diverse range of populations, including individuals with alcohol use disorders (AUDs; Garland et al., 2010); individuals receiving methadone-maintenance therapy (MMT) for opioid use disorders (OUD; Cooperman et al., 2021); chronic pain patients prescribed LTOT (Garland et al., 2014b, 2019b, 2022); individuals with co-occurring substance use and psychiatric disorders (Garland et al., 2016); and individuals with behavioral addictions (Li et al., 2017). A quantitative synthesis of this research is now needed to provide comprehensive evidence of MORE's effects on addictive behaviors, craving, opioid dose, pain, and psychiatric symptoms, as well as to explore potential moderators of its efficacy. Given the underrepresentation of participants from diverse racial/ethnic groups and marginalized backgrounds in research examining mindfulness-based interventions for addiction (Spears, 2019), we were particularly interested in examining whether the impact of MORE on these outcomes was affected by the racial,

gender, or socioeconomic composition of samples. Age was also identified as a salient moderating variable in light of research suggesting that older adults may have unique needs that can impact their responsiveness to SUD treatment (Choi et al., 2014; Kuerbis & Sacco, 2013). Therefore, the primary objectives of the present study were to (a) conduct a meta-analysis of randomized controlled trials examining the effects of MORE on addictive behaviors, craving, opioid dose, chronic pain, and psychiatric symptoms, and (b) examine whether the effects of MORE on clinical outcomes differed as a function of study and sample characteristics.

Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (Moher et al., 2009). A study protocol was submitted through PROSPERO, an international prospective register for review protocols (registration number, CRD42022319006).

Selection Criteria

Randomized controlled trials (RCTs) evaluating the effects of MORE on people with substance use disorders, substance use (including alcohol, nicotine, or prescription drugs including opioids), or behavioral addictions were eligible for inclusion. Studies were excluded if they did not evaluate MORE, used research designed other than RCTs (e.g., quasi-experimental, qualitative), did not include sufficient data to calculate an effect size, or were not published in peer-reviewed journals. No limitations were placed on studies based on the date of publication or language.

Search Strategy

A systematic, computerized search was conducted in the bibliographic databases *Web of Science*, *PsychInfo*, *Scopus*, and *PubMed*. Studies evaluating MORE were identified using the following search terms: *Mindfulness-Oriented Recovery Enhancement OR Mindfulness Oriented Recovery Enhancement AND intervention OR program OR treatment.* Searches were conducted in March 2022 and updated in July to identify any additional studies meeting inclusion criteria.

Following this initial search, two reviewers (A.P. and R.L.R.) worked independently to conduct a title and abstract review to assess articles' eligibility for inclusion. Next, both reviewers read each study in full and excluded those that did not meet prespecified inclusion/exclusion criteria. There was near unanimity with respect to the studies identified as eligible during the title-and-abstract review. Disagreements during the full-text review were few and resolved through mutual discussion until consensus was reached. Additional relevant publications were identified by manually examining the reference lists of included articles and contacting the authors of studies eligible for inclusion.

Data Extraction

Two reviewers (A.P. and R.L.R.) independently extracted the following information from each manuscript: author, publication year, study aims, study setting, inclusion/exclusion criteria, sample size, mean age of participants, percentage of female participants, percentage of white participants, percentage of participants earning less than $25,000, intervention characteristics, length of treatment, primary outcomes, outcome measures, follow-up time points, and the means and standard deviations of primary outcomes at the longest follow-up time point available. If demographic information, means, or standard deviations were not reported in primary studies or supplementary materials, corresponding authors were contacted to request this data. When studies reported results based on analyses of ecological momentary assessments (EMA), means and standard deviations of EMAs collected during the first and last available week of measurement were computed for each time period and used for the meta-analysis. Following data extraction, both authors categorized extracted effect sizes into one of five outcomes: addiction-related behaviors, craving, opioid dose, pain, and psychiatric symptoms.

Risk of Bias

Risk of bias was assessed using Cochrane's risk-of-bias tool for randomized trials (RoB 2; Sterne et al., 2019). Following the recommendation of the RoB 2, a code of "high risk", "low risk", or "some concerns" was assigned to the following five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was then used to rate the overall quality of evidence for each of our primary outcomes (Schünemann et al., 2008). Both assessments were conducted independently by two reviewers (A.P. and R.L.R.). Disagreements were rare and resolved through discussion.

Summary Measure

For addiction-related behaviors, craving, psychiatric symptoms, and chronic pain, standardized mean change (SMC) using raw score standardization was selected as our effect

size metric. Here, the SMC between scores at pretreatment and the last available follow-up point was estimated for MORE and control conditions separately and multiplied by a bias correction factor. We selected the last available follow-up point as a conservative measure of the long-term impact of MORE. The final effect size estimate was computed by calculating the difference in the SMC between the two groups (Morris, 2008). To calculate the variance for SMC, the correlation between measurement points is required. Because this estimate was not reported by primary studies, we imputed a conservative value of $r = 0.70$ and re-estimated models using r values of 0.30, 0.50, and 0.90 to ensure the robustness of our findings (Rosenthal, 1984). No substantive differences emerged from these analyses.

All studies examining opioid dosing reported this outcome in morphine milligram equivalents (MME). Consequently, our effect size metric for opioid dose was the difference between unstandardized change scores for MORE and control conditions between pretreatment and the last available follow-up point. Measures of variation for mean change were estimated by converting F statistics and p values to standard errors and standard deviations (Higgins et al., 2019).

Effect Size Dependency

Many studies included in this review reported more than one effect size for each of our meta-analytic outcomes. However, including more than one effect size per study violates the assumption of independence that underlies traditional two-level random effects models (Borenstein et al., 2009). To address this dependency, we used three-level random effects models to evaluate outcomes in which studies contributed multiple effect sizes (pain, addictive behavior, psychiatric symptoms, craving), and a two-level model to evaluate opioid dose, as studies reporting on this outcome each contributed only one effect size. As with two-level random effects models, three-level models estimate sampling variance from individual effect sizes (level 1) and the variance between effect sizes from different studies (level 3). However, three-level models also yield an estimate of the variance between effect sizes drawn from the same study (level 2). This approach enables the extraction of multiple effect sizes in a non-aggregated form, thereby maximizing statistical power (Fernández-Castilla et al., 2020; Van den Noortgate et al., 2015; Van Den Noortgate & Onghena, 2003).

Data Analyses

Meta-analyses were performed using a multi-staged approach. We first calculated intercept-only two- and three-level random effects models, which yielded an estimate of the effect of MORE relative to comparison conditions. Next, we examined the heterogeneity of effect size estimates. For two-level random effects models, the I^2 statistic and τ were used. For three-level models, heterogeneity was assessed by calculating three variance components: ${\sigma_1}^2$, ${\sigma_2}^2$, and the I^2 statistic, which was partitioned across levels 2 and 3 to provide an estimate of the percentage of variance at each level of analysis (Cheung, 2019). For two-level models, I^2 values above 25% were considered to reflect high levels of heterogeneity (Borenstein et al., 2009). For three-level models, independent log-likelihood ratio rests were conducted to test for heterogeneity at levels 2 and 3, and statistically significant tests were interpreted as evidence of heterogeneity (Assink & Wibbelink, 2016).

When significant heterogeneity was observed, we performed univariate random-effects meta-regressions to investigate study- and sample-level characteristics that may have impacted the effects of MORE on primary outcomes. Our moderating variables included the following: racial/ethnic composition (percentage of white participants), sample age, sample low-income socioeconomic status (percentage of the sample reporting an annual income of less than $25,000), gender composition (percentage of female participants), and year of publication. If studies reported income as a categorical variable, we used the closest available value when thresholds other than $25,000 were reported. As recommended by Fu et al. (2011) meta-regressions were only performed when six or more studies provided effect size estimates.

Publication bias was assessed through visual inspection of the symmetry of contour-enhanced funnel plots and Egger's tests, which were modified for use in three-level models by estimating the variance component of each outcome as a model covariate. All models were estimated using the Restricted Maximum-Likelihood (REML) estimator (Pastor & Lazowski, 2018) using the "rma" and "rma.mv" functions of the metafor package (Viechtbauer, 2010) in RStudio (2021).

Results

Characteristics of Selected Studies

We screened 122 citations and 30 full-text articles. Sixteen manuscripts reporting data from eight RCTs of MORE (total $N = 816$) were ultimately included (see Fig. 1). Seven manuscripts reported primary outcomes from clinical trials (Cooperman et al., 2021; Garland et al., 2010, 2014b, 2016, 2019b, 2022; Li et al., 2017), seven were secondary analyses (Garland et al., 2014a, 2017b, 2019a, 2020; Hanley & Garland, 2020; Parisi et al., 2022a; Roberts et al., 2022), and two reported data from the same sample of participants taking part in a randomized controlled mechanistic study (Garland et al., 2021; Hudak et al., 2021). All studies were published in English between 2010 and 2022. Key characteristics of included RCTs and their corresponding manuscripts are detailed in Table 1.

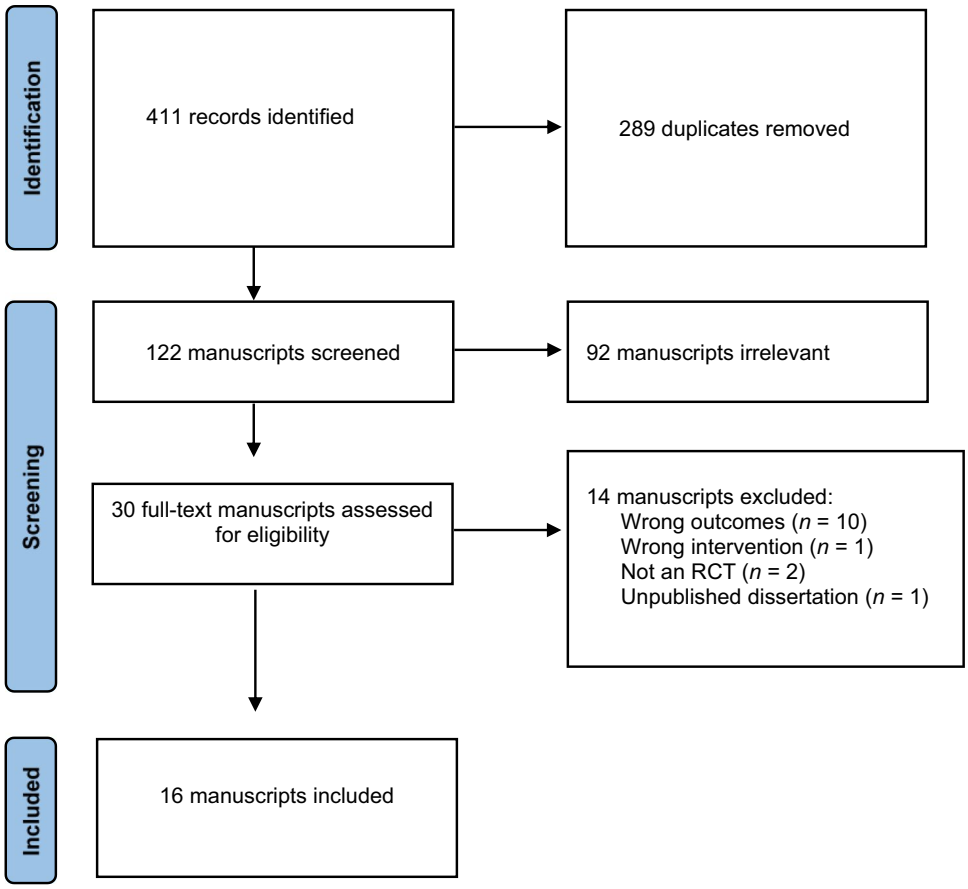

Fig. 1 Search and screening process

Interventions

Across all RCTs, MORE was delivered as a manualized, group-based intervention consisting of weekly, 2-h sessions. Two RCTs examined 10-session versions of MORE developed for individuals with AUDs (Garland et al., 2010) and SUDs (Garland et al., 2016). The remaining RCTs examined 8-session versions of MORE developed to address opioid use among individuals with chronic pain (Garland et al., 2014b, 2019b, 2021, 2022) and internet gaming disorder (Li et al., 2017).

The majority of RCTs (75%) compared MORE to supportive psychotherapy groups (SG) matched to MORE in terms of their structure, intensity, and homework requirements (Garland et al., 2010, 2014b, 2019b, 2021; 2022; Li et al., 2017). One RCT compared MORE to methadone treatment-as-usual (TAU; Cooperman et al., 2021), and another RCT employed two comparison conditions: cognitive-behavioral therapy (CBT) and TAU (Garland et al., 2016). Means and standard deviations from the CBT condition were used to generate effect sizes for this latter study, and models were re-estimated using the TAU condition as a sensitivity analysis. No substantive differences were found. Intervention fidelity (e.g., therapist adherence and competence) for MORE and active comparison conditions (SG, CBT) was monitored in all but one RCT (Garland et al., 2010), with no major deviations reported.

Participants

The eight RCTs included in this meta-analysis examined 816 adult participants. Sample sizes ranged from 30 to 250, and the mean age of study samples ranged from 25 to 59. Though the majority of participants were male (58.1%) and white (67.5%), a substantial proportion of participants were female or from diverse and underrepresented racial/ethnic groups. Four RCTs enrolled individuals prescribed LTOT for chronic pain. Of these, one included individuals who evidenced opioid misuse (Garland et al., 2022), one included individuals who did *not* evidence opioid misuse at the time of study enrollment (Garland et al., 2019b), and two did not restrict participants by opioid misuse status (Garland et al., 2014b, 2021). The remaining studies recruited individuals with AUD (Garland et al., 2010); comorbid substance use and psychiatric disorders (Garland et al., 2016); internet gaming disorder (Li et al., 2017); and individuals with OUD and chronic pain receiving methadone treatment (Cooperman et al., 2021).

Table 1 Study descriptions of randomized controlled trials examining Mindfulness-Oriented Recovery Enhancement

Author, year	*N*	Sample	Mean age	% white	% female	% income ≤ 25,000	Comparison	Intervention length	Measurement points	Outcomes
Garland et al., 2010	53	Adults in a therapeutic community for alcohol use disorder	40.3 (9.4)	23.4	20.8	52.8[a]	ASG	10 weeks	Baseline, midtreatment, posttreatment	BSI psychiatric symptoms, PSS stress PACS alcohol craving
Garland et al., 2014b	115	Chronic pain patients receiving long-term prescription opioids for analgesia	48.3(14)	65.2	67.83	23.5[a]	SG	8 weeks	Baseline, posttreatment, 3-months posttreatment	COMM opioid misuse BPI pain severity BPI pain interference NRS opioid craving C-SOSI depression C-SOSI anger C-SOSI sympathetic arousal
Garland et al., 2014a	49	Secondary data analysis of Garland et al., 2014a	46.6 (13.9)	Not reported	71.43	Not reported	SG	8 weeks	Baseline, posttreatment	NRS craving
Garland et al., 2017b	55	Secondary data analysis of Garland et al., 2014a	48.9 (11.6)	74.6	61.8	Not reported	SG	8 weeks	Baseline, last treatment week	NRS EMA pain intensity
Garland et al., 2016	180	Adult men in a therapeutic community for substance use disorders	37.1 (10.8)	42	0	100	CBT, TAU	10 weeks	Baseline, posttreatment	PCL-C PTSD BSI depression BSI anxiety PACS craving
Li et al., 2017	30	Students and university employees with internet gaming disorder	25 (5.4)	53.3	16.7	Not reported	SG	8 weeks	Baseline, posttreatment, 3 months posttreatment	BSI distress DSM-5 internet gaming disorder symptoms VAS video game craving OCS problematic internet use
Garland et al., 2019b	95	Chronic pain patients prescribed long-term opioid therapy for analgesia who did not exhibit opioid misuse	56.75 (11.7)	89.5	66.3	36.8	SG	8 weeks	Baseline, posttreatment, 3-months posttreatment	COMM opioid misuse BPI pain severity
Garland et al., 2020	95	Secondary analysis of Garland et al.,2019b	56.75 (11.7)	89.5	66.3	36.8	SG	8 weeks	Baseline, posttreatment, 3 months posttreatment	Opioid dose
Hanley and Garland., 2020	39	Secondary analysis of Garland et al., 2022	55.1 (10.6)	84.6	64.1	Not reported	SG	8 weeks	Baseline, posttreatment	NRS opioid craving

Table 1 (continued)

Author, year	*N*	Sample	Mean age	% white	% female	% income ≤ 25,000	Comparison	Intervention length	Measurement points	Outcomes
Roberts et al., 2022	95	Secondary analysis of Garland et al., 2019b	56.75 (11.7)	89.5	66.3	36.8	SG	8 weeks	Baseline, posttreatment, 3 months posttreatment	DASS distress
Parisi et al., 2022a	95	Secondary analysis of Garland et al., 2019b	56.75 (11.7)	89.5	66.3	36.8	SG	8 weeks	Baseline, last treatment week	NRS EMA pain intensity NRS EMA opioid craving
Cooperman et al., 2021	30	Individuals with chronic pain receiving MMT for OUD	50.4 (8.8)	36.7	50	33.3[b]	SG	8 weeks	Baseline, posttreatment, 2 months posttreatment	Days of substance use PACS opioid craving CESD depression BAI anxiety RAND pain RAND well-being
Garland et al., 2019a	30	Secondary analysis of Cooperman et al., 2021	50.4 (8.8)	36.7	50	33.3[b]	TAU	8 weeks	Baseline, last treatment week	EMA NRS pain intensity EMA NRS pain unpleasantness EMA NRS opioid craving EMA NRS stress
Garland et al., 2022	250	Chronic pain patients on long-term opioid therapy who exhibited opioid misuse	51.8 (11.9)	87.2	63.9	39.2	SG	8 weeks	Baseline, posttreatment, 1-, 3-, 6-, and 9 months posttreatment	BPI pain interference BPI pain severity COMM opioid misuse Opioid dose EMA NRS opioid craving PCL-C PTSD DASS depression DASS distress
Hudak et al., 2021	62	Veterans receiving prescribed long-term opioid therapy for chronic pain	59.3 (10)	82.3	14.5	35.2	SG	8 weeks	Baseline, posttreatment, 2-, and 4-months posttreatment	Opioid dose
Garland et al., 2021	63	Same sample as Hudak et al., 2021	59.2 (10.1)	82.5	17.5	Not reported	SG	8 weeks	Baseline, 4-months posttreatment	SHAPS anhedonia

Note. ASG = Alcohol supportive psychotherapy group; SG = supportive psychotherapy group; CBT = cognitive behavioral therapy; TAU = treatment-as-usual; BSI = Brief Symptom Inventory; PSS = Perceived Stress Scale; PAC = Penn Alcohol Craving Scale; COMM = Current Opioid Misuse Measure; BPI = Brief Pain Inventory; NRS = numeric rating scale; EMA = ecological momentary assessment; C-SOSI = Calgary Symptoms of Stress Inventory; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders: Fifth Edition; BAI = Beck Anxiety Inventory; VAS = Visual Analogue Scale; OCS = Online Cognitions Scale; DASS = Depression Anxiety Stress Scale; MMT = methadone maintenance therapy; OUD = opioid use disorder; CESD = Center for Epidemiologic Studies Depression Scale Revised ; BAI = ; RAND = RAND Short-Form Health Survey; SHAPS = Snaith-Hamilton Pleasure Scale

[a] Income measured as the percentage of participants earning less than $20,000 annually

[b] Income measured as the percentage of participants earning less than $30,000 annually

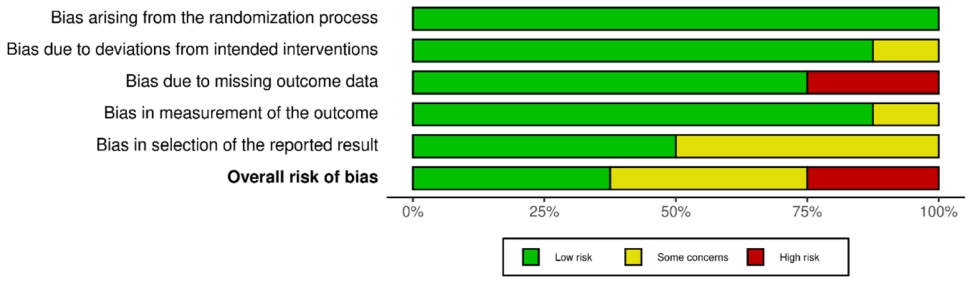

Fig. 2 Present review authors' judgements of the risk of bias items presented as percentages across all included randomized controlled trials

Methodological Characteristics

Figure 2 illustrates the methodological attributes of the eight included RCTs as assessed using the RoB 2. All trials reported the use of appropriate random sequence generation methods; likewise, intervention adherence was high across RCTs and supported by assessments of treatment fidelity. Most RCTs reported that assessors were blinded to treatment condition; however, as is common in psychosocial interventions, participants were not blinded in any study. Although several RCTs reported high levels of attrition, the quantity of missing data was comparable to other studies of psychosocial interventions for SUD (Lappan et al., 2020). Moreover, most studies ($n = 7$) performed intent-to-treat analyses with statistical techniques designed to account for missing data (e.g., maximum likelihood estimation of missing data). Standardized, validated measures were used to assess outcomes across studies. Although many study protocols ($n = 6$) were preregistered on clinicaltrials.gov, two studies were completed prior to when preregistration requirements became commonplace. As such, two trials were not registered, preventing us from ruling out the potential for biases in the selection of reported results for those trials. Details of the RoB 2 assessment are available in Online Resource 1.

Outcomes

The 16 included manuscripts produced 47 effect sizes reflecting the effects of MORE on addictive behavior, pain, psychiatric symptoms, craving, and opioid dose relative to comparison conditions. Results from all meta-analyses are reported in Table 2, and our summary of evidence is presented in Table 3.

Addictive Behaviors

Five RCTs (Fig. 3) produced six effect sizes on addictive behaviors, including opioid misuse (Garland et al., 2014b, 2019b, 2022), illicit drug use (Cooperman et al., 2021), and internet gaming disorder symptoms (Li et al., 2017). A statistically significant, moderate effect size was observed, suggesting that MORE participants experienced larger reductions in addictive behaviors than participants in comparison conditions (SMC = −0.54, 95% CI [−0.86, −0.23], $p = 0.007$).

Craving

Seven RCTs (Fig. 4) reported ten effect sizes related to opioid (Cooperman et al., 2021; Hanley & Garland, 2020; Garland et al., 2014a, 2014b, 2019a; Parisi et al., 2022a),

Table 2 Mean effect sizes of outcomes

Outcome	Studies	ES	SMC	95% CI	*p*	Level 1	σ_1^2	Level 2	σ_2^2	Level 3	τ	I^2	Egger's
Addictive behaviors	5	6	−0.54	[−0.86, −0.23]	.007	63.36	0.00	0.00	0.03	36.64			−0.40*
Chronic pain	4	10	−0.60	[−0.83, −0.37]	< .001	30.75	0.06	69.25	0.00	0.00			−0.73**
Psychiatric symptoms	8	18	−0.34	[−0.51, −0.17]	< .001	45.07	0.00	6.57	0.03	48.36			−0.10***
Craving	7	10	−0.42	[−0.73, −0.11]	.010	21.90	0.14**	78.10	0.00	0.00			−0.01
Opioid dose[ab]	3	3	−17.95	[−26.17, −9.72]	< .001						2.58	11.20	−6.81

Note. Studies, number of studies; ES, number of effect sizes; SMC, standardized mean change; CI, confidence interval; Level 1, variance attributable to sampling error at level 1; σ_1^2, variance estimate for effect sizes from the same study, with significant values indicating a significant log-likelihood test; σ_2^2, variance estimate for effect sizes from different studies, with significant values indicating a significant log-likelihood test; Level 2, I^2 for level 2; Level 3, I^2 for level 3; I^2, total I^2 for two-level random effects models; τ, estimated standard deviation of true effects across studies for two-level models

*$p < .05$, **$p < .01$, ***$p < .001$

[a]Outcome was evaluated using a two-level random effects model

[b]Effect sizes were generated using mean change scores

Table 3 Summary of evidence

Outcome	Studies	ES	*N*	SMC	95% CI	Egger's	Trim-and-fill	Heterogeneity	Meta-regressions	QOE	Comments
Addictive behaviors	5	6	520	−0.54**	[−0.86, −0.23]	−0.40*	−0.49	$\sigma_1^2 = 0.00$, $\sigma_2^2 = 0.03$	None conducted	Moderate	Downgraded one level due to small number of effect sizes examining non-opioid addictive behaviors in non-pain samples
Chronic pain	4	10	490	−0.60***	[−0.83, −0.37]	0.73**	−0.64	$\sigma_1^2 = 0.06$, $\sigma_2^2 = 0.00$	None conducted	Moderate	Downgraded one level due to non-overlapping CIs
Psychiatric symptoms	8	18	748	−0.34**	[−0.51, −0.11]	−0.10***	−0.22	$\sigma_1^2 = 0.00$, $\sigma_2^2 = 0.03$	Publication year, sample age, sample race, sample gender, and sample income insignificant	Moderate	Downgraded one level due to non-overlapping CIs, which were not accounted for in meta-regression analyses
Craving	7	10	609	−0.42*	[−0.73, −0.11]	−0.01	None conducted	$\sigma_1^2 = 0.14$**, $\sigma_1^2 = 0.00$	Publication year, sample age, sample race, sample gender, and sample income insignificant	Moderate	Downgraded one level due to non-overlapping CIs. which were not accounted for in meta-regression analyses
Opioid dose[a]	3	3	363	−17.95***	[−26.17, −9.72]	−6.81	None conducted	$I^2 = 11.20\%$	None conducted	Moderate	Downgraded one level due to small number of included studies and unclear risk of bias

Because included studies could provide effect sizes for multiple outcomes, sample sizes for each outcome will sum to a larger number than the total sample size for this meta-analysis. ES, effect sizes; QOE, quality of evidence as assessed using the Grading of Recommendations Assessment, Development, and Evaluation system; σ_1^2, variance estimate for effect sizes from the same study, with significant values indicating a significant log-likelihood test; σ_2^2, variance estimate for effect sizes from different studies, with significant values indicating a significant log-likelihood test

[a]Effect sizes were generated using mean change scores

*$p < .05$, **$p < .01$, ***$p < .001$

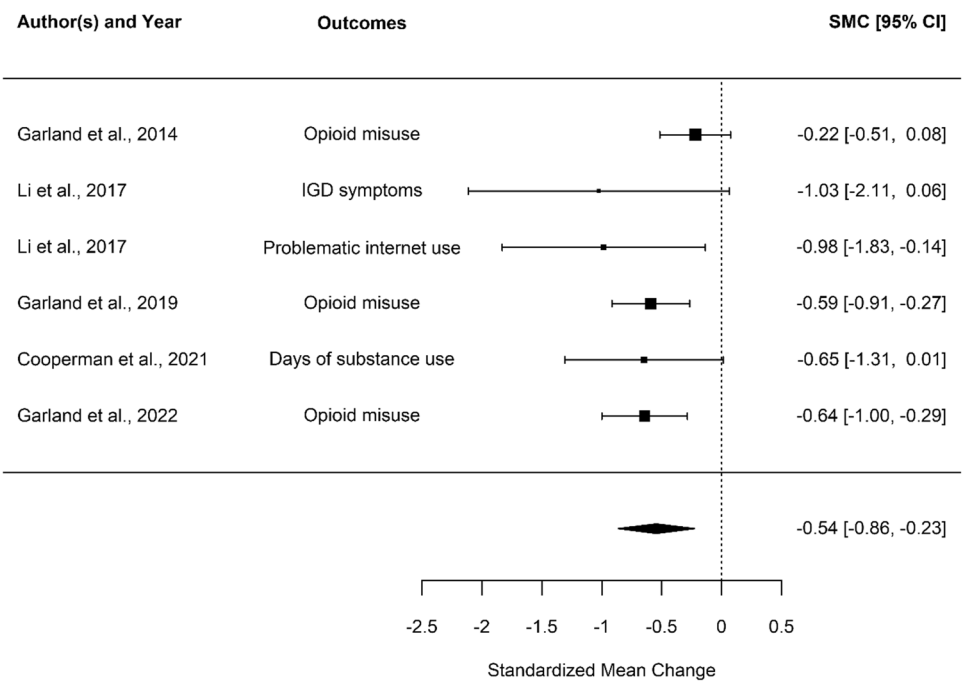

Fig. 3 Summary of studies examining the effects of mindfulness-oriented recovery enhancement on addictive behaviors

alcohol (Garland et al., 2010), video game (Li et al., 2017), and general substance craving (Garland et al., 2016). Follow-up points ranged from the last treatment week to 9 months posttreatment. A statistically significant, small-moderate effect size was observed favoring MORE (SMC = −0.42, 95% CI [−0.73, −0.11], $p = 0.014$), such that MORE participants demonstrated larger reductions in craving than participants in comparison conditions.

Opioid Dose

Three RCTs produced three effect sizes related to opioid dosing among chronic pain patients prescribed LTOT (Fig. 5). Follow-up points ranged from 3 to 9 months posttreatment. Results revealed a statistically significant effect in favor of MORE, such that MORE participants evidenced a greater decrease in MME (MC = −0.17.95 mg) relative to comparison conditions (95% CI [−26.17, −9.72], $p < 0.001$).

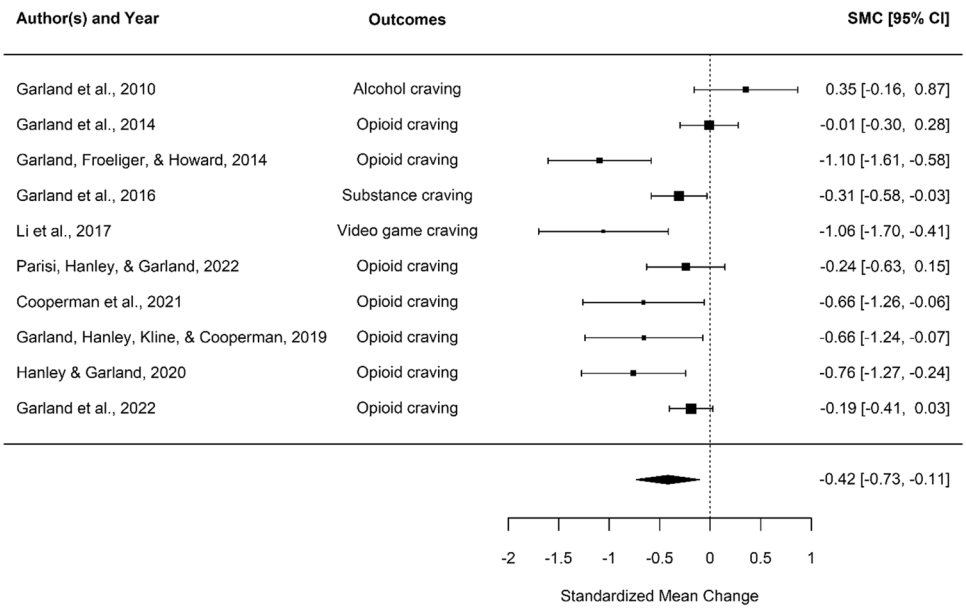

Fig. 4 Summary of studies examining the effects of mindfulness-oriented recovery enhancement on craving

Chronic Pain

Four RCTs (Fig. 6) produced 10 effect sizes examining the effects of MORE on chronic pain-related outcomes, including pain severity (Garland et al., 2014b, 2019b, 2022), interference (Garland et al., 2014b, 2022), unpleasantness (Garland et al., 2019a), and intensity (Garland et al., 2019a). Follow-up points ranged from the last week of treatment to 9 months posttreatment. Overall, MORE was associated with statistically significant, moderate effect size decreases in pain relative to comparison conditions (SMC = −0.60, 95% CI [−0.83, −0.37], $p < 0.001$).

Psychiatric Symptoms

Eight RCTs (Fig. 7) reported 18 effect sizes investigating the effects of MORE on a range of psychiatric symptoms, including general symptomatology (Garland et al., 2010), stress (Garland et al., 2010, 2014b, 2019a), distress (Garland et al., 2017b, 2022; Li et al., 2017; Roberts et al., 2022), well-being (Cooperman et al., 2021), depression (Garland et al., 2016, 2022), anxiety (Garland et al., 2016), and posttraumatic stress disorder symptoms (Garland et al., 2016, 2022). Follow-up points ranged from posttreatment to 9 months posttreatment. MORE was associated with statistically significant, small effect size reductions in psychiatric symptoms relative to comparison conditions (SMC = −0.34, 95% CI [−0.51, −0.17], $p < 0.001$).

Publication Bias

Visual inspections of contour-enhanced funnel plots showed moderate levels of asymmetry for the effects of MORE on addictive behaviors, pain, and psychiatric symptoms (see Online Resource 2). Moreover, Egger's regression tests were significant for all three outcomes, suggesting that publication bias or other sources of heterogeneity may have influenced the synthesized effect sizes (Table 2). Consequently, we re-analyzed these outcomes using trim-and-fill methods that account for the asymmetric distribution of studies around an omnibus effect. Nearly identical models were observed for addictive behaviors (SMC = −0.49, $p < 0.001$, 95% CI [−0.70, −0.28]), and pain (SMC = −0.64, $p < 0.001$, 95% CI [−0.83, −0.44]), while smaller yet significant effects were found for psychiatric symptoms (SMC = −0.22, $p = < 0.001$, 95% CI [−0.34, −0.10]).

Moderation Analyses

Significant log-likelihood estimates were observed for craving, indicating heterogeneity of effect sizes. Moreover, an inspection of forest plots revealed several non-overlapping confidence intervals for pain and psychiatric symptoms, suggesting that both outcomes also had high levels of study heterogeneity. We therefore examined sample race/ethnicity, sample age, sample socioeconomic status, sample gender, and the year of study publication as moderating variables for psychiatric symptoms and craving, as an insufficient number of studies were available to conduct meta-regressions for pain-related outcomes (Lipsey, 2003). No significant moderating variables emerged from these analyses (see Table 4),

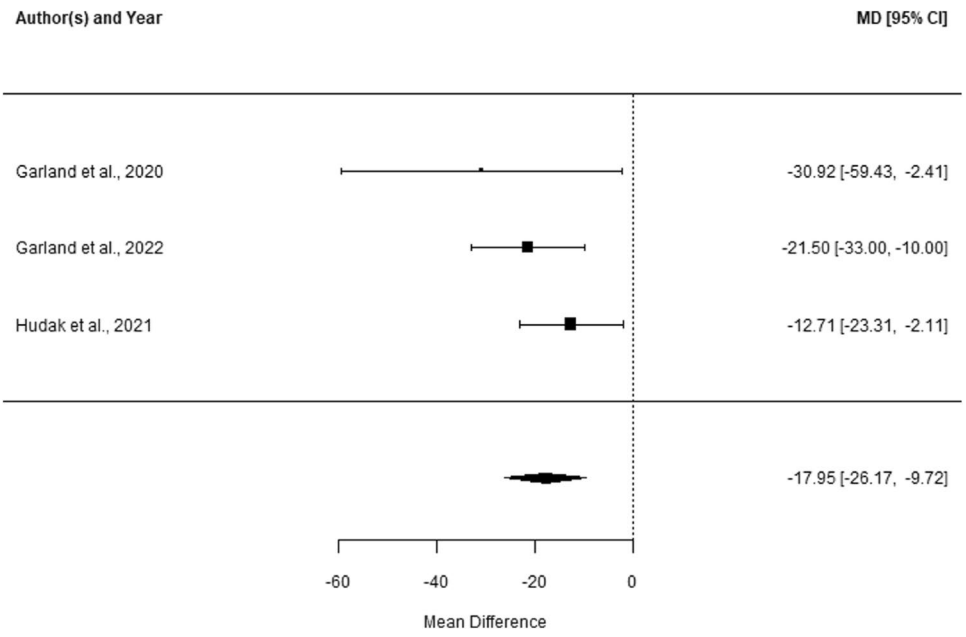

Fig. 5 Forest plot of studies examining the effects of Mindfulness-Oriented Recovery Enhancement on opioid dose. Squares indicate point estimates, with the size of the squares indicating weight. Horizontal lines indicate 95% CIs. The diamond indicates the pooled effect estimate

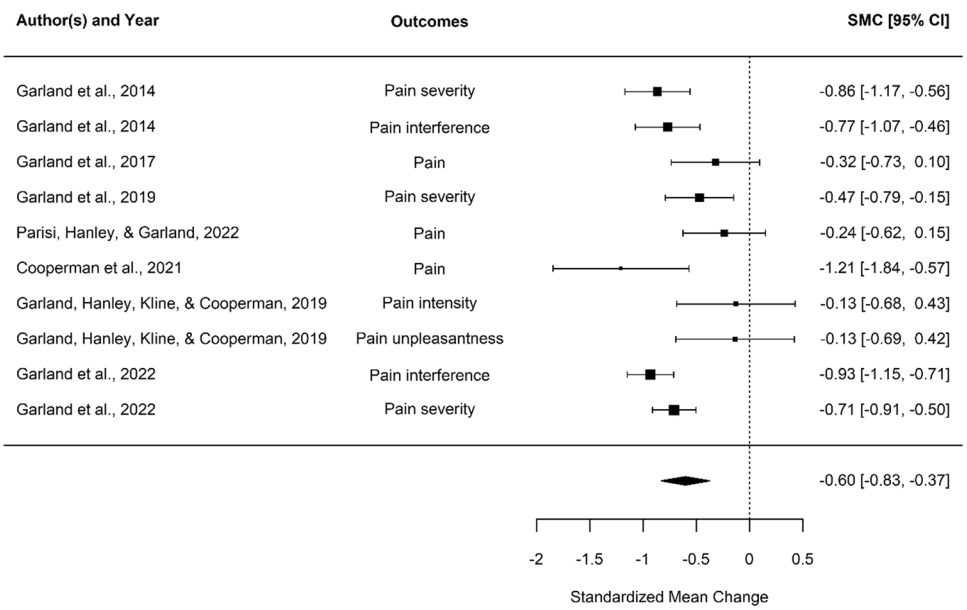

Fig. 6 Summary of studies examining the effects of mindfulness-oriented recovery enhancement on chronic pain

suggesting that the effect of MORE on both outcomes was robust to the year of publication, as well as the demographic characteristics of study samples.

Discussion

This meta-analysis quantitatively synthesized the therapeutic effects of MORE. Sixteen manuscripts reporting outcomes from eight RCTs were included, which examined 816 participants with a broad array of addictive disorders, psychiatric symptoms, and chronic pain conditions. Our findings demonstrate that MORE produced significantly larger improvements in addictive behaviors, craving, opioid dosing, chronic pain, and psychiatric symptoms than a range of active comparison conditions. The majority of trials reviewed focused on people with chronic pain at risk for opioid misuse or OUD; results from the present study demonstrate that MORE is clearly an efficacious treatment for this group of patients—a growing population for whom effective interventions are lacking. Moreover, despite the diversity of included participants, MORE's therapeutic effects on craving and psychiatric symptoms did not systematically differ as a function of participant age, race, gender, or income, suggesting that MORE may be efficacious for a wide diversity of individuals.

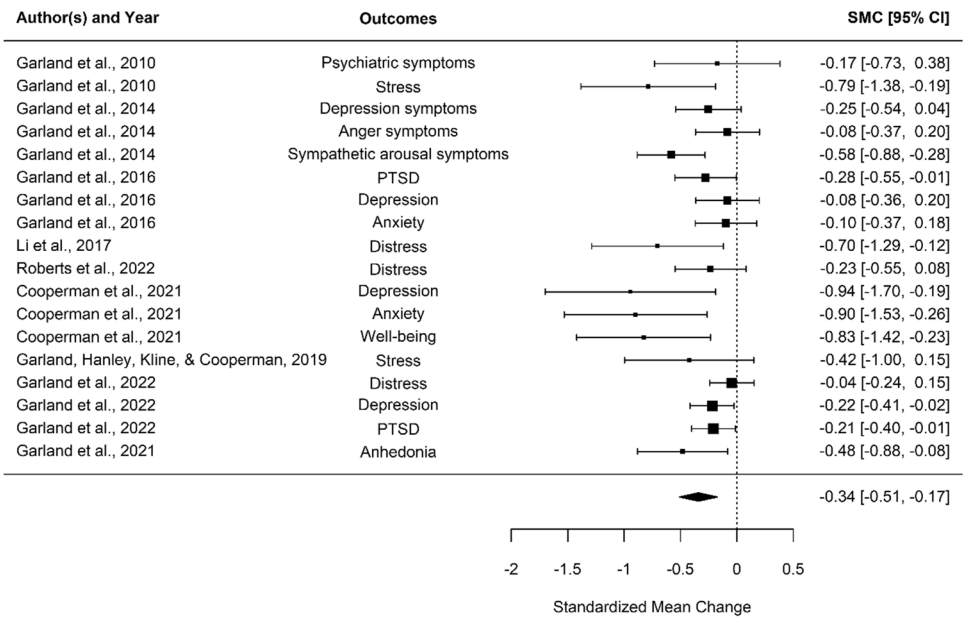

Fig. 7 Summary of studies examining the effects of mindfulness-oriented recovery enhancement on psychiatric symptoms

Table 4 Random effects meta-regressions

Outcome	Studies	ES	Intercept/mean SMC	95% CI	β	95% CI	F(df1, df2)	p	σ_1^2	σ_2^2
Psychiatric symptoms										
Publication year	8	18	−0.35**	[−0.53, −0.16]	0.00	[−0.05, 0.05]	$F(1, 16) = 0.00$	0.979	0.00	0.04
Sample age	8	18	−0.35**	[−0.53, −0.17]	0.00	[−0.02, 0.02]	$F(1, 16) = 0.06$	0.807	0.00	0.04
Sample race	8	18	−0.37***	[−0.54, −0.19]	0.00	[0.00, 0.01]	$F(1, 16) = 1.35$	0.263	0.00	0.03
Sample gender	8	18	−0.35**	[−0.54, −0.16]	0.00	[−0.01, 0.01]	$F(1, 16) = 0.06$	0.802	0.00	0.04
Sample income	6	16	−0.31**	[−0.51, −0.11]	0.00	[0.00, 0.01]	$F(1, 14) = 0.64$	0.437	0.00	0.03
Craving										
Publication year	7	10	−0.42*	[−0.75, −0.09]	−0.03	[−0.12, 0.06]	$F(1, 8) = 0.67$	0.438	0.15**	0.00
Sample age	7	10	−0.43*	[−0.76, −0.09]	0.01	[−0.03, 0.05]	$F(1, 8) = 0.17$	0.692	0.16**	0.00
Sample race	7	9	−0.32	[−0.69, 0.04]	0.00	[−0.02, 0.02]	$F(1, 7) = 0.00$	0.999	0.06	0.07
Sample gender	7	10	−0.42*	[−0.77, −0.08]	0.00	[−0.02, 0.01]	$F(1, 8) = 0.13$	0.726	0.16**	0.00
Sample income	6	7	−0.19	[−0.51, 0.14]	0.00	[−0.01, 0.01]	$F(1, 5) = 0.03$	0.868	0.00	0.06

Studies, number of studies; ES, number of effect sizes; SMC, standardized mean change; CI, confidence interval; σ_1^2, variance estimate for effect sizes from the same study, with significant values indicating a significant log-likelihood test; σ_2^2, variance estimate for effect sizes from different studies, with significant values indicating a significant log-likelihood test

*$p < .05$, **$p < .01$, ***$p < .001$

It is possible that MORE's broad spectrum effects stem from its unique integration of mindfulness, reappraisal, and savoring practices. Unlike other MBIs, in MORE formal mindfulness practices are used to synergize later training in reappraisal and savoring skills, providing participants with a range of regulatory strategies that may be flexibly employed to target the manifold mechanisms implicated in addiction, psychiatric disorders, and chronic pain. For example, mindfulness may facilitate meta-awareness of pain, negative emotions, and drug cue-reactivity, enabling individuals to recognize and disrupt automatic attentional biases (Garland & Howard, 2013; Garland et al., 2017a), and habitual behavioral responses that drive addictive behaviors (Garland et al., 2013b; Tiffany, 1990). The metacognitive stance afforded by mindfulness training may broaden awareness to encompass previously unnoticed contextual information that accommodates cognitive reappraisal of stressful life circumstances (Garland et al., 2015; Goldin et al., 2021)—an emotion regulatory process that has been linked to lower levels of craving, psychiatric distress, and substance misuse (Dryman & Heimberg, 2018; Hudak et al., 2022; Kober et al., 2010; Roberts et al., 2022). In a complementary fashion, the attentional capacities strengthened by mindfulness training may be leveraged in the service of savoring to (a) remediate dysregulated reward function by amplifying positive affective and neurophysiological responses to naturally rewarding, salutary objects and events (Garland et al., 2014a, 2019b, 2021) and (b) enhancing the motivational drive to sustain adaptive behavioral changes (Garland, 2016). As cited above, though a systematic mechanistic research program has obtained evidence of the effects of MORE on the aforementioned processes, multivariate mediational models are now needed to determine the independent and interactive causal effects of each of these components on MORE's clinical outcomes as revealed by the present meta-analysis.

Limitations and Future Research

Any conclusions or implications drawn from our findings should be tempered by the limitations of this meta-analysis. First, although we employed a multilevel analytic approach to maximize statistical power, the modest number of RCTs reviewed may have negatively impacted the reliability of effect size estimates. Additionally, half of the RCTs were stage 1 clinical trials with small samples and therefore may have been underpowered.

Second, we found evidence of heterogeneity for psychiatric symptoms, craving, and pain-related outcomes. Although random effects meta-regressions were performed, no moderating variable was found to be significant. Moreover, the few studies reporting pain-related outcomes precluded examination of effect size moderators. Consequently, the source of within- and between-study heterogeneity for all three outcomes remains unclear.

Third, an inspection of funnel plots and results from Egger's regressions revealed moderate levels of asymmetry for addictive behaviors, pain, and psychiatric symptoms, indicating that results for these outcomes may have been subject to publication bias. Although trim-and-fill analyses suggested that such bias, if present, had little impact on our primary findings, these tests may have been underpowered and should thus be interpreted in light of this limitation. That said, according to our review of clinicaltrials.gov, no trials of

MORE for addictive behaviors meeting our inclusion criteria were omitted from this meta-analysis.

Fourth, because the majority of RCTs assessed outcomes at posttreatment or 3 months posttreatment, additional research is needed to ascertain the long-term impact of MORE. Fifth, the majority of studies examining the effects of MORE on addictive behaviors focused on opioid misuse among individuals with chronic pain conditions, limiting the generalizability of findings. In that regard, we derived our effect size estimate of MORE for opioid misuse from a continuous measure of opioid misuse, the Current Opioid Misuse Measure (Butler et al., 2007). Use of this measure may underestimate MORE's actual effect on opioid misuse; in the largest clinical trial of MORE to date ($N = 250$; Garland et al., 2022), MORE reduced a composite, binary index opioid misuse (triangulating self-report, blinded clinical interview, and drug urine screen) by 45% at 9-month follow-up, nearly tripling the effect of the supportive psychotherapy control condition (OR = 2.94 at 9 months).

Finally, this meta-analysis may be limited by bias in that it involved authors (e.g., E.L.G., A.W.H.) of many of the primary trials reviewed. To mitigate such bias, study identification, data extraction, coding, and analysis were conducted by authors (A.P., R.L.R.) who were not involved in the conduct of any of the trials reviewed, and neither E.L.G. nor A.W.H. performed the aforementioned processes. It should also be noted that the developer of MORE (E.L.G.) was a coauthor on publications from all the trials reviewed in this meta-analysis, though two of the trials were conducted by independent principal investigators (Cooperman et al., 2021; Li et al., 2017). Given that MORE is a young therapy, the involvement of the developer in these initial trials is perhaps unsurprising. However, as the evidence base on MORE continues to grow, independent teams of investigators should evaluate MORE in future trials.

To advance the growing empirical foundation of MORE, we propose several directions for future research. Multi-site large-scale RCTs with longer follow-up periods are needed to support the strength and sustainability of outcomes reported in this review. To establish the efficacy of MORE for addictive behaviors, future RCTs should also examine its effects among non-pain populations and obtain quantitative estimates of substance use and other addictive behaviors. Although several studies in this meta-analysis tested MORE among low-income racial and ethnic minority populations, and the overall non-white proportion of participants in these trials is 32.5%, recruiting additional participants from diverse racial, ethnic, and socioeconomic backgrounds remains an ongoing research priority. Such research could strengthen the generalizability of our findings and provide the statistical power needed to support more granular investigations regarding the populations for whom MORE may work most optimally. Finally, the majority of RCTs in this meta-analysis compared the effects of MORE to active comparison conditions, providing evidence that our findings cannot be explained by non-specific therapeutic factors. However, MORE is a multimodal intervention that targets a number of interconnected and complex mechanisms designed to maximize its clinical effects among individuals with addictive disorders, chronic pain, and psychiatric comorbidities. Dismantling trials are now needed to determine to what extent the mindfulness, reappraisal, and savoring components in MORE contribute to its therapeutic benefits. With continued effectiveness and implementation research, MORE should advance towards more widespread dissemination in healthcare.

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Author Contribution A.P. participated in the design of the meta-analysis, wrote the search protocol and inclusion criteria, conducted literature searches, reviewed all selected studies, extracted study data, conducted meta-analyses, and wrote the first draft of the manuscript. R.L.R participated in the design of the meta-analysis, conducted literature searches, reviewed all selected studies, extracted study data, reviewed results of meta-analyses, and contributed to the final manuscript. A.W.H. and E.L.G. participated in the design of the meta-analysis and contributed to the final manuscript. All authors have approved the final manuscript.

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Declarations

Competing Interests Eric Garland, PhD, LCSW, is the Director of the Center on Mindfulness and Integrative Health Intervention Development. The Center provides Mindfulness-Oriented Recovery Enhancement (MORE), mindfulness-based therapy, and cognitive behavioral therapy in the context of research trials for no cost to research participants; however, Dr. Garland has received honoraria and payment for delivering seminars, lectures, and teaching engagements (related to training clinicians in MORE and mindfulness) sponsored by institutions of higher education, government agencies, academic teaching hospitals, and medical centers. Dr. Garland also receives royalties from the sale of books related to MORE. Dr. Garland is also a consultant and licensor to BehaVR, LLC.

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