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Mindfulness-Based Treatments for Co-Occurring Depression and Substance Use Disorders: What Can We Learn from the Brain?

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Abstract

Both depression and substance use disorders represent major global public health concerns and are often co-occurring. Although there are ongoing discoveries regarding the pathophysiology and treatment of each condition, common mechanisms and effective treatments for co-occurring depression and substance abuse remain elusive. Mindfulness training has recently been shown to benefit both depression and substance use disorders, suggesting that this approach may target common behavioral and neurobiological processes. However, it remains unclear whether these pathways constitute specific shared neurobiological mechanisms or more extensive components universal to the broader human experience of psychological distress or suffering. We offer a theoretical, clinical and neurobiological perspective of the overlaps between these disorders, highlight common neural pathways that play a role in depression and substance use disorders, and discuss how these commonalities may frame our conceptualization and treatment of co-occurring disorders. Finally, we discuss how advances in our understanding of potential mechanisms of mindfulness training may offer not only unique effects on depression and substance use, but also offer promise for treatment of co-occurring disorders.

Keywords

Mindfulness; Addiction; Depression; Substance Use Treatment; Functional Magnetic Resonance Imaging (fMRI); co-occurring disorders; dual diagnosis

Mindfulness training (MT) may target common underlying mechanisms of major depressive disorder (MDD) and substance use disorders (SUDs), providing an effective treatment for co-occurrence of these maladies where few currently exist. We will use “co-occurring disorder” and “dual diagnosis” to refer to the co-occurrence of MDD and an SUD in which “diagnoses of these disorders must occur simultaneously or within a one year time frame of each other” (1). As first-line treatment for substance-induced mood disorders is to treat the underlying SUD (2), substance-induced mood disorders will not be included in this discussion. Additionally, although co-occurring psychotic and anxiety disorders are common

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and warrant discussion, the majority of the current discussion will be limited to co-occurring MDD and SUDs.

(I.) MDD and SUDs: significant and growing problems

Both MDD and SUDs are major public health problems. Overall, unipolar depressive disorders were the fourth leading cause of disease burden in 2002, and are projected to be the second leading cause by 2030 (3). Further, MDD and SUDs have been found to co-occur frequently: about one third of individuals with MDD also have symptoms consistent with an SUD (4), and lifetime prevalence of a co-occurring SUD ranges from 30% to 42.8% (3,5). From 1992 to 2002, the rates of past-year major depressive episodes among people with a concurrent SUD increased from 10 to 15% (6). These data highlight the large and growing burden of co-morbid MDD and SUDs.

There are currently multiple empirically supported behavioral treatments for both MDD and SUDs as individual disorders. Well-supported behavioral treatments for depression include cognitive behavioral therapy (CBT), behavioral-activation therapy, mindfulness-based cognitive therapy and exercise (7). Similarly, substance abuse treatments include CBT, relapse prevention, motivational interviewing (MI), contingency management (CM), and 12-Step programs (8–10). Despite significant research on treating these disorders individually, few treatments have been evaluated for individuals with co-occurring MDD and SUDs (11). MI has demonstrated efficacy for many types of substance abuse, though few studies have been conducted with dual diagnosis patients (12,13). CBT has been modified for people with SUDs and depression and has shown moderate effects therein (14). CM has more recently been adopted for dually-diagnosed populations, though mood symptomatology was not measured in these studies, leaving its broader efficacy unverified (13).

(II.) Mindfulness training for co-occurring disorders: theoretical, clinical and neurobiological perspectives

Over the past two decades, the emergence of studies on treatments incorporating mindfulness training (MT) has offered promise for the treatment of MDD and SUDs independently. We offer a theoretical, behavioral and neurobiological exploration of MT for treatment of these disorders when they occur concurrently.

(a.) Theoretical perspectives

A recent consensus definition of mindfulness emphasizes two complementary elements: 1) the placement of attention on the immediate experience; and, 2) adopting an open, curious, accepting attitude toward that experience (15). It is believed that although the capacity for mindfulness is inherent, the majority of individuals move through life on “auto-pilot,” performing daily activities based on habitual behavioral patterns while their minds are elsewhere (16). Mindfulness is developed through a continual practice of “awakening” to present-moment experiences. Traditionally, this is taught through meditation practices that first focus on developing concentration capacities by repeatedly bringing attention to an object, such as the breath, then broadening the attention to include all physical and mental events that are experienced (*e.g.* bodily sensations, emotions and thoughts). Instruction for mindfulness practice can be as simple as, “when sitting, know you are sitting; when thinking, know you are thinking” (17). The intention is to bring a nonjudgmental, objective and accepting quality to this observation.

(b.) Clinical perspectives

While mindfulness practices are centuries old, they have only recently become popular in Western medicine and psychology. One of the earliest incorporations of mindfulness into medical treatment paradigms was through the mindfulness-based stress reduction (MBSR) program at the University of Massachusetts (18). MBSR showed efficacy in the treatment of chronic pain where other treatments had failed (19). After the initial success in treating chronic pain, the effectiveness of mindfulness-based therapies was investigated for treatment of other conditions including anxiety disorders (20–23), addiction (24–27), and depression (28,29), though methodological quality of these studies has been suboptimal (30). Mindfulness-based cognitive therapy (MBCT), based largely upon MBSR, has shown an absolute reduction of 44–50% in the relapse rate for individuals with three or more episodes of depression both in initial and replication studies (28,29). A study of incarcerated, substance-abusing individuals who were taught mindfulness meditation revealed significant reduction in substance use three months following release from incarceration, as well as reductions in anxiety and depression (31). Another study of individuals with alcohol and cocaine use disorders suggested that MT may be as effective as CBT in preventing relapse with specific effects on psychological and physiological stress pathways (25). A further study of a mindfulness-based treatment for substance use disorders suggested that participation in treatment was associated with greater decreases in craving and substance use as compared to a treatment as usual (32), and that the treatment may lessen the relation between depressive symptomatology and craving, thereby decreasing substance use. Taken together, these data provide a rationale for the hypothesis that MT may target shared underlying mechanisms in MDD and SUDs in a dually diagnosed population.

(c.) Neurobiological perspectives

Evidence for common underlying neural pathways in MDD and SUDs may explain some of the shared mechanisms in these disorders, offering a useful perspective on potential targets of treatment for dually-diagnosed individuals. Multiple approaches have investigated the pathophysiology of MDD and SUDs, including those based on genetics, neurotransmitters, and endocrine systems (reviewed elsewhere (33–36)). Regional brain activation studies have provided unique insight into the pathophysiology of both MDD and SUDs. Many regions have shown overlap between MDD and SUDs, suggesting possible mutual underlying pathophysiologies. For example, regions of the ventromedial prefrontal cortex (vmPFC), which is important for homeostasis, emotional regulation and decision-making, have shown dysfunction in both MDD (37–41) and SUDs (42–48). The dorsolateral PFC (dlPFC), which is involved in working memory, attention, initiation of cognitive control, and conflict-induced behavioral adjustment (49–51), the amygdala, which contributes to the formation and storage of memories associated with emotional events, memory consolidation, and reward learning and motivation (52–54), and the insula, which contributes to “sensing” of somatic states through its representation of bodily sensation (55), have all shown importance in both MDD and SUDs (37,40,56–63). While these data suggest overlapping neuroanatomical correlates for MDD and SUDs that may be reflected in common intermediary phenotypes or endophenotypes, they do not directly demonstrate functional commonalities.

The psychological and behavioral correlates of brain function in MDD and SUDs may provide insight into potential targets of effective treatments. For example, several studies suggest that rumination and stress are commonly seen in both MDD and SUDs. Rumination, described as self-focused attention on symptoms of distress without engagement in active problem solving (64), is conceived of as an automatic behavior often acquired during a first depressive episode (28). People who engage in rumination when distressed are more likely to become depressed and have longer periods of depression (64). Likewise, temporary

distraction, which may break the ruminative cycle, may lead to a decrease in dysphoria (65). Brain regions that are implicated in rumination include the amygdala and PFC (64). Ruminators have shown lower PFC activity than controls when attempting to inhibit negative distracters, as well as difficulty with cognitive shifting (66). These data are suggestive of dysfunctional cognitive control circuitry (67). Other studies suggest that rumination is associated with increased amygdalar activity during processing of emotional stimuli (68,69). A role for rumination in SUDs has been suggested by work showing that a tendency to ruminate is associated with greater inclinations to use alcohol or other substances (70). Though preliminary, these data suggest that dysfunction in specific brain regions may correlate with rumination and contribute to habitual behaviors in both MDD and SUDs.

Links between stress, depression and substance use have also been established (reviewed elsewhere (71,72)). For example, exposure to stressful life events has repeatedly been associated with MDD (33,72). Also, depressed patients often exhibit elevated plasma cortisol (the dominant circulating stress glucocorticoid hormone in humans) and abnormal cortisol suppression (73). Similarly, stress has been shown to be instrumental in SUDs: stress cross-sensitizes to both stimulant (74) and alcohol (75) use, induces craving (76), and increases self-administration of drugs such as amphetamines (77), cocaine (78), and alcohol (79). This is likely influenced by stress hormones, as in healthy volunteers, stimulants induce cortisol release, while the magnitude of the reported subjective “high” correlates with plasma cortisol concentrations (80).

The above data suggest that MDD and SUDs share several phenotypes such as stress vulnerability and rumination, pointing at possible mutual underlying neurobiological dysfunctions. Still unclear are the details of how specific this overlap may be. However, these commonalities may provide a sufficient framework from which to develop treatments targeted at shared brain and behavioral dysfunction.

(III) Mechanism of action in mindfulness training

Recent neurobiological, cognitive and behavioral data support two specific components of mindfulness, attention and acceptance, that may directly target the common intermediary phenotypes of rumination and stress, highlighting their potential utility in the treatment of MDD and SUDs. (Reviews of the general mechanisms of mindfulness can be found elsewhere (15,81–84).)

Attention

(a.) Theoretical perspectives—One primary aim of MT is to shift attention from a passive, wandering state (“default mode” –see below) to an active, intentional state. For example, during concentration meditation, when an individual’s mind strays from the object of attention or is distracted by other stimuli, the individual is instructed to intentionally “bring the attention back” to the intended focus. With practice, individuals retrain their minds to more continually “pay attention, on purpose, in the present moment” (18).

(b.) Clinical perspectives—The link between attention training and treatment of depression and addiction may not be initially apparent. It has been hypothesized that focusing and sustaining attention on present experience increases the ability to notice overlearned behavioral patterns as they arise, allowing for individualized interventions (whether cognitive or behavioral) that interrupt these patterns (15,85). For example, early in major depressive episodes, associations between mood and depressive thought patterns are established and can be reactivated in periods of dysphoria (86). In susceptible individuals, negative cognitive styles and tendencies to ruminate can interact to create the conditions for

the “perfect storm”: depression that is triggered by stressful events (87). With continued practice of mindfulness, individuals may be better able to notice these patterns, allowing for disengagement from ruminative thought patterns (*i.e.* not being caught up in the thoughts and believing them as “true”) and selection of how to relate to these experiences, rather than “automatically” reacting to them (16). Indeed, studies have suggested that decreases in distress scores following MT are mediated by a decreased tendency to ruminate (88). These findings suggest MT may be effective in targeting habitual ruminative thinking, with consequent reduction in stress and depression (28).

Stress and ruminative thought patterns have also been linked to SUDs. For example, individuals’ elevated rumination scores have been shown to predict substance abuse (70,89). And although efforts to avoid or suppress ruminative or “unwanted” thoughts are commonly used in attempts to manage cravings and relapse (90), thought suppression has been shown to lead to stronger expectancies after cue exposure (91). Interestingly, decreases in alcohol consumption following mindfulness-based treatment have been shown to be partially mediated by decreases in thought suppression indices such as avoidance (27). These findings suggest that in dually-diagnosed individuals, attentional focus on thoughts may be more effective than attempts to suppress them in decreasing their influence on behavior.

(c.) Neurobiological perspectives—It is hypothesized that specific areas of the medial PFC may be active during ruminative and/or wandering mindstates (dubbed the “default mode”)(92,93). These regions have been found to play a role in linking subjective experiences through time (94,95), holding memory of traits of the self (96,97), reflected self-knowledge (98,99), and aspirations for the future (100). Without this “narrative self reference,” or sense of identity through time, stress reactivity and rumination would not be possible (101,102).

The mechanisms by which MT influences default mode functioning are being explored. In a recent study in which participants were instructed to either elaborate on current cognitions (narrative focus, NF) or to attend to somatic sensations and merely note any cognitions without elaborating on them (experiential focus, EF), investigators found midline cortical activation during NF as compared to EF (103). After MT, midline cortical structures showed decreased activity in EF vs. NF (103). One interpretation of these data is that momentary self-experience may provide a non-self-related cortical “task” which may suppress midline cortical activity. These findings are corroborated by studies showing increased gamma-band oscillation in the brains of long-term meditators (suggesting increased neuronal synchronization (104)), and behavioral studies showing improved attentional regulation with meditation training (105–107). Together, these data suggest that present-centered attentional focus not only moves the individual away from the habitual default-mode thought process, but also manifests behaviorally. From these data, one might hypothesize that MT would benefit dually-diagnosed individuals through improved attentional focus, with consequent reduction in stress-induced ruminative thought patterns, as well as more rapid recognition of these once they have been engaged. These would likely be reflected in “lateralization” of brain activation patterns, as seen by Farb and colleagues in healthy individuals. Future studies in this population using neuroimaging attentional tasks will be informative in testing these hypotheses.

Acceptance

(a.) Theoretical perspectives—A second major component of mindfulness, acceptance, involves a non-judging/non-attached view of experiences. This perspective leads to an understanding of thoughts and sensations as “transient mental events” rather than as reality or a reflection of the self. As with attentional focus, non-attached observation, or meta-

cognition, has been hypothesized to reduce perpetuation of harmful thought patterns by shifting perspective of uncomfortable or unpleasant thoughts from “real” or “true” to viewing them as passing mental events. It should be noted that although acceptance is reported to be beneficial in MT as well as therapies that incorporate mindfulness (108,109), it is unclear whether a non-attached viewpoint fosters acceptance, acceptance fosters a non-attached viewpoint, or whether the effects are bidirectional, and to what degree these are an extension or result of insights gained from the practice of attention.

(b.) Clinical perspectives—The utility of a non-attached mode of experience in individuals with depression and/or addictions is gaining increasing support. Negative affect has been shown to predict relapse to both cigarettes and drug use (110–112). Also, higher intensity of negative affect has been correlated with longer duration of use (113), and worse distress tolerance has been associated with decreased abstinence (114). Acceptance of distressing thoughts lessens reactivity, and decreases attempts to avoid or suppress experiences, which have been linked to worsened outcomes (81,115). For example, in clinical populations, MT has been associated with increases in the ability to “let go of” (*i.e.*, disengage from) negative automatic thoughts and decreases in the tendency towards negative automatic thinking (116). Individuals with SUDs often report experiencing “urges” to use substances, and many state that the experience of an urge is increasingly tolerated and managed when working with a mindfulness approach (25,117–119). Additionally, decreases in substance use following MT have been shown to be partially mediated by decreased avoidance, but not frequency, of intrusive thoughts (27). Further, distress tolerance, drawing from Acceptance and Commitment Therapy-based approaches, has shown preliminary utility in smoking cessation (120). Finally, alcohol- and cocaine-dependent individuals have shown attenuation of self-reported anxiety and drug cravings during stress, with concomitant adaptive shifts in autonomic nervous system function, while remaining fully engaged with their experiences (25). One might expect associated normalization in plasma cortisol concentrations, as has been suggested by studies of individuals with heart disease and cancer who have undergone MT (121,122), though these studies are yet to be reported. Together, these suggest that through acceptance of both mood- and drug-related ruminative thought patterns, MT may show increased efficacy in individuals with co-morbid MDD and SUDs, where other treatments fail.

(c.) Neurobiological perspectives—Meta-cognitive skills, such as inhibition of secondary elaborative processing, may be fostered by MT, since attentional capacity is not being consumed by elaborative thinking (15,105). Supporting this, Farb and colleagues have shown a decoupling of insula-vmPFC activity and an increased coupling of the insula with dlPFC after MT (103). Further, meditation practice has been associated with thickened right insular and somatosensory cortices (123,124). These data suggest a movement away from self-referential experiences (related to midline PFC activation) towards those that are more objectively observed/felt and easily accepted. As stress has been shown to be associated with reduced dlPFC activation during particular tasks, with concomitant increased activation of the default-mode network, this lateralized brain activation pattern may also signal more adaptive responses with MT: neural resources are reallocated away from self-referential, elaborative thinking towards task-specific responses, such as more accurate assessment of internal/external situational stimuli and resultant skillful responses (125). Consistent with this hypothesis, a recent study using the Stroop color-word interference task (which may predict treatment outcomes in addicted individuals (48)), showed that MT was associated with improved cognitive flexibility (126). We would hypothesize that dually-diagnosed individuals would show similar adaptive patterns after MT with concomitant increased insular and dlPFC activation patterns, resulting in decreased perceived stress, drug use, and depression severity.

Section 8: Conclusions and future directions

Mindfulness training has shown promise in the treatment of both SUDs and MDD. Examination of the common neurobiological and behavioral dysfunction in these disorders suggests the promise of MT for dually-diagnosed individuals. MT may help those with dual diagnosis decrease avoidance, tolerate unpleasant withdrawal and emotional states (stress-related), and unlearn maladaptive behaviors (rumination). Additionally, it may lessen the interactions between these processes, thus weakening their additive effects on depression and substance use.

We can now ask: do the commonalities in regional brain dysfunction between MDD and SUDs begin to approximate potential neural correlates of human suffering? If so, is this common to other psychiatric disorders, such as anxiety disorders, that share core features with both MDD and SUDs (*e.g.* unpleasant emotional states)? Would individuals with these disorders and co-morbid SUDs be helped by MT as well? Given the burgeoning research in discerning mechanisms of mindfulness and integrating MT in the treatment of psychiatric disorders, careful studies in dually-diagnosed individuals have the potential to greatly expand our knowledge of common pathophysiology and provide effective treatments where few currently exist.

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ADDICTION MESSENGER - October 2011

Mindfulness and Addiction Treatment

Do not dwell in the past. Do not dream of the future. Concentrate the mind on the present moment.

Buddha

Mindfulness as a practice for health and well-being has been around for centuries. Lately it has received attention in the addiction treatment field and is showing promising outcomes across a broad spectrum of uses. The widespread use of cognitive behavioral approaches in addiction treatment created fertile ground for the inclusion of mindfulness-based practices, which enhance treatment using a combination of meditation, movement and cognitive skills.

Mindfulness can be a way to cope with feelings, stress, triggers and urges and a way to manage stress and anxiety. Being mindful increases engagement with the present moment and allows for a clearer understanding of how thoughts and emotions can impact health and the quality of life. It is a way of staying present with pain and discomfort, rather than fleeing it, suppressing it or seeking to “medicate” it in some way. When confronted with an urge, a person practicing mindfulness observes and accepts the urge, and rides it like a wave – knowing that urges have a beginning, middle and end - and that this one too will pass.

Mindfulness frames strong urges or feelings not as commands to be acted upon immediately or automatically, but rather as invitations to accept or decline after careful consideration. Mindfulness practitioners say it allows them to remain calm under fire, enabling them to choose a more adaptive response to a particular stressor or stimulus.

Mindfulness: What it is...and what it isn't

Dr. Jon Kabat-Zinn is credited with bringing mindfulness to the modern treatment world. His basic definition of mindfulness is “paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally” (Kabat-Zinn, 1994). Efforts to operationalize the definition, in part so that treatment practices can be standardized, replicated and their outcomes measured, have resulted in expanded definitions that include concepts such as acceptance, commitment, openness and cognitive flexibility.

Mindfulness Skills

Mindfulness can evolve from learning, practicing and regularly applying several specific meditative and cognitive skills, including the following which are described in “Using Mindfulness Techniques in Substance Abuse Treatment”

(http://kimh039.hubpages.com/hub/Using_Mindfulness_Techniques_in_Substance_Abuse_Treatment):

Awareness: The ability to focus attention on one thing at a time, while at the same time recognizing that there are many things going on. Some of these things are external such as sounds, odors, touch, and sights, while some of these things are internal, such as feelings, thoughts, urges, impulses, etc.

Non-judgmental: The ability to observe without judging or labeling things as “good” or “bad.” For example, one can observe their angry feelings without judging them as bad or feeling a need to get rid of them or do something about them.

Present Moment: The ability to fully participate in the present without being distracted by guilt from the past or worry and anxiety about the future. It means not just mindlessly doing what you have always done or going through the motions, but paying deliberate attention to what you are experiencing.

Open (or Beginner’s) Mind: The ability to be open to new experiences and see them as they are, not how you have judged them to be or think they should be. A “Beginner’s Mind” is as open as that of a child who experiences something for the first time.

How does one develop mindfulness skills? Through exercises such as those briefly highlighted below from the aforementioned “Using Mindfulness Techniques in Substance Abuse Treatment”:

Mindful Breathing: *Mindful breathing involves focused attention on breathing. Notice how you are breathing. Notice slower breathing and fuller breaths. Notice your belly rise and fall as you breathe in and out. When your mind drifts away from your breathing, and it will, simply notice what caught your attention and gently shift your attention back to your breathing.*

Meditation: *The purpose of mindfulness meditation is to become more aware and accepting of internal processes; thoughts, feelings, urges, sensations, cravings, triggers, etc. People who are extremely anxious about internal processes or have difficulty sitting still may need to work up to a full session of 20 minutes, beginning with only 2-3 minutes at a time and working on other exercises more at first. The goal is 20 minutes of meditation two times a day. During meditation, if your mind drifts to thoughts about the past or worries about the future, gently re-direct your attention to the present moment. Mindfulness meditation is about staying in the present, not necessarily about achieving a heightened state of awareness or bliss.*

Beginner’s Mind: *Pick an object in the room that is familiar to you, and examine it with your beginner’s mind; that is, as if you have never seen the object before. Some people imagine they are an alien from another planet or an alien on another planet, and are seeing the object for the first time. Notice the shape, weight, texture and color of the object. Try to imagine what the object could be used for. As you continue to examine the object, do you notice anything about it that you may not have noticed before? When you put the object away, reflect on what you learned about the object that you didn’t already know. Consider*

what would happen if you approached other areas of your life with a beginner's mind; people, places, objects, situations. How would these other areas of your life be the same or different if you approached them with beginner's mind? What expectations do you now have that you would not have if you saw them for the first time?

There are many other exercises one can practice towards becoming more mindful, including those which focus specifically on emotions, eating, and physical sensations. Mindfulness can be applied to any activity at any time during the day. Mindfulness can be practiced in the shower, during a walk, at work, during exercise, in a store, in the waiting room, etc.

It is also important to note what mindfulness isn't. It is not a relaxation technique, although relaxation can occur. Likewise, mindfulness meditation should not be promoted as a path to religious or spiritual enlightenment of some sort. It is not a mystical or religious endeavor. It doesn't produce trances or altered states of consciousness. It should not be the sole component of treatment; rather, it is one of several potentially useful tools to offer clients and train them to use. The training and practice components are very important if clients are to receive the full benefits from mindfulness meditation.

Research on Mindfulness Meditation Outcomes

The research on mindfulness is relatively new and emerging. Some combination of mindfulness-based interventions have been applied to the treatment of chronic pain, skin disorders, and anxiety disorders· borderline personality disorders, relapse prevention, neurological activity, immune functioning, stress levels with cancer patients and addiction treatment. (Hoppes, 2006) A few significant examples follow (Brewer et al 2010):

Mindfulness-based stress reduction (MBSR) showed efficacy in the treatment of chronic pain where other treatments had failed.

Mindfulness-based cognitive therapy (MBCT) has shown an absolute reduction of 44–50% in the relapse rate for individuals with three or more episodes of depression both in initial and replication studies.

Incarcerated, substance abusing individuals who were taught mindfulness meditation showed significant reductions in substance use three months following incarceration, as well as reductions in anxiety and depression.

Mindfulness-based treatment for substance use disorders was associated with greater decreases in craving and substance use compared to a treatment-as-usual by lessening depressive symptoms and craving.

Research on the Neurobiology of Mindfulness Meditation

Research on the neurobiological mechanisms by which mindfulness meditation works has shown that physical and physiological changes in the brain occur with sufficient practice and use. Specifically, mindful meditation has been shown to “thicken” the brain in areas in charge of decision making, emotional flexibility, and empathy. Changing your thought processes causes changes in the brain (Lazar et al. 2005).

Mindfulness practice may positively affect the activity in the amygdala, the center of the brain which regulates emotions (Davidson 2000). When the amygdala is relaxed, anxiety lessens: heart rate lowers, breathing becomes slower and deeper, and the body stops releasing cortisol and adrenaline, two chemicals which are adaptive in some circumstances, but which can have a negative effect, if too much is released over the long term.

According to neuroscientist Daniel Siegel, mindfulness meditation practice may create new neural networks for self-observation, optimism, and well-being. Mindfulness meditation benefits the left-prefrontal cortex (associated with optimism, self-observation, and compassion), potentially reducing the effect of the right-prefrontal cortex (associated with fear, depression, anxiety, and pessimism) (Alexander, 2010).

Mindfulness-Based Stress Reduction (MBSR)

Modern foundational work on mindfulness came from Mindfulness-Based Stress Reduction (MBSR), a program developed by Jon Kabat-Zinn of the University of Massachusetts <http://www.umassmed.edu/cfm/stress/index.aspx>. The highly participatory 8-week course includes: guided instruction in mindfulness meditation, gentle stretching and mindful yoga, group dialogue and discussions aimed at enhancing awareness in everyday life, individually tailored instruction, daily home assignments, four home practice CDs and a home practice manual.

Research has shown MBSR to be effective for patients with chronic pain, hypertension, heart disease, cancer, and gastrointestinal disorders, as well as for psychological problems such as anxiety and panic. The success of this approach led directly to the application of similar principles for other mental health and addiction problems, brief descriptions of which follow.

Mindfulness-Based Cognitive Therapy (MBCT)

Mindfulness-Based Cognitive Therapy (<http://www.mbct.com/>) is designed to help people who suffer repeated bouts of depression. It combines the ideas of cognitive therapy with meditative practices and attitudes based on the cultivation of mindfulness. Participants become acquainted

with the modes of mind that often characterize mood disorders while simultaneously learning to develop a new relationship to them. MBCT was developed by Zindel Segal, Mark Williams and John Teasdale, based on the MBSR program previously described. Research has shown that people who have been clinically depressed 3 or more times (sometimes for twenty years or more) find that taking the program and learning these skills helps to reduce considerably their chances that depression will return. In fact, evidence from two randomized clinical trials of MBCT indicates that it reduced rates of relapse by 50% among patients who suffer from recurrent depression.

Mindfulness in the Treatment of Substance Use Disorders

Mindfulness-based approaches, which include the work of Linehan, with dialectical behavior therapy (DBT), Kabat-Zinn with MBSR, Segal and colleagues and their adaptation of MBCT for depression, have been called the “Third Wave of CBT” (Hoppes, 2006). Mindfulness-based interventions “can enhance the effectiveness of cognitive-behavioral therapy (CBT) for addiction, particularly in relation to problems with affective regulation that often co-occur with substance abuse disorders. “ (Hoppes, 2006)

Michael Waupoose, program manager for Gateway Recovery, a University of Washington Health addiction treatment center, provides a relevant example “if a patient has a very bad argument with his spouse or children, his anxiety will increase; he may get frustrated and angry; and, commonly, he will automatically leave that situation and go out for a drink to relieve stress and tension. Obviously, this is an example of unhealthy coping with discomfort. Mindfulness meditation would teach that person how to be present in that situation, how to be conscious of what's happening to their body, and how to deal with it without reacting to it automatically,” Waupoose continued. “It teaches people how to be conscious of their feelings or thoughts without having to follow them all the way through.” (UW Health News, 2010)

Why is this important? According to Dr. Kimberly Hoppes of Mt. Sinai Medical Center, “facing the damages of addiction (occupational, familial, social, economic, etc.) without the mood numbing effects of substances, poses an additional challenge for the recovering individual. For many individuals in early recovery, the negative thoughts and feelings they experience about their lives are not based upon distortions in perception, but upon real problems which have often been compounded by avoidance and denial. Individuals attempting to achieve abstinence face the daunting task of trying to abstain while simultaneously confronting the reality of serious consequences of their addiction. The lack of preparation, skills, or resources to handle what can feel like an unbearable “wake up call” can greatly contribute to the risk of relapse, particularly during the early months of heightened addiction-related emotion deregulation... through mindfulness skills that focus on dealing with these painful realities without becoming

consumed by negative emotions and thoughts, the recovering individual is more likely to build the motivation to pursue positive changes in behavior in the present.” (Hoppes, 2006)

Mindfulness meditation is also beginning to be discussed as a promising component in the treatment of co-occurring substance use and mental health disorders (Brewer, et al, 2010).

Mindfulness and Relapse Prevention

Mindfulness-Based Relapse Prevention (<http://www.mindfulrp.com/default.html>), developed by the late Dr. Alan Marlatt and colleagues (Bowen, Chawla & Marlatt, 2010) at the University of Washington, is an aftercare program integrating mindfulness practices and principles with cognitive-behavioral relapse prevention. MBRP practices foster increased awareness of triggers, habitual patterns, and “automatic” reactions. These practices help those in recovery develop the ability to pause, observe present experience, and bring awareness to the range of choices before them.

MBRP developers believe it is best suited to individuals who “have undergone initial treatment and wish to maintain their treatment gains and develop a lifestyle that supports their well-being and recovery.” Before enrolling, participants typically have at least 30 days of active sobriety, and participate in a short interview to discuss suitability for the MBRP class. The program involves 8 weeks of curriculum-based classes. Each class includes mindfulness meditation and/or mindful movement, along with cognitive-behavioral strategies to maintain and reinforce sobriety. Participants are expected to do daily home practice. The primary goals of MBRP are to develop awareness of personal triggers and habitual reactions, and learn ways to create a pause in this seemingly automatic process; change the relationship to discomfort, learning to recognize challenging emotional and physical experiences and responding to them in skillful ways; foster a nonjudgmental, compassionate approach toward oneself and experiences; and build a lifestyle that supports both mindfulness practice and recovery.

The outcomes of MBRP (<http://www.mindfulrp.com/Research.html>) have been promising, including: significantly lower rates of substance use, decreases in craving, and increases in acceptance and acting with awareness among those who received MBRP as compared to treatment as usual. Free mp3s audios featuring techniques used in MBRP such as: Body Scan, Sober Space, Urge Surfing, Mindful Movement, and Meditation are available on the MBRP website at <http://www.mindfulrp.com/For-Clinicians.html>.

Is Mindfulness Meditation for Everyone?

Of course not, there are side effects and contraindications identified in the literature regarding the use of mindfulness meditation. A good reference article on this topic, *Mindfulness Meditation Research: Issues of Participant Screening, Safety Procedures, and Researcher Training* (Lustyk,

Chawla, Nolan, Marlatt, 2009) notes: "Side effects of meditation with possible adverse reactions are reported in the literature. Mental health consequences were the most frequently reported side effects, followed by physical health then spiritual health consequences." For each of the potential adverse effects identified in the article, the authors offer methods to assess the relative risks and deal with them.

Conclusion

According to one mindfulness researcher, "mindfulness seems to represent an emotional balance that involves acceptance of internal experiences, affective clarity, an ability to regulate one's emotions and moods, cognitive flexibility, and a healthy approach to problems. Mindfulness may indeed represent a solid ground from which to experience the vicissitudes of life without losing one's balance or distorting one's experience." (Hoppes, 2006) Indeed, the words and ancient wisdom of the Buddha quoted at the beginning of this issue seem to have found an increasingly legitimate place in modern, effective addiction treatment and recovery practices.

Additional Resources

The following are recommended in addition to the websites and other resources mentioned in this issue:

Monthly updates on published research on the application of mindfulness to various fields can be found in the newsletter *Mindfulness Research Monthly* at <http://www.mindfulexperience.org/newsletter.php>

Several instruments have been developed for measuring mindfulness. A listing of the instruments and their supportive psychometric studies is available at <http://www.mindfulexperience.org/measurement.php>.

Sample mindfulness exercises can be heard/downloaded from UCLA's Mindful Awareness Research Center website at <http://marc.ucla.edu/body.cfm?id=22>

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Mindfulness Meditation for Substance Use Disorders: A Systematic Review

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Abstract

Relapse is common in substance use disorders (SUDs), even among treated individuals. The goal of this article was to systematically review the existing evidence on mindfulness meditation-based interventions (MM) for SUDs.

The comprehensive search for and review of literature found over 2,000 abstracts and resulted in 25 eligible manuscripts (22 published, 3 unpublished: 8 RCTs, 7 controlled non-randomized, 6 non-controlled prospective, 2 qualitative studies, 1 case report). When appropriate, methodological quality, absolute risk reduction, number needed to treat, and effect size (ES) were assessed.

Overall, although preliminary evidence suggests MM efficacy and safety, conclusive data for MM as a treatment of SUDs are lacking. Significant methodological limitations exist in most studies. Further, it is unclear which persons with SUDs might benefit most from MM. Future trials must be of sufficient sample size to answer a specific clinical question and should target both assessment of effect size and mechanisms of action.

Keywords

mindfulness; meditation; addiction; relapse prevention; substance abuse

INTRODUCTION

According to the United Nations Office on Drugs and Crime,(1) approximately 200 million people worldwide are current drug users. In the U.S., an estimated 22.6 million were diagnosed with substance dependence or abuse in 2006.(2) The cost of drug abuse worldwide, in terms of crime, loss of work and health care costs, was estimated at 180.9 billion USD in 2002.(3) The human suffering related to substance use disorders is immeasurable.

Substance use disorders (SUDs) have been described as "chronic relapsing conditions," with rates of relapse exceeding 60% and being relatively consistent across substances of abuse.(4–6) A range of treatments have been developed to target relapse. Among behavioral

interventions, cognitive behavioral therapy (CBT), including relapse prevention,(7) has received considerable support. However, in spite of best "standard of care" therapy, relapse rates continue to be high, highlighting the need for development of new treatment modalities to better assist individuals in their recovery.

The theoretical framework for mindfulness meditation suggests that it may be a promising approach to treating addictive disorders.(8,9) *Mindfulness* has been defined as the intentional, accepting and non-judgmental focus of one's attention on the emotions, thoughts and sensations occurring in the present moment.(10) Such a purposeful control of attention can be learned through training in techniques such as *meditation*.(11) The "observe and accept" approach, characteristic of meditation, refers to being fully present and attentive to current experience but not being pre-occupied by it. Thus, meditation can become a mental position for being able to separate a given experience from an associated emotion,(12) and can facilitate a skillful or *mindful* response to a given situation.(8) Meditation is often contrasted with everyday, habitual mental functioning or being on "auto-pilot." As such, meditation may be a valuable technique for SUD-affected persons, whose condition is often associated with unwanted thoughts, emotions and sensations (e.g. craving), the tendency to be on "auto-pilot", and pre-occupation with the "next fix", rather than "being in the present moment." Meditation may also be a component of maintaining lifestyle balance, with meditation-acquired skills complementing and enhancing CBT effects for SUDs.(7,8,13,14)

Traditionally, meditative techniques have been taught and practiced through formal and informal meditation centers. More recently, meditation has also become a component of many therapeutic programs; in 1997, over 240 meditation programs were a part of U.S. health care systems,(15) and the basics of meditation are taught in many U.S. medical schools. Mindfulness Based Stress Reduction (MBSR) (10) is the most frequently cited method of mindfulness training in the medical context.(16) Based on the MBSR model, other therapies, combining both mindfulness and CBT elements have been developed, including the Mindfulness Based Cognitive Therapy (MBCT) for relapse related to recurrent depression (17) and Mindfulness Based Relapse Prevention (MBRP) for relapse related to SUDs.(9,18) Mindfulness is also a central part of Dialectical Behavior Therapy (DBT) for individuals with borderline personality disorder,(19) Acceptance and Commitment Therapy (ACT) (20) for individuals with a variety of mental health problems, and Spiritual Self-Schema (3-S) therapy designed for clients with SUDs.(21)

While the use of mindfulness meditation as a therapy for SUDs is not new and has been associated with anecdotal clinical success,(14) until recently there has been a paucity of research to support its empirical efficacy. The growing interest in complementary and alternative medicine (CAM), especially mind-body therapies,(15,22) has brought a surge of interest in research evaluating the effects of meditation in a range of clinical contexts, including addictive problems. The current evidence on the clinical applications of mindfulness meditation for SUDs has not been rigorously reviewed.

The goal of this article was to systematically review and assess the existing evidence on the effects of mindfulness or mindfulness meditation based therapies for addictive disorders. Although there are various forms of meditation, it is not known whether these approaches have similar effects on the problems or disorders under consideration. This review focused specifically on mindfulness meditation, and the term "meditation", as used in this manuscript, refers exclusively to mindfulness meditation.

METHODS

Criteria for selection of studies

Inclusion criteria: 1) study intervention was mindfulness or mindfulness meditation-based (MM), 2) used as a therapy for substance use, misuse or related disorders; 3) the study was longitudinal, with pre- and post-intervention assessments; and 4) it involved human subjects.

Exclusion criteria: 1) lack of a sufficient description of the study intervention to determine if it was rooted in mindfulness; 2) non-English; and 3) only interim results of an unpublished study were available. We anticipated that the number of eligible studies would be limited; therefore, we did not exclude studies based on design (experimental vs. non-experimental), methodological quality or specific intervention protocol. Both published and unpublished reports were eligible for inclusion.

Search strategy

The research librarian (RK) worked closely with the co-authors (AZ, KK) to refine search strategies. Comprehensive searches (Table 1) were conducted through Mar 9, 2008 of the following electronic databases: Cochrane Database of Systematic Reviews (since 1995), EMBASE (since 1993), PubMed (including PreMed and Old Med, since 1950), PsycINFO (since 1967), CINAHL (since 1982), and Allied and Complementary Medicine (since 1985). The National Institutes of Health (NIH) CRISP electronic database of relevant institutes (National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse, National Institute of Mental Health, National Center for Complementary and Alternative Medicine) was searched from 1995 – Mar 9, 2008 with keywords: “meditation” OR “mindfulness”. The Scientific Research on The Transcendental Meditation® Program: Collected Papers (Volumes 1 to 4) were hand-searched. The reference lists of relevant articles were reviewed to identify potentially eligible studies. E-mail or phone contact was attempted with relevant author(s) or Principle Investigator(s) of included articles or abstracts when additional information was needed.

Identification of eligible studies

The titles and abstracts of all identified studies were screened (RK and AZ, “initial screening”). Studies that clearly described using only Transcendental Meditation, Progressive Muscle Relaxation, Biofeedback or Autogenic Training as their interventions were excluded. The full-text of studies describing the use of meditation, mindfulness, relaxation, yoga, breath practices or other techniques that were compatible or potentially compatible with mindfulness meditation (as the primary or comparison interventions) were then reviewed (AZ, “secondary screening”). Practices that were included as compatible with MM are described in the following section. The secondary screening resulted in an exclusion of ineligible articles (AZ); articles that were considered potentially eligible were then additionally reviewed (“tertiary screening”) by 3 independent reviewers (NC, GAM, KK), experts in psychology, meditation and relapse prevention for SUDs.

Data extraction and study assessments

Data from all eligible articles were extracted, and the methodological quality of controlled and prospective case series studies was assessed for internal validity by two unblinded reviewers (AZ, DR). We used an adapted version of a scoring instrument suited for studies using behavioral interventions and developed for the systematic review of alcohol treatment trials. (23) This instrument (Table 2) was adapted for use in SUDs with input from Dr. William Miller, co-developer of the original scale (personal communication, Mar-Apr, 2008).

Using this instrument, the studies were assigned the following sub-scores (Table 3): *a) Population Severity Rating (PSR)*, *b) Methodological Quality Score (MQS)*, *c) Clinical Benefit Score (CBS, called the Outcome Logic Score in the original scale (23))*, and *d) Cumulative Evidence Score (CES)*, where: $CES = CBS \times MQS$. *e) The Overall CES* was also calculated for subgroups of studies (e.g., RCTs), as a sum of CES of individual studies.

When possible, *absolute risk reduction (ARR)*, *number needed to treat (NNT)* and *effect size (ES)* were calculated by the authors (AZ, DR) for the main substance-use related outcomes. The following formulas were used: *a) ARR* = absolute difference in outcome rates between the control and treatment groups; *b) NNT* = $1/ARR$; and *c) ES*, Cohen's *d*, was either converted from correlations (where $r=0.37$ corresponded to $d=0.8$, $r=0.24$ corresponded to $d=0.5$, and $r=0.1$ corresponded to $d=0.2$) or calculated from the mean values (*M*) and standard deviations (*SDs*); Cohen's *d* for controlled trials (formula #1) was calculated as $d = [M1 - M2] / SD_{pooled}$, where *M1*, *M2* were the means in the two groups, and $SD_{pooled} = \sqrt{[(SD1^2 + SD2^2)/2]}$; Cohen's *d* for uncontrolled pre-post trials (formula #2) was calculated as $d = [\text{mean of the pre-post difference}] / [\text{SD of this mean}]$. In cases where it was not possible to use formula #2, then formula #1 was used.

RESULTS

1. Literature search results (Figure 1)

The search identified 1,095 abstracts of published articles. After removing 595 duplicates (RK), 500 abstracts were reviewed (AZ, initial screening). Of those, 276 were excluded. The full-texts of 224 articles were then reviewed (AZ, secondary screening), and 34 articles were submitted for a tertiary screening. Twelve of the 34 articles (24–35) did not meet the eligibility criteria and were excluded. Of the excluded studies, two deserve an additional comment. (24, 34) Both studies used the body scan technique as a study intervention. Although the body scan was derived from a mindfulness meditation-based program, in isolation, this technique did not meet the criteria for mindfulness or mindfulness meditation because MM-based body scan involves not only instructions on paying attention to the various parts of the body, but also encourages focused awareness, without attempt to change or manipulate body sensations, thus promoting non-judgmental and compassionate acceptance of whatever is occurring in the body at any given moment.

The 22 published articles included 7 RCTs, (36–42) 6 controlled non-randomized trials, (43–48) 6 prospective case series, (49–53) 1 case report (54) and 2 qualitative studies. (55,56) Seventeen of these reports were based on separate clinical trials and 5 on secondary database analyses. (45,48,52,55,57) The CRISP database search found 324 “hits,” resulting in 9 additional relevant abstracts. Through personal communication, 2 ready-for-submission, but unpublished articles (58,59) and 1 PhD dissertation (60) were additionally identified as eligible, resulting in a total of 25 included studies. Of note, after completion of this manuscript, results of one of the “unpublished studies” (58) have been published. (61)

The heterogeneity of the included studies and interrater agreement on methodological quality scoring were not formally assessed. The wide variety of conditions treated, treatment protocols and outcome measures used was apparent on inspection, and made the pooling of data impossible. Disagreements between the reviewers were resolved by consensus.

2. Methods of the included published studies (Table 3 – Table 5)

a) Studied population—Three studies focused on adolescents, (49,52,57) while the remaining 19 studies evaluated adults. Of the 22 studies, 12 evaluated severely impaired subjects (*Population Severity Rating*, PSR 4/4), treated for alcohol and/or drug dependence in

residential (36,46,51,56) or outpatient settings,(37,40,⁴¹,⁴⁷,⁵³,55,62) three described a clinical sample of adolescents with SUDs (PSR 3/4),(49,52,57) three included a non-clinical sample of substance-using prisoners (PSR 2/4),(44,45,48) and four were based on community-recruited adults (PSR 2/4) with tobacco (38,43,50) or marijuana (54) dependence.

b) MM intervention—The MM interventions used in the included studies were based on 5 main models:

Vipassana meditation: (<http://www.dhamma.org>) is a form of MM that is deeply rooted in the Buddhist tradition. Most contemporary forms of MM derive from traditional Vipassana meditation. Typical Vipassana courses are group-based, last ten consecutive days, are conducted in silence, and involve meditating for 10–11 hours per day. They are available at no charge and follow a similar curriculum world-wide.

Three articles,(44,45,48) based on one study,(44) described the effects of a traditional vipassana training led by a traditionally trained teacher, in a prison settings. The intervention was standardized (followed a traditional vipassana format), but its delivery was not monitored.

Mindfulness Based Stress Reduction (MBSR): Originally developed for management of chronic pain and stress-related disorders,(10) MBSR has been shown to be effective or potentially effective for many mental health and medical conditions.(16) MBSR is the most frequently cited method of meditation training in the medical context,(16) and has a published curriculum.(10) The usual MBSR course consists of 8 weekly, therapist-led group sessions (2–2.5 hours per session), one full-day retreat (7–8 hours) and daily home assignments. The MBSR curriculum served as a model for the manualized *Mindfulness Based Cognitive Therapy (MBCT)* (17) that combines meditation (10) and traditional, cognitive therapy strategies (63) to prevent relapse in recurrent depression. MBCT has been shown to reduce the rate of depressive relapse among persons with recurrent depression,(64,65) and may be efficacious for symptom reduction in "active" depression (66) and anxiety disorders as well.(67) Using the MBCT model in turn, a manualized *Mindfulness Based Relapse Prevention (MBRP)* program has been developed for outpatient clients with SUDs.(9,18) The elements of cognitive therapy in MBRP are based on relapse prevention cognitive therapy strategies (7) that have demonstrated efficacy for SUDs.(68) Evaluation of the MBRP program for SUDs is currently ongoing.(69)

Ten articles,(36,43,⁴⁶,⁴⁹–⁵³,56,57) based on 8 separate studies,(36,43,⁴⁶,⁴⁹–⁵¹,53,56) reported use of the MBSR-based intervention. Only one study did not report modifications to the MBSR curriculum;(43) the other studies implemented modified MBSR programs, tailored to the targeted population. The modifications were reported as “minor” in 3 studies (46,50,51) – in these studies, the intervention, delivered by trained MBSR teachers, was labeled as "MBSR" and scored as “manualized.” Two studies (four reports: ³⁶,49,52,57) used modified MBSR, with modifications being quite substantial and not manualized – therefore, these interventions were scored as “not manualized.” Two studies developed and used an MBSR-based, manualized intervention: one patterned after MBSR and adjusted to the needs of therapeutic community residents,(56) and one patterned after MBRP and adjusted to the needs of recovering, alcohol dependent adults.(53) The meditation course intensity in the included studies ranged from five 90-minute sessions over seven weeks (with less than 50% of the session content devoted to MM) (49,52,57) to eight 2–2.5-hour sessions over eight weeks, with the majority of each session devoted to MM.(36,43,⁴⁶,50,53) In addition, two studies implemented a full-day retreat.(36,50) Only one study reported monitoring the integrity of intervention delivery.(56)

Spiritual Self Schema (3-S): therapy has been developed for the treatment of addiction and HIV risk behavior.(21) Its curriculum is manualized (www.3-S.us) and consists of an 8- or 12-week long course, designed for clients at risk for, but not infected with HIV or clients with HIV, respectively. The 3-S therapy teaches meditation and mindfulness skills in the context of comprehensive psychotherapy, integrating Buddhist principles with modern cognitive self-schema theory that is tailored to each patient's spiritual/religious faith.(21)

Four reports,(37,42,47,55) based on 3 separate studies,(37,42,47) used manualized 3-S therapy delivered in an individual and/or group format, during 1–2 hour-long sessions per week, by a trained therapist over eight (37,42,55) or twelve (47) weeks. Integrity of the intervention delivery was monitored in all the studies.

Acceptance and Commitment Therapy (ACT): Theoretically based in contemporary behavior analysis, ACT applies both mindfulness/acceptance, as well as commitment and behavior change processes.(62) These core processes, conceptualized as positive psychological skills, aim to increase psychological flexibility that is defined as the ability to better connect to one's experience, and to make overt behavioral choices in the service of chosen goals and values ("committed action").(62) Originally developed for psychological disorders,(20) ACT has been applied to a variety of conditions, including SUDs.

Three studies used manualized ACT,(38,39,54) delivered by a trained therapist in either an individual (54) or both individual and group (38,39) therapy format. The ACT sessions took place weekly, ranging in duration from 1½ (54) to 3½ (39) hours per week, over seven (38) to sixteen (39) weeks. Integrity of intervention delivery was monitored in all the studies.

Dialectical Behavior Therapy (DBT): DBT originated as a therapy for chronically suicidal clients with borderline personality disorder,(19,70) and was subsequently adapted for SUDs. (71) DBT comprises strategies from cognitive and behavioral therapies (with a problem-solving focus) and acceptance strategies (with mindfulness as its core) adapted from Zen teaching and practice. It provides a comprehensive long-term treatment that includes psychotherapy (therapist-led, in group and individual formats), case and medical management.

Two studies used a 1 year-long manualized DBT program for SUDs, with individual and group therapy lasting from three (41) to six (40) hours per week. Integrity of intervention delivery was monitored in these studies.

c) Methodological quality

Randomization: All 7 RCTs (Table 4) received 4 points for randomization on the MQS scores, including the study that reported unequal effects of randomization (36) – in this case, a full MQS score was assigned since the "inequality" favored the controls. Two of the 7 RCTs used randomization techniques that require a comment. One of these RCTs initially randomized subjects into 2 arms: MM and "standard of care" control, and then sub-randomized the MM group into two different protocols of MM delivery. Since no differences were found between the two MM subgroups, they were later combined into one group for the final analysis, and compared to controls.(42) Another RCT randomly assigned subjects to two different modes of MM delivery, but found no differences between these groups (no details described); thus, the groups were combined into one, and assessed as a prospective case series, with detailed results presented for pre-post analyses only.(37)

Blinding: "Double-blinding," interventionist or subject blinding are not feasible and/or desirable in studies using MM interventions for practical and ethical reasons, and none of the treatment studies used such methods. Three RCTs reported assessor blinding.(39–41)

Sample size: The included studies were "pilots" with small sample sizes. One published RCT (39) and one unpublished RCT (59) provided sample size assumptions, however, a high attrition rate resulted in their being underpowered.

Analysis: Only one study described evaluation of the distributional characteristics of the variables, and the use of parametric or non-parametric tests, when appropriate.(53) One published study (43) and one unpublished study (58) did not use statistical analyses for the assessment of intervention effects. Other studies used parametric analyses that assume normal data distribution. However, in the context of small sample sizes and high variability of some data (as indicated by SDs), it is possible that some variables did not have normal distribution. Six studies either reported 100% follow-up data collection,(50) 100% retention (46) or analyzed data per intention-to-treat (ITT) protocol, imputing missing data.(38–41)

Quality of MM intervention delivery: MM was manualized in 15 separate studies, described in 18 articles.(37–48,^{50,51},53–56) Integrity of the intervention delivery (therapist protocol adherence and/or competence) was monitored in 10 separate studies.(37–42,^{47,50,54,56})

Retention rate: among the MM subjects ranged from about 45% (39,44) to 100%.(46) with an average rate of 75%. One study with a 72% retention rate collected primary outcome data for all enrolled subjects.(50)

Methodological Quality Score (MQS) and Cumulative Evidence Score (CES; Table 3): Among the included 22 reports, 15 were based on separate studies. As expected, among these 15 studies, the highest MQSs were for RCTs, followed by non-randomized controlled trials and case series. Only one RCT (40) received a score of "excellent", defined as MQS \geq 14. (23) Evaluating by the type of MM intervention used, the highest MQSs were achieved by studies of DBT and ACT, followed by 3-S and MBSR-based therapies. The MBSR-based intervention was the most commonly studied MM therapy (7/15 studies). Grouping by subject population, the highest mean MQSs were achieved by studies evaluating adults with SUDs in the outpatient setting, which were also the most common population / settings (N=7: opiate dependent, medically managed subjects – five studies; poly-SUDs – one study; and alcohol dependence – one study); these studies were followed by studies of community-recruited adults with tobacco dependence (N=3), and studies of adults treated for SUDs in residential settings (N=3). The Overall CES, calculated for subgroups of studies, indicated that, in general, the studies yielded positive evidence (Overall CES ranging from +10 to +143) with 50% to 85% of the studies reporting positive outcomes by ITT (N=6) or per protocol (N=13) analyses, respectively (Table 3).

d) Side effects or adverse events—Only two reports directly stated that no MM-related significant side effects, adverse events or problems occurred.(53,55) Other reports did not address this topic, implicitly suggesting lack of negative effects.

3. Results of the published treatment RCTs (Table 4)

Seven RCTs, including a total of 383 (63% female) adult subjects, followed for an average of 38 weeks post-entry (from eight (37,42) to sixty eight (40,41) weeks), offered the most detailed assessment of MM interventions. Methodological quality of the RCTs was moderate (MQS 8-14/17). Six RCTs evaluated severely impaired populations (PSR 4/4), and one (38) focused on tobacco dependent adults (PSR 2/4).

Six of 7 RCTs used two-arm, and one used a three-arm design.(39) Three studies compared MM + "standard of care" (SOC) to SOC alone,(36,42) with both MM and SOC provided at the same clinical site. One study compared MM to SOC, with SOC subjects referred out for therapy

("naturalistic control").(41) Finally, four studies (37–40) compared MM to an active intervention: three to a different therapy (behavioral (39,40) or pharmacotherapy (38)) and one compared MM delivered in "individual" versus "individual + group format".(37)

All RCTs reported some positive results. Compared to SOC, the MM intervention showed positive effects as indicated by the ITT (40,41) and per protocol (38–42) analyses. Differential improvement in both substance use-related and other outcomes was noted in 5 of 7 studies. (38–42) One study (36) noted a differential improvement in medical symptom severity only ($p < 0.05$, effect size 0.2), and one study,(37) comparing 3-S "individual" to 3-S "individual + group" therapy did not find differences between the study arms, but noted pre-post improvements ($p < 0.05$, effect size 0.5) in substance use outcomes.

Overall, studies using SOC (39,41,42) or active, but "non-matching" interventions (38) as a comparison group, tended to report greater statistically significant between-group differences, with results favoring MM, than studies using a "matching" behavioral intervention.(39,40) The 3-arm study by Hayes et al.,(39) with the largest sample size but low retention rate, of 124 poly-substance abusing methadone maintenance patients suggested, in a per protocol analysis, that MM + SOC may result in a substantial reduction of substance use compared to SOC alone (ARR 33%). This finding was consistent across 3 other RCTs comparing MM to SOC (ARR 30% (42) with medium to large effect size (41)) or to pharmacotherapy with medical management (ARR 12–20% per ITT and per protocol analyses).(38) Two methodologically strong RCTs compared MM to a different behavioral intervention that "matched" MM by subject involvement and therapy format.(39,40) These studies did not find significant in-between group differences in substance use (ARR 5–12%, $p > 0.05$) or psychological outcomes at the study end-point at forty two (39) or sixty eight (40) weeks, however, they both noted a tendency to a more accurate drug use reporting among MM compared to comparison subjects. (39,40) Regarding non-substance use related measures, MM subjects, compared to SOC controls, increased their motivation for HIV prevention, their spiritual practices and showed a cognitive shift from "addict" to "spiritual qualities" ($p < 0.05$);(42) they also improved their Global Adjustment and Global Social Adjustment Scale scores ($p < 0.05$).(41)

4. Results of the published non-randomized controlled studies, case reports and case series (Table 5)

Table 5 summarizes four controlled non-randomized trials (described by 6 articles (43–48)), four case series (described by 6 articles (49–53,57)) and one case report.(54) These studies included 609 subjects, 13 to 67 years old, suffering from various SUDs, and recruited from the outpatient treatment,(46,47,^{49,51}–53,57) community,(43,50) or jail (44,48) settings.

While the methodological quality of the scored studies was limited (MQS 4-8/17), collectively they reported overall positive outcomes. On average, substance use tended to decrease at follow-up compared to baseline (43,50,53) or compared to a control group,(44,47) with effect sizes ranging from small (47,53) to medium.(44) One study (49) reported an increase in substance use at follow-up compared to low-use at baseline, but no detailed results were presented, and substance use was not the primary focus of the study. Severity of potential relapse triggers (such as stress, mental health and sleep problems, certain coping styles) also tended to improve compared to both baseline (49,50,53) and control conditions.(44,46,47) and the average effect size for these changes ranged from medium to large. Bowen et al. (44) also noted a reduction of alcohol-related negative consequences (small effect size) among subjects who underwent MM training compared to controls. Only one uncontrolled trial (among all included studies) of alcoholics treated with MM therapy, adjunctive to SOC, assessed craving severity and the degree of mindfulness.(53) Although craving severity decreased (medium effect size), this change was not statistically significant; degree of mindfulness, or the ability to be attentive to a present-moment experience in daily life, improved (medium effect size),

and this change correlated to improved stress severity (large effect size) at 16 week follow-up. (53)

Participation in the MM therapy correlated to or mediated the improvements in substance use and relapse-related outcomes, with small-to-large effect size. (44,45, 47, 48, 50,53) One uncontrolled study compared "relapsers" (N=7; subjects reporting at least one heavy drinking day during the study) to non-relapsers (N=8), and found that relapsers had more severe symptoms of anxiety, depression and craving, reported lower degree of mindfulness and meditated fewer minutes per day ($p<0.05$). (53) The same study also reported that drinking level as well as the change in drinking correlated to the severity of relapse risk factors such as anxiety, depression, stress, and craving (large effect sizes) and the change in their severity, respectively. In turn, severity of relapse risk factors negatively correlated with the intensity of a daily meditation practice (large effect size). (53)

Two uncontrolled trials assessed pre-post levels of biological outcomes: stress-responsive and illness-sensitive biomarkers, in addition to self-reported psychological measures. A study of recovering alcoholics evaluated serum interleukin-6 (IL-6), liver enzymes and diurnal profile of salivary cortisol at baseline and 16-week follow-up. (53) While cortisol (N=10) and liver enzymes (N=12) did not significantly change over time (small effect size), IL-6 level decreased (N=12; medium effect size, $p=0.05$), suggesting a reduction in chronic stress level and improved health. After MM intervention, SUD-affected residents of a therapeutic community showed a decrease in an awakening salivary cortisol level compared to baseline (medium effect size). (51)

5. Subject treatment experiences related to MM intervention (Table 4 and Table 5)

Two qualitative studies, (55,56) derived from mixed-methods primary projects, (42,47,72) focused on subject treatment experiences related to MM therapy (Table 5). Several other studies also evaluated subject experiences, using quantitative (e.g. Likert scales) or qualitative techniques. (38,39,43,53) Taken together, MM therapy was well-received by the subjects with different degrees of problem severity (PSR 2-4/4) and in various settings: residential, (56) outpatient (39,53,55) and community. (38,43) Subjects reported high degree of satisfaction with MM therapy and its usefulness as a recovery-enhancing tool. They also viewed MM-related skills as unique, "brand new" and different from those taught in a traditional, professional addiction treatment. (53,55)

Four studies evaluated individual ("at-home") MM practices among the subjects who underwent an 8-week MM intervention. (36,42,43,53) Two of these studies, using the MBSR-based intervention, reported that about 47% of the subjects continued meditation practice at twelve (43) and twenty two (36) weeks post-entry. A study evaluating MBSR + CBT-based intervention found that 100% of the study completers (79% of the sample, with all drop-outs occurring after the 1st or 2nd MM session) meditated at 16 weeks, on average 3.9 days/week, 27.4 minutes/meditating day. (53) Likewise, an RCT evaluating 3-S therapy found that at 8 weeks all study completers (82%) continued meditating, on average 26 minutes/day. (42)

6. Unpublished studies (Table 6)

Two treatment trials using ACT (58,59) and one laboratory-based study of a mindfulness-based coping technique (60) provide additional insights into the potential efficacy and mechanisms of MM interventions for smoking cessation. An RCT of 10-week MM intervention (ACT, combined with CBT and nicotine replacement therapy, NRT) found a significantly higher quit rate (small effect size) and higher treatment satisfaction (medium effect size) among the MM subjects compared to controls, receiving NRT alone, at 52 weeks; in addition, acceptance-based responding mediated effects of MM on smoking outcomes. (59) A set of prospective case

series (N=16 subjects), designed for pilot-testing and refinement of the study methods, evaluated effects of combined ACT, CBT and NRT. Although smoking quantity and frequency have not been compared "pre-post," and all study completers resumed smoking at 26 weeks post-quit date, the longest continuous abstinence period was longer after the MM intervention than during subjects' previous attempts when abstinence had lasted less than 3 days. Further, 82% of the subjects reported that they learned skills that were "very" or "extremely useful" in helping them quit smoking.(58) Finally, one RCT (PhD dissertation) described an experiment evaluating efficacy of mindfulness-based coping compared to "usual" coping strategies aimed to prevent relapse after quitting smoking.(60) In this study, during a cue exposure paradigm, the MM group used MM strategies, as instructed, while controls used primarily distraction-based techniques to cope with smoking cravings and urges. During the 7 day follow-up, the MM group smoked fewer cigarettes/day than controls (medium effect size, $p < 0.05$). Overall, the results of these unpublished trials support the existing preliminary evidence provided by published studies.

DISCUSSION

This is the first systematic review of mindfulness or mindfulness meditation based interventions (MM) for substance use, misuse or disorders. Although existing data is preliminary and does not allow a consensus recommendation for any particular type of MM intervention for any single substance use-related condition, several findings are of clinical, theoretical and research interest.

The majority of the reviewed studies showed some positive outcomes among SUD-affected subjects treated with MM intervention, compared to baseline or other therapy (most commonly SOC). The case studies illustrated how MM has been practiced from a historical and clinical perspective. The focus on real-life trial methods has been termed pragmatic.(73) Pragmatic studies have the advantage of assessing effectiveness under conditions that patients encounter in real-life settings, thereby avoiding confounders associated with highly standardized clinical trial settings. Though lacking methodological strengths of control and randomization, the case studies, documented here, consistently showed positive patient outcomes and the general treatment satisfaction of subjects with chronic, often refractory, SUDs who were treated with MM therapy. Pragmatic aspects of these studies included meeting patient's expectations of receiving a "promised treatment," the ability of the therapist to better select the patient, and study methods that more closely resemble real clinical settings. Data from the controlled trials suggest that subjects receiving MM, adjunctive to SOC or pharmacotherapy, do as well or better than those receiving SOC or pharmacotherapy alone. When compared to other behavioral interventions in RCT settings, MM appears to produce comparable results. All these conclusions require assessment with more formal methodology in adequately powered clinical trials.

The promise of MM as an efficacious treatment for SUDs is supported by the consistency of positive results, demonstrated in this review across different study designs, MM modalities, subject populations and addictive disorders treated. Additional support for the potential efficacy of MM in SUDs can be drawn from the results of studies of other clinical samples. MM-based therapies have been shown to be effective or potentially effective (with, on average, medium pooled effect size, Cohen's d 0.5–0.7 (16,62)) for a variety of medical and mental health disorders, including stress, anxiety, depression, emotion dysregulation, avoidance coping,(16,62,74–77) all known risk factors for relapse in SUDs.(78,79) In this context, MM may be particularly helpful for patients with co-occurring substance use and mental health disorders ("dual diagnosis").

Although long-term MM practice patterns have not been assessed in the context of SUDs, its use in other clinical samples suggests that MM can have long-lasting effects. For example, after a meditation course, 60–90% of subjects still meditated up to 4 years later, and reported that the course "had lasting value" and was highly important.(16) Patient satisfaction is an important consideration when choosing between treatment alternatives.(80) MM also appears safe - rigorous studies have not reported any side effects or adverse events.(64,65) This review corroborates these findings.

It is appealing to assume that the preliminary positive results in MM studies are direct outcomes of MM interventions; however, such a hypothesis is premature. The theoretical framework behind MM as well as early indirect evidence supports the use of MM for SUDs (8,9,13,14) and suggests unique therapeutic properties of MM. On a conceptual level, MM stands out as distinctive and, in many ways, different from other existing behavioral modalities, specifically from cognitive behavioral therapy (CBT) that is commonly used to treat SUDs.(81,82) While CBT promotes adaptive, antecedent-focused coping strategies (e.g. targeting emotion cues), meditation targets maladaptive, response-focused strategies, such as emotional avoidance, suppression or impulse control; thus, MM-related skills can complement skills acquired through CBT.(8,9,13,14) The integration of meditation and traditional CBT strategies may improve overall treatment efficacy, e.g. by increasing awareness of sensations, such as craving, emotional states, and physiological arousal.(83) Recent pilot trials of clinical cohorts add support to the above hypotheses, indicating that MM and CBT can produce different effects on mental health outcomes.(62,84,85) Two reviewed qualitative studies (53,55) reported that subjects viewed MM-related skills as different from those acquired through "traditional" SOC therapy for addiction.

Limitations

of this review include limiting the inclusion criteria to studies published in English, potentially excluding relevant studies. Lack of reviewer blinding and lack of assessment of inter-rater agreement could have introduced bias. Although the included interventions were based on the MM principles, they were heterogeneous; evaluating them together as one "MM intervention" could have introduced bias.

Strengths

of this review include an exhaustive literature search and application of statistical methods allowing direct comparison of included studies.

Directions for Further Research

Existing studies of MM therapy for addictive disorders are far from definitive and the research methods are evolving. These clinical and research fields would benefit from the development of: 1) standardized scientific parameters to be used in future studies of MM as a therapy for addictive disorders, 2) a comprehensive conceptual model of possible mechanisms underlying MM efficacy in SUDs, and 3) recommendations on MM implementation in clinical addiction medicine settings. Below we elaborate on each of these recommendations:

1. Research methods of MM studies in addiction settings require refinement and standardization.
 - A written manual should be used to guide the meditation intervention. It has been suggested that best therapeutic effects are achieved when the meditation intervention is adjusted to accommodate the specific needs of the targeted population.(86) While several "manualized" MM therapies are currently used in the treatment of SUDs (MBSR, MBRP, DBT, ACT, 3-S), most have been modified and adjusted to the needs of individual studies; however, only

a minority of these studies developed a separate intervention manual. It is not known whether even relatively minor adaptations could have affected outcomes. Standardization of treatment manuals would facilitate study replication and data pooling.

- A theory for, and measures to assess, the evaluation of treatment outcomes in the context of MM also require development.
 - Assessment of subjects' MM practice intensity and changes in the degree of mindfulness should be considered. These are essentially the "dose" and "quality" of the intervention and as such have the potential to influence findings similar to medication dose-response effects in pharmacotherapy trials. This data would also provide information on the ability of subjects to sustain MM practice over time. Many clinical MM programs "interview" potential clients before enrollment to ensure appropriate selection. In research settings, including the reviewed studies, the eligibility criteria are usually diagnosis-driven; results may therefore be skewed away from a positive effect, should one exist.
2. Research of MM has the potential to create a comprehensive bench-to-bedside explanatory model of its effects. Therefore, the mechanism of MM should be assessed in tandem with clinical assessment. Possible mechanisms have been hypothesized; (8,9,13,14) however, no comprehensive model, encompassing bio-psychological aspects of addiction, has been developed. None of the included studies was designed as a "dismantling" study or focused on "active ingredients" underlying MM effects. Appropriate control therapies and targeted assessments, including "objective" measures (e.g. biomarkers, imaging studies) are needed to assess treatment efficacy and to elucidate a mechanism of action for MM interventions in addictive disorders.
 3. While MM techniques are already used in the clinical setting to treat addictive disorders,(14) it is premature to formally recommend for or against such practice. Researchers and clinicians involved in MM research should collectively address effectiveness of MM therapies in the form of consensus statements, and thereby provide guidelines on the best ways to implement MM therapies in clinical settings as a part of comprehensive addiction treatment programs.

CONCLUSIONS

Conclusive data for MM as a treatment for addictive disorders are lacking. However, the preliminary evidence indicate MM efficacy. MM therapies appear safe when performed in clinical research settings. Significant methodological limitations exist in most studies published to date, and it is unclear which persons with addictive disorders might benefit most from MM. Future clinical trials must be of sufficient sample size to answer a specific clinical question and should include carefully designed comparison groups that would allow assessment of both the effect size and mechanism of action of MM.

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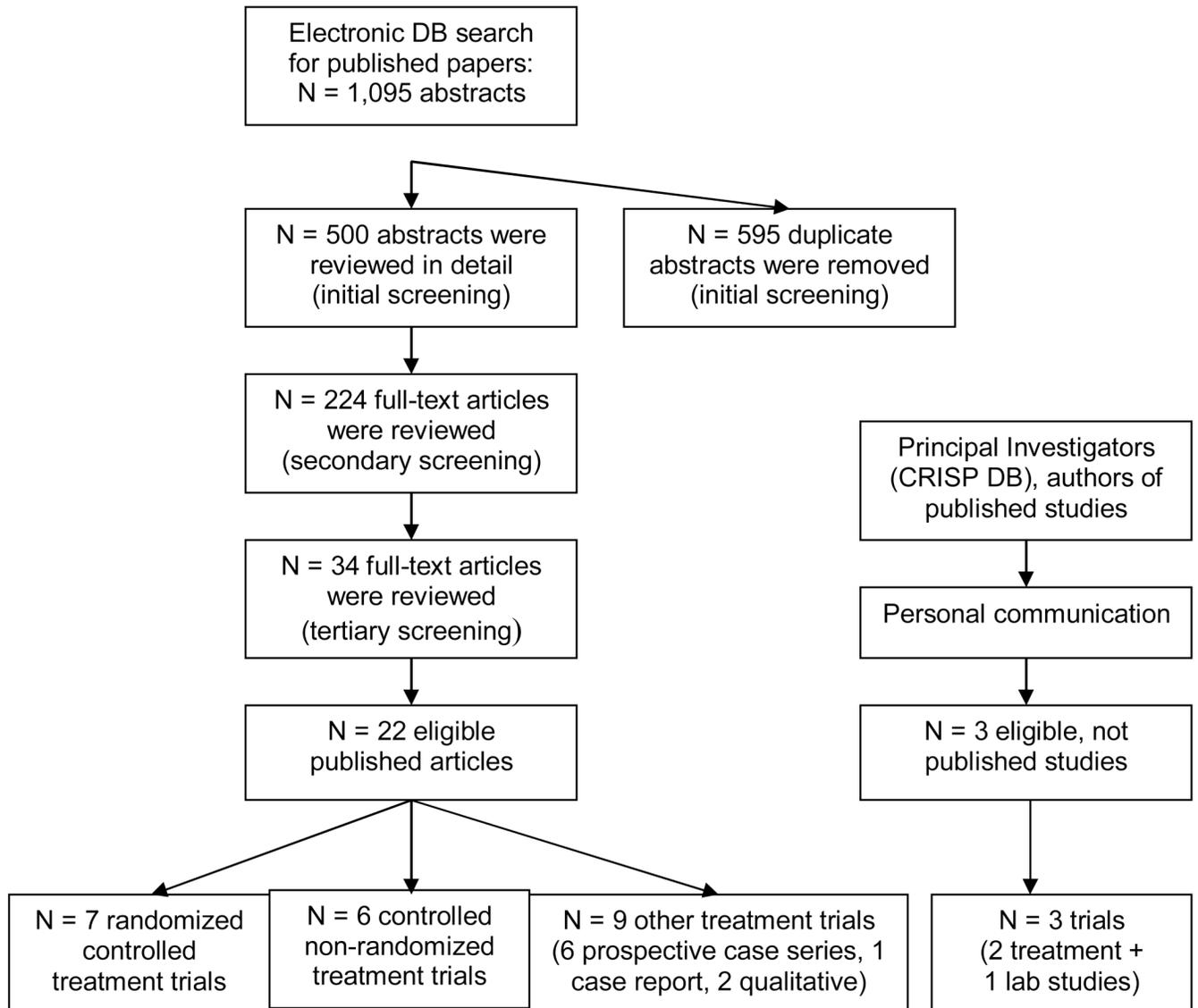


Figure 1.
Results of the literature search (DB – database).

Table 1

Electronic database search strategy.

Step	Search Strategy
1	Meditation [tw] or relaxation [tw] or mindfulness [tw] or “breathing technique” [tw] or “breathing exercises” [tw]
2	Smoking [tw] or tobacco [tw] or caffeine [tw] or “substance-related disorder” [tw] or “drug abuse” [tw] or addiction [tw] or “drug dependence” [tw] or “drug habituation” [tw] or “drug usage” [tw] or “substance abuse” [tw] or “substance dependence” [tw] or “substance use” [tw] or alcohol [tw] or alcoholism [tw] or “street drugs” [tw] or cocaine [tw] or marijuana [tw] or marihuana [tw] or opioid [tw] or heroin [tw] or morphine [tw] or stimulant [tw] or ecstasy [tw] or nicotine [tw]
3	1 and 2

Table 2

Scoring* of the prospective studies (range of points): Population Severity Rating (PSR); Clinical Benefit Score (CBS); Methodological Quality Score (MQS); and Cumulative Evidence Score (CES).

<p>PSR (range: 0 – 4)</p>	<p>0 = insufficient information; 1 = non-clinical sample, mild or no problems; 2 = non-clinical sample of nicotine dependent smokers; or drug users or problem drinkers who did not seek treatment and did not have severe problems or dependence; 3 = clinical sample of drug users or problem drinkers who sought treatment for substance use related problems, but who did not have dependence; 4 = severely impaired clinical population in treatment for drug or alcohol dependence.</p>
<p>CBS (range: -2 / +2)</p>	<p>+2 = <u>controlled trials</u>: MM was significantly better than ‘no Tx’ ($MM > 0$); or MM combined with other Tx was significantly better than that Tx alone ($MM+A > A$); <u>non-controlled trials</u>: significant improvement on primary outcome post- vs. pre-intervention.</p> <p>+1 = <u>controlled trials</u>: MM was significantly better than an alternative Tx (including SOC), or better than a briefer form of the same MM therapy, without control ($MM > A$); <u>non-controlled trials</u>: significant improvement post- vs. pre-intervention on secondary outcome only.</p> <p>-1 = <u>controlled trials</u>: MM outcomes were comparable to those of an alternative Tx ($MM = A$) or MM combined with other Tx ($MM = MM+A$), or briefer form of the same MM therapy, or mixed differences among active Tx arms, without control; <u>non-controlled trials</u>: no significant change in any outcomes post- vs. pre-intervention.</p> <p>-2 = <u>controlled trials</u>: MM was worse than a comparable other Tx of similar intensity without control ($MM < A$), or not better than a briefer dissimilar Tx without control, or MM combined with other Tx produced worse results than other Tx alone ($MM +A < A$), or MM is not better than no-Tx ($MM \leq 0$); <u>non-controlled trials</u>: no improvement, but presence of worsening in the outcomes post- vs. pre-intervention.</p>
<p>MQS (range: 0–17) non- controlled trials: maximum score = 12</p>	<ul style="list-style-type: none"> • Group allocation: 4 = randomization, 3 = within-S counterbalanced, 2 = case control / matching, 1 = quasi-experimental design, arbitrary assignment, sequential, cohorts; 0 = violated randomization or nonequivalent groups (or non-controlled trial); • Quality control: 1 = Tx standardized by manual, specific training, content coding, etc.; 0 = no standardization is specified; • Follow-up rate (at any follow-up point): 2 = 85–100%; 1 = 70–84.9%; 0 = fewer than 70%, or longest follow-up < 3 months; • Follow-up length: 2 = at least 12 months; 1 = 6–11 months; 0 = less than 6 months, or unspecified; • Contact: 1 = personal for $\geq 70\%$ of completed cases; 0 = non-personal or unspecified, or in < 70% of cases; • Collateral interviews: 1 = present in > 50% of cases; 0 = present in $\leq 50\%$ of cases, or unspecified; • Objective verification: 1 = present in > 50% of cases (records, biomarkers); 0 = absent in $\leq 50\%$ of cases, or unspecified; • Attrition: 2 = both Tx drop-outs AND cases lost to follow-up are enumerated, AND are considered in outcome; 1 = meets “considered” criteria for either drop-outs OR cases lost to follow-up, but not both; 0 = dropped and lost cases are not considered in outcome (e.g. all non-completers are excluded from outcome analyses). • Independent: 1 = assessors are independent and blind to group; 0 = follow-up non-blind, unspecified (or non-controlled trial); • Analyses: 1 = acceptable analyses of group differences (or pre-post analyses for non-controlled trials); 0 = no statistical analysis, inappropriate, or unspecified; • Multisite: 1 = parallel replications at ≥ 2 sites, separate research teams; 0 = single site or sites offering different Tx.
<p>CES</p>	<p>CES score = CBS x MQS (range for an individual study: -34 / +34)</p>

Negative (–) CES indicates studies showing a comparable or worse Tx outcome, positive (+) CES indicates studies showing a significant benefit of the MM therapy, compared to a comparison group in controlled trials, or baseline in uncontrolled trials.

MM: Mindfulness or Mindfulness Meditation based intervention; SOC: standard of care; Tx – treatment.

* Adapted with permission from William Miller (personal communication, 2008) (23).

Table 3

Summary of the Cumulative Evidence Scores of the published included studies, grouped by study design, type of Mindfulness or Mindfulness Meditation intervention (MM) and subject population, sorted within groups by the mean Methodological Quality Score of the studies.

Studies	Number of studies	Methodological Quality Score, MQS (mean / 17)	Population Severity Score, PSS (mean / 4)	Cumulative Evidence Score, CES (sum of scores of the individual studies)	% positive (% studies with +CES)
Total	15*	8.0	3.3	ITT: +10 (6 studies) PP: +143 (13 studies)	ITT: 50% PP: 85%
By design					
RCTs	7	11.3 (range: 8–14)	3.7	ITT: +2 (4 studies) PP: +93 (6 studies)	ITT: 50% PP: 83%
Controlled, non-randomized	4*	6.8 (range: 6–8)	3	ITT: –8 (1 study) PP: +16 (3 studies)	ITT: 0% PP: 67%
Case series	4	5.8 (range: 4–8)	3.25	ITT: +16 (1 study) PP: +34 (4 studies)	ITT: 100% PP: 100%
By MM intervention					
DBT	2 RCTs	13.5 (13,14)	4	ITT: +27 (2 studies) PP: +13 (1 study)	ITT: 100% PP: 100%
ACT	2 RCTs	12.5 (12,13)	3	ITT: –25 (2 studies) PP: +50 (2 studies)	ITT: 0% PP: 100%
3-S	3 (2 RCT, 1 controlled)	8.7 (range: 7–11)	4	ITT: – (0 studies) PP: +26 (3 studies)	ITT: – PP: 67%
MBSR-based	7* (1 RCT, 2 controlled, 4	6.4 (range: 4–8)	3.3	ITT: +8 (2 studies) PP: +42 (6 studies)	ITT: 50% PP: 83%

Studies	Number of studies	Methodological Quality Score, MQS (mean / I7)	Population Severity Score, PSS (mean / 4)	Cumulative Evidence Score, CES (sum of scores of the individual studies)	% positive (% studies with +CES)
	case series)				
Vipassana	1 controlled	6	2	ITT: - (0 studies) PP: +12 (1 study)	ITT: - PP: 100%
By subject population					
SUDs, adults, outpatient settings	7 (5 RCTs, 1 controlled, 1 case series)	10.3 (range: 7-14)	4	ITT: +15 (3 studies) PP: +69 (6 studies)	ITT: 67% PP: 83%
SUDs, adults, tobacco dependence	3* (1 RCT, 1 controlled, 1 case series)	9 (6,8,13)	2	ITT: +3 (2 studies) PP: +42 (2 studies)	ITT: 50% PP: 100%
SUDs, adults, residential settings	3 (1 RCT, 1 controlled, 1 case series)	6.7 (4,8,8)	4	ITT: -8 (1 study) PP: +12 (3 studies)	ITT: 0% PP: 67%
Substance use, adults, jail	1 controlled	6	2	ITT: - (0 studies) PP: +12 (1 study)	ITT: - PP: 100%
Substance use, adolescents	1 case series	4	3	ITT: - (0 studies) PP: +8 (1 study)	ITT: - PP: 100%

* one non-randomized controlled study did not use statistical analysis to compare results

Table 4

Published RCTs of mindfulness or mindfulness meditation based interventions (MM) used for the treatment of substance use, misuse or disorders. In the Outcomes section, values presented in [square brackets] were calculated by the authors for this systematic review.

Feature	Study 1. Alterman et al. 2004 (36)	Study 2. Avants et al. 2005 (37)	Study 3. Margolin et al. 2006 (42)	Study 4. Hayes et al. 2004 (39)	Study 5. Gifford et al. 2004 (38)	Study 6. Linehan et al. 1999 (41)	Study 7. Linehan et al. 2002 (40)	
Subjects	31 (17 F); mean age 36.5 yrs	29 (17 F); mean age 41.7 (28–51 yrs)	72 (47 F); mean age ~ 41 (21–56 yrs)	124 (63 F); mean age 42.2 (23–64 yrs); Axis II - 52%, anxiety and/or mood disorders ~ 42%	76 (45 F); mean age 43 (19–71 yrs)	28 F; mean age 30.4 (18–45 yrs); 50% depression, 38% PTSD	23 F; mean age 36.1 (18–45 yrs); anxiety and/or mood disorders 40–50%; past suicide or self-injury, attempt 65%	
Addictive disorder	PSR 4; SUDs, recovery house residents; alcohol + drugs 68%; prior Tx: 4.9 times for drug, 1.9 times for alcohol abuse.	PSR 4; opiate & cocaine dependent methadone maintenance out-patients; heroin use 17.1, cocaine use 16.5 yrs; majority with prior methadone Tx, and drug use in a prior month.	PSR 4; opiate dependent methadone maintenance out-patients; heroin use 17.7 yrs; cocaine use disorder 89%; prior methadone Tx 57%; majority used drugs in a prior month.	PSR 4; poly-SUDs; opiate dependent methadone maintenance out-patients, with other SUDs; 35% alcohol, 46% cocaine, 10% sedative dependent, who have continued drug use; prior residential or out-pt Tx: 6.3 times.	PSR 2; tobacco dependent community-recruited adults, with at least one past-year quit attempt; on average, smoked 21.4 cig/day, had 4 prior quit attempts (median success: 30 days) in the past 2 yrs.	PSR 4; BPD + SUDs; recruited from the clinic patients; 74% poly-SUDs, 58% cocaine, 52% alcohol; pre-study % days abstinent (alcohol, drugs): ~ 25–35%.	PSR 4; BPD + opiate dependence; recruited from variety of out-pt settings; 52% cocaine, 26% alcohol, 13% sedative dependent; prior methadone Tx: 83%.	PSR 4; BPD + SUDs; DBT for SUDs, 52 wks: therapist-led individual (40–90 min/wk) & group (150 min/wk) sessions + optional individual coaching (30 min/wk) + diary cards.
MM group & MM intervention	N=18; MBSR-based, 8 wks: therapist-led group sessions (120 min/wk) & one retreat (7 hrs) + 30–45min meditation group meetings (4 times / wk).	N=11; 3-S (individual), 8 wks: therapist-led individual sessions (60 min/wk).	N=38; 3-S (two groups), 8 wks: one educational session (60 min), AND N=20; therapist-led individual sessions (60 min/wk), OR N=18; therapist-led individual (60 min/wk) & group (60 min/wk) sessions.	N=42; ACT, 16 wks: therapist-led 32 individual (60 min) & 16 group (90 min) sessions.	N=33; ACT, 7 wks: therapist-led individual (50 min/wk) & 7 group (90 min/wk) sessions.	N=12; DBT for SUDs, 52 wks: therapist-led individual (60 min/wk) & group (120 min/wk) sessions + skills coaching calls + optional 39-wk methadone or methylphenidate Tx for opiate or stimulant dependence.	N=11; DBT for SUDs, 52 wks: therapist-led individual (40–90 min/wk) & group (150 min/wk) sessions + optional individual coaching (30 min/wk) + diary cards.	
Comparison group	N=13, SOC only.	N=18; 3-S (individual & group); 8 wks: therapist-led individual (60 min/wk) & group (60 min/wk) sessions.	N=34; 'waitlist' SOC only.	N=44; ITSF, 16 wks: 32 individual (60 min) therapist or AA sponsor-led, + 16 group (90 min) therapist-led sessions. N=38; SOC only.	N=43; NRT + medical Tx (physician-led): one 90 min group education session; then weekly clinic visits (physician visit as needed).	N=16; SOC only (subjects were referred to other clinics for SOC).	N=12; CVT + 12-Step, 52 wks: individual (40–90 min/wk) + NA group (120 min/wk) + optional 12-Step sponsor meetings.	
Ancillary treatment (all groups)	SOC	One 60 min individual HIV educational	SOC	SOC	None	None	ORLAAM (52 wks), physician-led medical Tx, weekly UTtox for opiates	

Feature	Study 1. Alterman et al. 2004 (36)	Study 2. Avants et al. 2005 (37) session + SOC	Study 3. Margolin et al. 2006 (42)	Study 4. Hayes et al. 2004 (39)	Study 5. Gifford et al. 2004 (38)	Study 6. Linehan et al. 1999 (41)	Study 7. Linehan et al. 2002 (40)
Follow-up	0, 8, 22 wks	0, 8 wks	0, 8 wks	0, 8, 16, 42 wks	0, 7, 26, 52 wks	0, 16, 32, 52, 68 wks	0, 16, 32, 52, 68 wks
Retention (at the end of follow-up):	<ul style="list-style-type: none"> MM (MBSR-based) 83%; SOC 77% 	<ul style="list-style-type: none"> MM (3-S Individual) 64%; MM (3-S Individual+Group) 89% 	<ul style="list-style-type: none"> MM (3-S) 82%; SOC 88% 	<ul style="list-style-type: none"> MM (ACT) 43%; ITSF 57%; SOC 68% (differential retention: p<0.07) 	<ul style="list-style-type: none"> MM (ACT) 61%; NRT 81% (differential retention: p=0.07) 	<ul style="list-style-type: none"> MM (DBT) 58%; SOC 50% 	<ul style="list-style-type: none"> MM (DBT) 82%; CVT+12-Step 83%
Outcome measures	Drug use (self-report, UTTox); psychological health, problem level (ASI composite scores); meditation practice	Drug use (self-report, UTTox); HIV risk behavior, spirituality, religious practices (surveys, reaction time task); Tx experiences.	Drug use (HIV risk behavior survey, with "yes/no" question on injection drug use or unprotected sex; UTTox), HIV prevention; motivation; spirituality, religious practices (surveys, reaction time task); Tx experiences.	Drug use (self-report, UTTox); psychopathology; Tx satisfaction.	Tobacco use (self-report, exhaled CO); dependence, withdrawal symptoms, coping styles, psychological health; Working Alliance Inventory; Tx satisfaction.	Drug use (self-report, UTTox); prior Tx, parasuicide history, the global adjustment and the global social adjustment, Brief Symptom Inventory.	Drug use (self-report, UTTox); parasuicide history, the global adjustment and the global social adjustment, Brief Symptom Inventory.
Substance use related outcomes (per ITT & PP analyses, at the end of follow-up, unless stated otherwise)	ITT: N/A; PP: • no differences between the groups (ES < 0.1); • compared to baseline, both groups decreased substance use.	ITT: N/A; PP: • no differences between the groups; • compared to baseline, the groups (combined) decreased heroin and cocaine use (p<0.05 [ES 0.5]) and HIV risk behavior (p=0.08 [ES 0.4]); • all but one subject reported positive 3-S effects on drug use, craving, motivation for abstinence and HIV prevention.	ITT: N/A; PP: • compared to SOC controls, fewer 3-S subjects injected drugs and/or had unsafe sex (53% vs. 23%, p<0.05 [ARR 30%, NNT 3.3]); • receipt of 3-S therapy was an independent protective factor against engaging in these behaviors (OR 8.9, p<0.05); • 3-S attendance was correlated to HIV risk behaviors (r= -0.33, p<0.05; [ES 0.7]).	ITT: • no significant differences between the ACT, ITSF and SOC groups (no details provided); PP: • the ACT and ITSF groups, compared to SOC, had more "clean" UTTox for opiates (61%, 50%, 28%, p<0.05 [ACT vs. SOC: ARR 33%, NNT 3.0; ACT vs. ITSF: ARR 11%, NNT 9.1]) and all drugs (50%, 38%, 12%, p<0.05 [ACT vs. SOC: ARR 38%, NNT 2.6; ACT vs. ITSF: ARR 12%, NNT 8.3]); • the ACT group tended to more accurately report drug use than the ITSF group (p<0.1).	ITT: • no significant difference in quit rate between the ACT and NRT groups (21% vs. 9%, p>0.05 [ARR 12%, NNT 6.3]); PP: • ACT had a better quit rate than the NRT group (35% vs. 15%, p<0.05 [ARR 20%, NNT 5]); • quit status was predicted by change in acceptance skills in the ACT group, and change in acceptance skills mediated effects of ACT on smoking status (p<0.05).	ITT: • DBT group had a higher proportion of drug/alcohol abstinent days compared to SOC (0.94 vs. 0.58, p<0.05, ES 0.59); PP: • The above difference was significant (ES 1.0).	ITT: • at 52 wks, DBT group reduced opiate use compared to CVT group (p<0.05), however, this difference disappeared at 68 wks (positive UTTox for opiates: 27% vs. 33%, p>0.05 [ARR 5%; NNT 22]); • during the 52-wk long Tx, the DBT group was more accurate in substance use reporting than CVT group (p<0.05). PP: N/A.
Other outcomes	ITT: N/A; PP: • the	ITT: N/A; PP: • compared to	ITT: • no differences between the groups in	ITT: N/A; PP: • the ACT subjects	ITT: N/A; PP: • the ACT subjects	(unclear whether ITT or PP was	ITT: • no differences between

Feature	Study 1. Alterman et al. 2004 (36)	Study 2. Avants et al. 2005 (37)	Study 3. Margolin et al. 2006 (42)	Study 4. Hayes et al. 2004 (39)	Study 5. Gifford et al. 2004 (38)	Study 6. Linehan et al. 1999 (41)	Study 7. Linehan et al. 2002 (40)
(per ITT & PP analyses, at the end of follow-up, unless stated otherwise)	Addiction Severity Index medical composite score improved in the MM, but not SOC group ($p<0.05$, ES 0.195); • 47% MM subjects continued meditating (4 hrs during the prior month).	baseline, 3-S subjects increased spiritual practices, and showed a cognitive shift from 'addict' to 'spiritual' self ($p<0.05$); • spirituality correlated to drug abstinence ($r=0.6$, $p<0.05$ [ES 0.4]) and to decrease in HIV risk behavior ($r=0.67$, $p<0.05$ [ES 0.45]).	SOC, 3-S group increased spiritual practices and motivation for HIV prevention, and showed a cognitive shift from 'addict' to 'spiritual qualities' ($p<0.05$); • all 3-S subjects reported meditating (mean 25.7 min/day) and planned continuing it.	psychological health scores or Tx satisfaction ratings; • compared to baseline, the groups improved on majority of psychological outcomes ($p<0.05$). PP: Results as above.	endorsed better relationship with their providers than the NRT subjects ($p<0.05$); • Tx satisfaction ratings were comparable between the groups.	used): • compared to SOC, the DBT group received more psychotherapy ($p<0.05$), and improved the global adjustment and global social adjustment scores ($p<0.05$).	the groups in psychopathology or jail time; • compared to baseline, both groups improved the Brief Symptom Inventory scores and global adjustment ratings.
Adverse effects	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
MQS / 17	8	8	11	12	13	13	14
CBS (ITT & PP analyses)	ITT: N/A PP: +2	ITT: N/A PP: -1	ITT: N/A PP: +2	ITT: -1 PP: +2	ITT: -1 PP: +2	ITT: +1 PP: +1	ITT: +1 PP: N/A
Comments	All subjects lived in the same recovery house.	The sample was randomized to individual or individual + group therapy, however, detailed results are reported as for pre-post one group.	After the initial randomization, the MM group was sub-randomized to individual (N=20) or individual + group therapy (N=18); in the final analysis, these subgroups were combined into one MM group.	3-arm RCT, with two 'active' interventions (MM and ITSF) that were "matched" by subject involvement and therapy format (but not therapist contact time).	None	Low Tx completion rate, especially in the SOC group (DBT 55%, SOC 19% per ITT).	Two interventions were "matched" by subject involvement and therapy format (but not therapist contact time). One subject was randomized incorrectly, removed before the study onset and not analyzed (resulting in N=23). All dropouts took place in the DBT group led by the only male therapist.

Values (presented in [square brackets]) calculated for the systematic review: ARR: Absolute Risk Reduction; CBS: Clinical Benefit Score; CES: Cumulative Evidence Score; ES: Effect Size (Cohen's d); MQS: Methodological Quality Score; NNT: Number Needed to Treat; PSS: Population Severity Score.

ACT: Acceptance Commitment Therapy; BPD: borderline personality disorder; CO: carbon monoxide; CVT: Comprehensive Validation Therapy; DBT: Dialectical Behavior Therapy; MM: mindfulness meditation; HIV: Human Immunodeficiency Virus; ITSF: Intensive Twelve Step Facilitation; ITT: intention to treat analysis; MBSR: Mindfulness-Based Stress Reduction; min: minutes; mos: months; NRT: Nicotine Replacement Therapy; ORLAAM: oral solution levomephthal acetate, opiate agonist; PP: per protocol analysis; PTSD: post-traumatic stress disorder; 3-S: Spiritual Self Schema; SOC: "standard of care" therapy; SUDs: Substance Use Disorders; TSF: Twelve Step Facilitation; Tx: treatment; UTox: urine toxicology test; wks: weeks; yrs: years.

Table 5

Published controlled non-randomized trials, case series, case report and qualitative studies of mindfulness or mindfulness meditation based interventions (MM) used for the treatment of substance use, misuse or disorders: methods and results. Results from the final follow-up are reported, unless stated otherwise.

Study	Indication	Subjects	Intervention	Outcome measures	Results	Methodological quality/ comments
Controlled non-randomized trials						
Study 1. Margolin et al. 2007 (47)	Substance use (as a part of HIV risk behavior) in HIV-positive, opiate dependent, methadone maintenance out-patients.	38 (19 F); mean age 45.3 (33–57 yrs); PSR 4; 55% cocaine use disorder; 45% have continued using drugs; 71% were prescribed an HIV Tx.	Per subject choice: • MM (N=21), SOC + 3-S, 12 wks, therapist-led individual (60 min/wk) & group (60 min/wk) sessions; • CG (N=17): SOC only.	• Collected at 0, 12 wks; • substance use (self-report, UTOx); • drug- and sex-related HIV risk behaviors; • impulsivity, spirituality, religiosity; • Tx experiences.	• Retention: MM 67%, CG 65%; PP: • compared to CG, MM showed trend to decreased alcohol and drug use ($p=0.08$ [ES 0.25]), and improved impulsivity, spirituality and motivation for abstinence ($p<0.05$); • 3-S attendance correlated to decreased substance use ($t=0.49$ [ES 0.2], impulsivity, and increased influence of spirituality on abstinence and HIV prevention motivation ($p<0.05$).	MQS: 7/17; CBS: N/A per ITT (+2 PP) Subject meditation practice was not reported; adverse effects and side effects were not mentioned.
Study 2a. Bowen et al. 2006 (44)	Substance use among prisoners of the minimum-security jail.	305 (63 F), mean age 37.5 (19–58 yrs); PSR 2; alcohol use 83%, tobacco use 83%, drug use 73% during 90 days prior to incarceration.	Per subject choice: • MM (N=63): SOC + vipassana meditation (VM), 10 consecutive days: silent, gender-specific course, 8–10 hrs/day, led by a trained instructor; • CG (N=242): SOC only.	• Collected at 0, 1 wk post-intervention, 3 & 6 mos post-release; • substance use (self-report), related adverse consequences; • psychological health.	• Retention at 3 & 6 mos: MM 46% & 43%; CG 24% & 21%. PP: • at 3 mos, compared to CG, MM reduced ($p<0.05$) alcohol [ES 0.6], cocaine [ES 0.35] and marijuana [ES 0.5] use, and alcohol-related consequences [ES 0.35], and improved psychiatric symptoms, drinking-related locus of control and optimism; the changes were related to the VM participation; • at 6 mos, recidivism rates (the only results reported for 6 mos) were low, and comparable between the groups.	MQS: 6/17; CBS: N/A per ITT (+2 PP) Subject post-intervention meditation practice was not recorded; adverse effects and side effects were not mentioned.
Study 2b. Bowen et al. 2007 (45) (secondary analysis of Study 2a).	Relationship between substance use & thought suppression; prisoners.	See Bowen et al. 2006 (44) N=81 (for the main analysis of 0–3 month outcomes)	See Bowen et al. 2006 (44)	See Bowen et al. 2006 (44)	PP: • at 3 mos, compared to CG, MM decreased thought avoidance ($p<0.05$); this change partially mediated the relationship between the VM participation, and alcohol use and related consequences.	See Bowen et al. 2006 (44)
Study 2c.	Relationship	See Bowen et al.	See Bowen et al.	See Bowen et al. 2006	PP: • no differences in the PTSD	See Bowen et al. 2006 (44)

Study	Indication	Subjects	Intervention	Outcome measures	Results	Methodological quality/ comments
Simpson et al. 2007 (48) (secondary analysis of Study 2a).	between substance use & PTSD severity; prisoners	2006 (44) ~ 22% of the subjects scored positively for PTSD; N=88; 29 MM and 59 CG; (for the main analysis of 0–3 month outcomes)	2006 (44)	(44)	symptom severity between the MM and CG groups; VM participation and baseline substance use, but not PTSD severity, predicted alcohol and drug use at 3 mos; baseline PTSD severity predicted adverse drinking consequences and psychological distress at 3 mos; PTSD subjects tolerated the VM course well;	MQS: 6/17; CBS: N/A* *No statistical assessment of the significance of in-between group differences or pre-post changes was provided; only descriptive statistics were used. Exhaled CO-related results were not reported.
Study 3. Altner 2002 (43)	Smoking cessation among tobacco dependent hospital employees	114 (71 F), mean age ~ 38.5 (20–65 yrs); PSR 2	Per subject choice: • MM (N=49); NRT + MBSR, 8 wks; therapist-led (2.5 hr/wk) group sessions; • CG (N=65); NRT only	• Collected at 0, 1.5, 3, 6, 15 mos (quit date likely at '0'); • % subjects who stopped, reduced or did not reduce smoking (self-report, exhaled CO); • Tx experiences among meditators (N=23, qualitative) at 3 mos.	• Retention: MM 100%; CG 97%. Descriptive statistics: • MM vs. CG subjects reported quit rate of 32.6% vs. 24.6% [ARR 8%, NNT 12.5], reduced smoking by 42.3% vs. 26.2%, continued smoking by 22.4% vs. 46.2%; • qualitative data: meditators reported positive opinions on the MBSR therapy and its usefulness as a coping strategy.	
Study 4. Marcus et al. 2001 (46)	Psychological health in alcohol or drug dependent patients of therapeutic community	36 (2 F), mean age ~ 34 years; PSR 4	Per subject choice: • MM (N=18); SOC + MBSR, 8 wks, therapist-led (2.5 hrs/wk) group sessions; • CG (N=18); SOC only	• Collected at 0, 8 wks; • psychopathology (SCL-90R), coping styles	• Retention: MM & CG 100%; ITT=PP: • compared to CG, MM group tended to report a more self-controlling coping style (p=0.05, eta squared effect size: 0.11); no other differences between the groups were found (p>0.05); • effect sizes (eta squared 0.05–0.06) tended to favor the MM group in seeking social support, on hostility and paranoid ideation scores (per authors, eta squared effect size: 0.01–small, 0.06–medium, 0.14–large).	MQS: 8/17; CBS: -1 per ITT (-1 PP) CES: -8 per ITT (-8 PP) Group were derived from separate residential facilities.
Case series						
Study 5. Zgierska et al. 2008 (53)	Relapse prevention in alcohol dependent adults, graduates of the Intensive Outpatient Program	19 (10 F), mean age 38.4 (21–50 yrs); PSR 4; in alcohol-related Tx the past: 63%	Mindfulness Based Relapse Prevention, 8 wks, therapist-led (120 min/wk) group sessions; MM component was based on the MBSR & MBCT programs,	• Collected at 0, 4, 8, 12, 16 wks; • alcohol use (self-report); • severity of alcohol relapse triggers: stress, anxiety, depression, craving; • salivary cortisol,	• Retention: 78.9% PP: • During the study, HDD decreased (p=0.056, ES 0.3), total number of drinks (ES 0.3) and PDA (ES 0.03) did not significantly change; • stress, depression, anxiety	MQS: 7/17; CBS: N/A per ITT (+1 PP) The only study that directly reports (lack of) side effects and adverse events, and describes evaluating distributional characteristics of the data, with the use of parametric or non-parametric

Study	Indication	Subjects	Intervention	Outcome measures	Results	Methodological quality/ comments
Study 6. Davis et al. 2007 (50)	Smoking cessation, community setting	18 (10 F), mean age 45.2 (22–67 yrs); PSR 2; on average, subjects smoked 19.9 cigarettes/day for 26.4 yrs.	MBSR-based, with minor modifications, 8 wks, therapist-led group sessions (six 150 min/wk sessions + one 7 hr retreat); quit date at wk 7 (after the retreat).	<ul style="list-style-type: none"> • serum IL-6, liver enzymes at 0, 16 wks; • meditation-related outcomes; Tx services utilization; Tx experiences. 	<ul style="list-style-type: none"> • Retention: 72% (however, 100% data collection rate for self-reported smoking). ITT=PP: • 10/18 (56%) quit smoking; PP: • compared to non-quitters, those who quit meditated more ($p<0.05$), with a possible dose-effect: 100% highly compliant, 40% moderately compliant, and 0% non-compliant mediators quit; • compared to moderately compliant, highly compliant mediators decreased severity of stress one day post-quit ($p<0.05$); baseline interest in meditation and affective distress were related to abstinence ($p<0.05$). 	MQS: 8/17 CBS: +2 per ITT (+2 PP) Due to 100% data collection rate for the primary outcome, the primary analysis includes all subjects.
Study 7a. Boozin & Stevens 2005 (49)	Sleep and sleepiness problems as relapse triggers among adolescents with SUDs	55 (21 F), age 13–19 yrs; PSR 3; sleep or daytime sleepiness problems, graduates or graduating from outpatient addiction Tx programs.	MBSR-based, therapist-delivered in a small group format over 5 sessions, during 7 wks: 1st session – other interventions, not MBSR; 2nd–6th sessions: 45 min MBSR + 45 min other Tx (stimulus control, bright light therapy, sleep hygiene, CT).	<ul style="list-style-type: none"> • Collected at 0–8 wks weekly, then 6 wks post-quit (12 wks post-entry); • smoking (self-report, exhaled CO); • stress, psychopathology symptom severity. 	<ul style="list-style-type: none"> • Retention: 93%; PP: • drug use, low at baseline, increased during the Tx - no details provided; • substance problem index plateaued for Tx completers (42% of the subjects), while it kept rising for those who did not complete Tx ($p<0.2$, no details provided); • sleep improved ($p<0.05$) among Tx completers only; sleepiness, worry and mental health distress decreased during the study ($p<0.05$). 	MOS: 4/17; CBS: N/A per ITT (+2 PP) Study focused on methods description; only preliminary results were reported, without details on substance use outcomes. The study intervention included MM (MBSR-based; slightly less than 50%), but MM was not its primary focus.

Study	Indication	Subjects	Intervention	Outcome measures	Results	Methodological quality/ comments
Study 7b. Haynes et al. 2006 (57) (secondary analysis of Study 3a)	Is sleep improvement related to improved aggressive behavior among adolescents with SUDs	23 (13 F), mean age 16.4 (13–19 years); see Bootzin & Stevens 2005 (49) for other details	See Bootzin & Stevens 2005 (49)	<ul style="list-style-type: none"> See Bootzin & Stevens 2005 (49); two questions on presence or absence of aggressive thoughts or actions. 	<ul style="list-style-type: none"> Retention: 91%; PP: • Those reporting aggression at baseline, compared to others, had lower self-efficacy in resisting substance use urges ($p < 0.05$); • post-Tx, those reporting aggression, compared to others, reported more frequent substance use, especially alcohol use ($p < 0.05$); • all subjects improved some aspects of their sleep; poor sleep was related to aggression, after controlling for substance use. 	See Bootzin & Stevens 2005 (49); Substance use was used as a covariate in the analysis, but was not the focus. No details on substance use are reported.
Study 7c. Stevens et al. 2007 (52) (secondary analysis of Study 3a)	Is sleep improvement related to improved trauma symptoms severity among adolescents with SUDs	20 (10 F), mean age 16.3 (13–19 years); see Bootzin & Stevens 2005 (49) for other details.	See Bootzin & Stevens 2005 (49)	<ul style="list-style-type: none"> See Bootzin & Stevens 2005 (49); Trauma Severity Index. 	<ul style="list-style-type: none"> Retention: unclear; PP: • Those with elevated trauma score at baseline, compared to others, had higher Substance Problem Index ($p < 0.05$). Substance use did not play a significant role in the analyses. • Those with better sleep characteristics had greater improvements in trauma scores than others. 	See Bootzin & Stevens 2005 (49); Substance use was used as a covariate in the analysis, but was not the focus. No details on substance use are reported.
Study 8. Marcus et al. 2003 (51)	Stress severity among substance dependent patients in residential Tx settings	21 (3 F), mean age 33.4 (21–51 yrs); PSR 4; therapeutic community patients with SUDs.	SOC + MBSR, 8 wks. therapist-led (150 min/wk) group sessions.	<ul style="list-style-type: none"> Collected at 0, 8 wks; salivary cortisol upon awakening; Perceived Stress Scale. 	<ul style="list-style-type: none"> Retention: 85.7% (data collection rate: 57% cortisol, 76% surveys); PP: • cortisol level decreased ($p < 0.05$, ES 0.65); • perceived stress severity did not change ($p > 0.05$, ES 0.44). 	MQS: 4/17; CBS: N/A per ITT (+1 PP) The study did not report substance use data.
Other studies						
Study 8 – case report. Twohig et al. 2007 (54)	Marijuana dependence, community settings	3 (1 F), ages 19, 20, 43; PSR 2; marijuana dependent (5 were enrolled, 2 dropped out)	ACT, 8 wks. therapist-led (90 min/wk) individual therapy sessions.	<ul style="list-style-type: none"> Collected at 0–8 wks (daily), and 13 wks; marijuana use (self-report, salivary swab); withdrawal severity, psychological outcomes; 	<ul style="list-style-type: none"> Retention: 3/5 (60%); although the 3 subjects did not use marijuana at 8 wks, they resumed its use by 13 wks (one to the pre-Tx level, and two at less than pre-Tx levels); • withdrawal, anxiety and depression severity seemed to improve compared to baseline. 	Methodological quality not scored. Manualized intervention.

Study	Indication	Subjects	Intervention	Outcome measures	Results	Methodological quality/ comments
Study 9- qualitative study. Carroll et al. 2008 (56)	MBSR-related treatment experiences among substance dependent patients in residential Tx settings	36 (6F), mean age 32.6 (19-54 yrs); PSR 4; residents of therapeutic community with SUDs.	MBSR, adapted to therapeutic community settings, 6 wks. therapist-led (180 min/wk) group sessions.	<ul style="list-style-type: none"> 356 stories were reviewed (written as a part of guided expressive writing); 38 stories of stress that referenced the MBSR therapy were identified and analyzed. 	Analysis of 38 stories identified 3 main MBSR qualities: <ul style="list-style-type: none"> utility (usefulness for calming self, stress-reduction, coping), portability (ability to apply learned skills in real-life), and sustainability (application of skills to a variety of different situations, goals). 	This report was based on the ongoing unpublished trial.(72) Manualized intervention - the intervention description (MBSR for therapeutic community, MBSR-TC) was published elsewhere.(87)
Study 10- qualitative study. Betel et al. 2007 (55) (based on Margolin et al. 2006 (42) and 2007 (47) studies)	3-S treatment experience in methadone maintenance patients, a part of the studies by Margolin et al. 2006 (42) and 2007.(47)	39 (34 F), mean age 43 (28-54 yrs); PSR 4; opiate dependent patients of methadone maintenance program, cocaine use disorder 77%, HIV-positive 38%.	3-S therapy: individual (46%) or individual + group (54%) - see Margolin et al. 2006 (42) and 2007 (47) for details.	<ul style="list-style-type: none"> Collected at post-Tx (8-12 wks post-entry); Tx experiences questionnaire and interview. 	<ul style="list-style-type: none"> Preferred Tx format: 43% group, 14% individual, and 43% equally liked individual and group sessions; all subjects meditated, on average 26 min/day; 3-S was viewed as helpful for recovery, and different from the received SOC; meditation was the most liked and helpful aspect of the 3-S therapy; 49% reported a positive change resulting from 3-S therapy; subjects were satisfied with 3-S, and 97% would like to continue it; no significant adverse events were reported. 	See Margolin et al. 2006 (42) and 2007 (47) for details. Subjects did not describe any significant negative effects (side effects or adverse events) or problems associated with 3-S therapy.

Values (presented in [square brackets]) calculated for the systematic review: ARR: Absolute Risk Reduction; CBS: Clinical Benefit Score; CES: Cumulative Evidence Score; ES: Effect Size (Cohen's d); MQS: Methodological Quality Score; NNT: Number Needed to Treat; PSS: Population Severity Score.

CG: comparison group; CO: carbon monoxide; MM: mindfulness meditation; HIV: Human Immunodeficiency Virus; ITT: intention to treat analysis; MBCT: Mindfulness-Based Cognitive Therapy; MBSR: Mindfulness-Based Stress Reduction; min: minutes; mos: months; NRT: Nicotine Replacement Therapy; PP: per protocol analysis; PTSD: post-traumatic stress disorder; 3-S: Spiritual Self Schemat. SOC: "standard of care" therapy; SUDs: Substance Use Disorders; Tx: treatment; UTox: urine toxicology test; VM: vipassana meditation; wks: weeks; yrs: years.

Table 6

Unpublished treatment trials and a laboratory-based study of mindfulness or meditation based interventions (MM) used for the treatment of substance use, misuse or disorders: methods and results. Results from the final follow-up are reported, unless stated otherwise.

Study	Design & Indication	Subjects	Intervention	Outcome measures	Results	MQS
Study 1. Gifford et al., 2008, submitted (59)	2-arm RCT: smoking cessation, community settings	303 (10 F), mean age 46.0 (18–75 yrs); PSR 2; tobacco dependent, community-recruited adults; on average, 24 cigarettes/day, 2.2 prior quit attempts in the past 2 yrs, with a median abstinence of 21 days.	<ul style="list-style-type: none"> MM intervention, <u>10</u> wks: ACT + Functional Analytic Psychotherapy (therapist-led, weekly 120 min group and 50 min individual sessions) + bupropion. Control group: bupropion only (medical management, one 60 min educational meeting, handouts) 	<ul style="list-style-type: none"> Collected at 0, 10, 26, 52 wks; smoking (7-day point prevalence; self-report, exhaled CO); withdrawal severity, psychological health; Working Alliance, Tx satisfaction. 	<ul style="list-style-type: none"> Retention: 45.2%; PP: • quit rate was higher at the MM than control group (31.6% vs. 17.5%, $p < 0.05$, ES 0.3 [ARR 14.1, NNT 7]); during 52 wks, MM was more effective in reducing smoking than control Tx (OR 2.2, $p < 0.05$); • acceptance-based responding and the therapeutic relationship mediated effects of MinM on Tx outcomes; • MM group reported higher Tx satisfaction than controls at all time points ($p < 0.05$, ES 0.7 at 52 wks). 	MQS: 10/17 CBS: N/A per ITT (+2 PP) Manualized MM intervention.
Study 2. Brown et al., 2008*, submitted (58)	Case series: smoking cessation, community settings	16 (12 F), mean age 41.9 (18–65 yrs); PSR 2; tobacco dependent, community-recruited adults; on average, 20.4 cigarettes/day, smoked for 26.3 yrs, unable to abstain for longer than 3 days in the past 10 yrs.	<ul style="list-style-type: none"> MM intervention, <u>10</u> wks, therapist-led: ACT + Cognitive Behavioral Therapy (wks 4–10) + NRT (wks 6–14). 	<ul style="list-style-type: none"> Collected at 0, 10, 14, 19, 32 wks (quit date: week 6); smoking (self-reported, exhaled CO); withdrawal and depressive symptom severity. 	<ul style="list-style-type: none"> Retention: 75%; quit rates at 10, 14, 19, 32 wks: 31%, 25%, 19%, and 0%. during the study, the longest continuous abstinence was median 24 days (mean 41.6), number of days abstinent was median 40.5 (mean 58.8, out of 180 study days), time to relapse (7 consecutive smoking days) was median 45.5 days (mean 49.9), and number of quit-smoking attempts was median 2.5 times (mean 4.1). 82% reported that the learned skills were “very” or “extremely useful” in helping quit smoking. 	MQS: 5/17 CBS: N/A* *No statistical assessment of the significance of pre-post change was provided; only descriptive statistics were used. Follow-up psychological outcomes were not reported. Manualized intervention.
Study 3. Bowen 2008, PhD dissertation (60)	2-arm RCT, laboratory study: smoking, and related craving and negative affect; community settings	123 (34 F), mean age 20.3 (18–46 yrs); PSR 2; undergraduate psychology students; on average, low dependence scores, smoked 5.3 cigarettes/day in the past week, had 8.4 quit attempts	Subjects did not smoke for 12 hrs prior, then underwent 4 brief cue (cigarette) exposures in a 90-min long laboratory session, during which they were asked to cope with arising thoughts, sensations and emotions using: • MM intervention (n=61); guided, audio-	<ul style="list-style-type: none"> Collected post-exposure (4 in-person assessments), at 1 and 7 days; smoking (self-reported); smoking urges, affect; brief written description of used coping strategies. 	<ul style="list-style-type: none"> Retention: 90.2%; PP: • during the follow-up week, MM group smoked fewer cigarettes/day than controls ($p < 0.05$, ES 0.6) – compared to baseline, MM decreased smoking by 26%, while controls increased it by 11%; • no significant differences between groups were found in latency to the first cigarette, negative affect 	MQS: 9/17 CBS: N/A per ITT (+2 PP) Manualized intervention.

Study	Design & Indication	Subjects	Intervention	Outcome measures	Results	MQS
		of minimum 24 hrs in the past year.	recorded, mindfulness-based coping strategies; <ul style="list-style-type: none"> • Controls (n=62): their "usual" coping strategies. 		and smoking urges; • during cue exposures, to cope with cravings and urges, MM group used MM strategies, while controls used primarily distraction-based techniques.	

* After completion of this manuscript, a report from this study has been published.(61)

Values (presented in [square brackets]) calculated for the systematic review: ARR: Absolute Risk Reduction; CBS: Clinical Benefit Score; CES: Cumulative Evidence Score; ES: Effect Size (Cohen's d); MQS: Methodological Quality Score; NNT: Number Needed to Treat; PSS: Population Severity Score.

ACT: Acceptance Commitment Therapy; CO: carbon monoxide; MM: mindfulness meditation; ITT: intention to treat analysis; min: minutes; mos: months; NRT: Nicotine Replacement Therapy; PP: per protocol analysis; Tx: treatment; UTox: urine toxicology test; wks: weeks; yrs: years.