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Mind-Body Treatments for the Pain-Fatigue-Sleep Disturbance Symptom Cluster in Persons with Cancer

Kristine L. Kwekkeboom, PhD, RN, **Catherine H. Cherwin, MS, RN**, **Jun W. Lee, MS, RN**, and **Britt Wanta, MS, RN**
University of Wisconsin-Madison, School of Nursing

Abstract

Purpose—To synthesize evidence regarding mind-body interventions that have shown efficacy in treating two or more symptoms in the pain-fatigue-sleep disturbance cancer symptom cluster.

Design—A literature search was conducted using CINAHL, Medline, and PsychInfo databases through March 2009.

Methods—Studies were categorized based on the type of mind-body intervention (relaxation, imagery / hypnosis, cognitive-behavioral therapy / coping skills training [CBT/CST], meditation, music, and virtual reality), and a preliminary review was conducted with respect to efficacy for pain, fatigue, and sleep disturbance. Mind-body interventions were selected for review if there was evidence of efficacy for at least two of the three symptoms. Forty-three studies, addressing five types of mind-body interventions met criteria and are summarized in this review.

Findings—Imagery / hypnosis and CBT / CST interventions have produced improvement in all three cancer-related symptoms individually: pain, fatigue, and sleep disturbance. Relaxation has resulted in improvements in pain and sleep disturbance. Meditation interventions have demonstrated beneficial effects on fatigue and sleep disturbance. Music interventions have demonstrated efficacy for pain and fatigue. No trials were found that tested the mind-body interventions specifically for the pain-fatigue-sleep disturbance symptom cluster.

Conclusions—Efficacy studies are needed to test the impact of relaxation, imagery / hypnosis, CBT / CST, meditation and music interventions in persons with cancer experiencing concurrent pain, fatigue, and sleep disturbance. These mind-body interventions could help patients manage all symptoms in the cluster with a single treatment strategy.

Keywords

Pain; Fatigue; Sleep Disturbance; Cancer; Mind-body and Relaxation Techniques

Persons with cancer experience a range of symptoms related to both the disease and its treatment. Recent evidence has demonstrated that certain symptoms tend to co-occur or “cluster” together, exacerbating the overall symptom experience (1–2). In some cases, there may be shared mechanisms causing each of the symptoms to occur (e.g., cytokine induced nausea and vomiting). In other cases, having one symptom may cause or exacerbate another (e.g., uncontrolled pain may interrupt one’s sleep). Finally, treatment strategies used for a particular symptom may produce side effects that manifest as new symptoms (e.g., using opioids to control pain may leave one feeling fatigued). Most studies have focused on identifying treatments for individual symptoms, but given new awareness of symptom

Address Correspondence to: Kristine Kwekkeboom, PhD, RN, University of Wisconsin-Madison School of Nursing, K6/336 Clinical Science Center, 600 Highland Ave., Madison, WI 53792, kwekkeboom@wisc.edu.

clusters, it now appears that this piecemeal approach may be flawed. Treatment approaches may have greater effects if they target a cluster of symptoms rather than one single symptom. This paper will review evidence for mind-body interventions to identify those that may be efficacious in treating the symptom cluster of co-occurring pain, fatigue and sleep disturbance in cancer.

Background

The focus of cancer symptom management research has recently shifted as investigators acknowledge that symptoms typically do not occur in isolation. Symptom clusters are defined as combinations of two or more co-occurring symptoms that are related to each other and that are independent of other symptoms or symptom clusters (3–4). Symptoms within the cluster may share the same etiology, but are not required to do so. Some of the symptoms may be related to the cancer itself, while others are brought about by cancer treatment strategies. When occurring together, the symptoms may have a greater impact on physical function, emotional distress and overall quality of life than was previously attributed to symptoms occurring in isolation.

Barsevick (5) used the term “crossover” in suggesting that treatments shown to benefit a single symptom may have a broad spectrum of effect and could also impact other symptoms in the cluster. Williams (6) hypothesized that a single intervention may impact the entire symptom cluster, noting that: 1) the symptoms may share a common etiology, 2) diminishing one symptom may prevent exacerbations in others, and 3) single interventions may be indicated for more than one symptom. She also noted possible benefits of using a single intervention in that it simplifies treatment, reduces the risk for side effects, and may reduce costs. In this paper, the term “crossover” is used to describe treatments that have demonstrated efficacy for more than one of the cluster component symptoms and may therefore be beneficial in treating the symptom cluster as a whole. It is our position that such crossover treatments should be given priority in symptom cluster management trials.

The most well-documented and studied symptom cluster is the combination of pain, fatigue, and sleep disturbance. Pain, fatigue, and sleep disturbance are among the most common symptoms experienced by persons with cancer (7). Pain is reported by 59% of persons receiving anticancer treatment and 64% of those with advanced, metastatic or terminal disease (8). Fatigue, the most common symptom experienced by all persons with cancer, impacts more than 75% of patients (9–11). Sleep problems, such as difficulty falling asleep, frequent nighttime wakening, waking too early in the morning, or excessive daytime sleeping, are reported by up to 72% of persons with cancer (12–13). These three symptoms have been found to cluster, co-occurring in more than 40% of patients, particularly those receiving cancer treatment (14–17). Moderate positive correlations between the three symptoms have been documented in persons with various cancer diagnoses and stages of disease (14). If not adequately managed, the symptoms in this cluster may interfere with mood, role and social functions, ability to tolerate and continue cancer therapies, and overall quality of life (18–23).

Traditional medical management of pain, fatigue, or sleep disturbance has focused on the use of pharmaceutical treatments such as analgesics, psychostimulants, hematopoietic growth factors, or sedatives. Specific medications prescribed for one symptom, however, may unintentionally worsen the other symptoms. For example, opioid pain medications may cause feelings of tiredness and increase daytime napping, which, in turn, leads to less restful nighttime sleep. Disruptions in sleep may exacerbate daytime fatigue, causing increased sensitivity to pain. Sleep disturbance related to steroid use may result in inadequate rest and intensify fatigue. On the other hand, use of sedatives or sleep enhancers may result in

sensations of grogginess or lack of alertness throughout the day, which could intensify fatigue and contribute to muscle aches and pain. It appears that the pain-fatigue-sleep disturbance symptom cluster cannot be optimally managed with the use of medications alone. Nonpharmacologic, mind-body interventions may provide a beneficial addition to the treatment regimen.

Mind-body interventions are techniques that "focus on the interactions among the brain, mind, body, and behavior, and on the…ways in which emotional, mental, social, spiritual, and behavioral factors can directly affect health" (24). Examples of mind-body interventions include relaxation, hypnosis, imagery, meditation, and cognitive or behavioral techniques, among others. The goal of mind-body interventions is to provide patients with the knowledge and skills to cope with and achieve personal control over their symptoms. Mind-body interventions are particularly appealing options to explore for the treatment of cancer symptom clusters as they are inexpensive, can be used in addition to pharmacologic strategies, have relatively few negative side effects, and can be implemented by patients independently with sufficient training.

Pain, fatigue, and sleep disturbance share a psychological component. Factors such as anxiety and meaning of the cancer symptoms may intensify how the symptoms are perceived and experienced (25). The Theory of Unpleasant Symptoms suggests that psychosocial factors such as mental state, reaction to illness, and anxiety are antecedents to symptoms that help define the overall symptom experience (26–27). Depression is often noted as being related to pain, fatigue, and sleep disturbance in cancer, and some investigators have included depression as a component of the symptom cluster itself (17). Interventions to enhance coping, diminish stress and anxiety, and improve mood may therefore help to improve the pain-fatigue-sleep disturbance symptom cluster (28). Mind-body interventions may be useful in altering negative thoughts about cancer, the underlying cause of symptoms, or in reframing how the symptoms are interpreted. The interventions may improve mood and provide a more optimistic attitude toward one's ability to cope with pain, fatigue, and sleep disturbance. Mind-body interventions may also enhance relaxation and reduce stress and anxiety related to the symptom experience. The physical and mental effects of relaxation may reduce sensitivity to pain sensations, allow more restful sleep, and reduce fatigue.

The purpose of this literature review is to identify mind-body interventions for which evidence suggests beneficial effects on at least two of the three cluster component symptoms (pain, fatigue, and sleep disturbance), and to synthesize that evidence. These interventions may hold potential for use as treatment for the full symptom cluster.

Method

CINAHL, Medline, and PsycINFO databases were searched through March 2009 using selected terms for mind-body interventions (*guided imagery, hypnosis, relaxation, biofeedback, cognitive-behavioral therapy, coping skills training, meditation, virtual reality*, and *music*) combined with the term *cancer* and terms for any of the three symptoms of interest (*pain, fatigue, sleep disturbance, sleep difficulty, insomnia*). We restricted our search to those mind-body interventions that involve primarily mental activity, as they can be performed by nearly all patients, including those with advanced disease. Although yoga is classified as a mind-body intervention by the National Center for Complementary and Alternative Medicine (24), there is disagreement in the literature with some investigators describing the intervention as physical exercise involving "vigorous…aerobic activity" (pg. 127) (29). Thus, we did not include "yoga" in our search. Results were limited to English language, research, and adults (age ≥ 18).

Abstracts were reviewed and articles were selected for inclusion if they tested one of the mind-body interventions in a sample of patients with cancer and if pain, fatigue, or sleep disturbance was among the dependent variables. We eliminated studies in which patients were undergoing diagnostic testing for cancer (i.e., a cancer diagnosis had not yet been established), as well as studies that included both persons with and without cancer in their samples.

Next we placed studies into one of six categories by intervention type: 1) Relaxation, 2) Imagery / Hypnosis, 3) Cognitive-behavioral therapy / Coping skills training [CBT/CST], 4) Meditation, 5) Music, 6) Virtual Reality. We categorized studies based on the description of the intervention provided in the research report. If the study included more than one intervention, it was categorized based on the most complex intervention included in the study. For example, if a CBT intervention was compared to a simple relaxation intervention, the study was categorized as a test of the more complex intervention, CBT. Descriptions of each type of intervention are provided in *Results*.

We conducted a preliminary review and identified those mind-body interventions for which beneficial effects were demonstrated on at least two of the three symptoms. Studies of those interventions were then reviewed in detail using a systematic narrative approach. We did not compute study quality scores, as our intent was to cast a broad net for those mind-body interventions that currently hold promise as treatment for the symptom cluster. Those interventions can then be targeted for immediate study.

Results

Evidence for Crossover Mind-Body Interventions

A total of 47 published articles were identified that tested a mind-body strategy for pain, fatigue, and / or sleep disturbance in persons with cancer. Of the six types of mind-body interventions searched, all but virtual reality had studies supporting beneficial effects on at least two of the three symptoms of interest (Figure 1). The four studies that tested a virtual reality intervention provided evidence for effects on fatigue only, and are not addressed in this review. The 43 studies of 1) relaxation 2) imagery / hypnosis, 3) CBT / CST, 4) meditation, and 5) music are described and their findings synthesized in the following pages.

Relaxation

Studies were categorized as “Relaxation” if they tested a technique designed to elicit a state of relative freedom from mental and / or physical tension (30). The use of relaxation as a therapeutic intervention dates back many decades. In the early 1900s, Jacobsen developed the progressive muscle relaxation (PMR) technique to stimulate physical and mental relaxation by focusing attention on the sensations associated with systematically tensing and relaxing groups of muscles (31). A variety of other relaxation exercises have been developed such as jaw relaxation (relaxing muscles of the face, mouth, and jaw), focused breathing (focusing attention on a relaxing word or phrase and slow, regular respirations) or abdominal breathing (slow deep breathing using muscles of the abdomen). Relaxation exercises minimize sympathetic nervous system response, which decreases oxygen demand, slows heart rate and respirations, and lowers blood pressure (32). Relaxation interventions may improve symptoms by eliminating physical tension and emotional stressors, and by facilitating the ability to become comfortable, rest, and fall asleep (25).

Relaxation interventions were implemented as the experimental treatment in six studies (Table 1). Pain was the most frequently studied outcome. It was the primary focus of four efficacy trials, with beneficial effects demonstrated in three. Samples included hospitalized patients with cancer pain, and outpatients with chronic cancer pain, and women with early

stage breast cancer. Significantly greater pain relief was obtained with PMR when compared to massage, treatment-as-usual (33), positive mood manipulation, distraction, and a no treatment control condition (34). Biofeedback-assisted relaxation resulted in greater pain relief when compared to attention control (e.g., time spent with a nurse) (35). Domar, Noe & Benson (36), however, found no significant differences in pain between a daily relaxation exercise and a distraction condition among patients having surgical skin cancer resection.

One study each explored the effect of relaxation training on fatigue and sleep disturbance. Training in PMR did not improve fatigue in patients receiving radiotherapy when compared to an informational intervention (37), but PMR training did improve sleep in patients with insomnia when compared to treatment-as-usual (38).

Two additional studies used relaxation interventions as comparison conditions in studies of imagery interventions. Both compared PMR to standard care in hospitalized patients. One demonstrated a significant reduction in pain with PMR (39), but the other found no differences in pain or fatigue (40).

Imagery / Hypnosis

Studies were categorized as “Imagery / Hypnosis” if they tested an intervention that asked participants to create specific mental images with the intent of bringing about positive physical or emotional effects (41). Despite their different names, imagery and hypnosis have been noted to be quite similar in terms of practice. Both interventions focus on the creation of mental representations, through recall of memories or creative imagination, that change the desired outcome (e.g., symptom experience) (42). Pleasant images may be created to distract attention away from the noxious symptom. Alternatively, images of the unpleasant symptom may be modified to change the symptom experience (43). Investigators have suggested that the body mimics neurohormonal responses to the mental images, as if they were actually occurring (41, 44). The mental images may also alter expectations for outcome, such that the desired outcome occurs automatically in response to the new image (44).

Imagery / hypnosis interventions served as the experimental intervention in six studies (Table 2). Four studies tested imagery interventions in hospitalized patients with cancer pain, and all reported beneficial effects; one in a pretest-posttest design (45) and three when compared to treatment-as-usual or attention control conditions (39,46–47). Conversely, Hasse et al. (40) found no significant differences in pain and no differences in fatigue between patients receiving an imagery intervention and those receiving standard care with colorectal surgery. Elkins (48) tested a hypnosis intervention among women with breast cancer who were experiencing hot flashes and reported a significant improvement in sleep scores in the hypnosis group compared to a no treatment control condition.

Four additional studies used imagery interventions as comparison conditions in studies of CBT / CST. All combined imagery with relaxation instructions. One study reported no change in pain or fatigue (49), but two reported significant reductions in pain (50–51) and one reported significant reductions in fatigue and sleep disturbance (52).

CBT / CST

Studies were categorized as “CBT / CST” if the intervention aimed to change patients’ thoughts as a way to influence their feelings and behaviors, helping patients to recognize and subsequently control their response to symptoms using a programmed education or counseling approach. Interventions that combined training in more than two cognitive or behavioral coping strategies in a single treatment group were also included in this category as coping skills training. What an individual thinks and believes about his / her symptoms,

including thoughts about the symptom's meaning, controllability, and consequences influence how symptoms are experienced. In CBT / CST interventions, participants are taught to understand how their thoughts influence their feelings and behavior, to recognize and acknowledge when this is occurring, and to use cognitive strategies and coping skills to change their thoughts and behaviors. The interventions are usually delivered over several weeks and involve assignments to practice what has been learned outside of the training sessions. If the patient experiences difficulty with the skills, problem-solving and additional training are carried out at the next treatment session. As applied to symptom management, CBT / CST interventions focus on helping participants to identify and change maladaptive cognitions about their symptoms and use various cognitive and behavioral coping strategies that change how the symptoms are perceived and experienced (53).

A total of twenty-one studies (24 publications) tested a program of CBT / CST in persons with cancer-related pain, fatigue, or sleep disturbance (Table 3). Four studies tested CBT / CST interventions for pain. Robb, Williams, Duvivier, & Newham (54) demonstrated a significant reduction in pain intensity among adults with chronic cancer pain after participating in a 6-month pain-focused CBT intervention. Syrjala and colleagues (50–51) conducted two trials of a CBT intervention, comparing the treatment to treatment-as-usual for mucositis pain experienced by persons having a bone marrow transplant to treat hematologic malignancies. In the first study, pain reported by the CBT group was no different from pain reported by the control group. In the second study, CBT resulted in significantly less pain than the control condition (51). Dalton (55) tested a similar self-care program among adults with cancer-related pain, but found no differences in pain ratings when compared to control.

Cancer-related fatigue was the primary focus of three studies of CBT / CST interventions; all demonstrated beneficial effects. Samples included patients receiving chemotherapy, patients who had completed treatment, and patients with malignant melanoma. Significantly greater improvements in fatigue were achieved with a 6–12 week CBT / CST intervention when compared to treatment-as-usual (56), waitlist control (57–58) and a no treatment control condition (59).

Three studies tested the effects of CST in managing the combination of pain and fatigue. Samples included women with metastatic breast cancer experiencing pain (49), patients undergoing curative radiation therapy (60), and women undergoing bone marrow transplant for breast cancer (61). All studies compared a one-session CST intervention to a treatment-as-usual control condition. No significant differences in pain or fatigue were noted between groups in any of these studies.

Seven studies evaluated the effects of CBT / CST interventions on the combination of fatigue and sleep disturbance. Six of these studies involved samples of women with breast cancer (52,62–66,68–69) and one study included patients with a variety of cancer diagnoses (67). Williams and Scheier (62) found decreased incidence of fatigue and sleep disturbance using a 20-minute coping skills audio-recording before each chemotherapy cycle compared to treatment-as-usual. In one group designs, both Quesnel (64) and Berger (68–69) reported significant improvement in sleep with a 4–8 week CBT intervention, but only Quesnel also reported improvement in fatigue. Epsie (67) found greater improvements in sleep and less fatigue after a 5-session nurse-led CBT intervention compared to treatment-as-usual. Savard et al. and Epstein and Dirksen reported greater improvement in sleep, but no change in fatigue when 4–8 weeks of CBT was compared to treatment-as-usual (63) or sleep education (65–66). And Cohen and Fried (52) reported no improvement in either fatigue or sleep disturbance with a 9-week CBT intervention compared to standard treatment.

Finally, four studies measured the effect of CBT / CST interventions on all three symptoms concurrently: pain, fatigue, and sleep disturbance. One study documented improvement in two of the three symptoms. Davidson, Waisberg, Brundage, & Maclean, (70) tested an 8-week sleep focused CBT program in persons with cancer-related insomnia using a one-group pretest posttest design. Significant improvements were documented in both fatigue and sleep disturbance, but pain remained unchanged. Arving et al. (71) and Dalton, Keefe, Carlson & Youngblood (72) both tested individually-tailored CBT interventions. Arving reported significantly less sleep disturbance but no differences in pain or fatigue among women starting treatment for breast cancer following a nurse-led CBT intervention compared to control. Dalton et al. (72) reported significantly lower ratings of "worst" pain immediately after the tailored CBT program, and greater reductions in pain and fatigue 6-months after the intervention compared to treatment-as-usual control. There were no differences in sleep. Vilela et al. (73) found no significant differences in pain, fatigue, or sleep disturbance in patients with head and neck cancer using a CST intervention compared to control.

Meditation

Studies were categorized as "Meditation" if they provided training in a self-directed mental exercise to intentionally and continually focus the mind on a single target perception. Meditative techniques grew largely out of Eastern religious practices such as Hindu, Buddhist, and Taoist meditation (74). Mindfulness-based stress reduction (MBSR), a meditative technique that has grown in popularity over the last decade, involves awareness of body sensations and focused breathing to calm the mind and give the individual a sense of non-judgmental awareness of bodily experiences (75). Some MBSR techniques include training in meditative exercises such as gentle yoga poses to help bring about the meditative state (76). Symptoms such as pain, fatigue, and sleep disturbance may be modified through meditation by focusing attention away from the symptom experience, by focusing on strengths and positive thoughts, by eliminating the evaluation or judgment of sensations associated with the symptom (77–79).

Although no studies tested the effects of meditation on cancer-related pain, four studies evaluated the impact of meditation interventions on fatigue and / or sleep disturbance (Table 4). Three studies specifically identified the type of meditation as MBSR; one used similar techniques, but simply described the intervention as meditation. Only one study reported beneficial effects, and that study used a one group pretest-posttest design. Carlson and Garland (77) reported a significant improvement in both fatigue and sleep disturbance among outpatients with cancer who participated in an 8-week MBSR intervention. Kieviet-Stijnen et al. (80) studied and 8-week MBSR intervention in patients with various cancer diagnoses and found no within group improvement in fatigue. Moadel et al. (81) studied a 12-week meditation intervention in a sample of women with breast cancer and found no significant differences in fatigue when compared to a wait list control condition. Similarly, Shapiro et al. (82) tested a 6-week MBSR intervention among women with breast cancer and found no differences in sleep disturbance when compared to a choice of other self-directed stress management techniques.

Music

Studies were categorized as tests of "Music" interventions if they promoted health and well-being through listening to or participating in music in some way (83). Music therapists sometimes involve persons in exploring thoughts and beliefs through music or expressing emotions by creating music, singing or dancing, but simple music listening can also be an efficacious strategy in managing symptoms. Music can stimulate both physiologic and emotional reactions based on its pitch, intensity, tone, and rhythms (84). Certain styles of

music may trigger relaxation while others enhance mood, and still others energize the mind and body. In general, music provides a source of distraction by holding one's attention on the specific musical qualities. Particularly engaging music may distract attention from pain, relaxing music may release muscle tension and reduce pain, or stimulate muscle relaxation to enhance sleep and rest (30,85). Fast paced, up tempo, positive music may energize and elevate the mood of someone who is feeling fatigued (86–87).

Four studies evaluated the effects of music interventions on pain (Table 5). Cholburi et al. (88) and Zimmerman et al. (89) both reported significant pre- to post-treatment reductions in pain using 30-minutes of preferred music among hospitalized patients with cancer pain. Beck (90) and Kwekkeboom (91), however, found no differences in pain when music listening was compared to a control condition (white noise, book on tape, or resting quietly).

Two studies tested a music intervention on cancer-related fatigue. Ferrer (92) compared live music to a no treatment control condition among cancer patients receiving chemotherapy and reported significantly less fatigue in the music group. Burns et al. (93) compared music with standard care in a sample of hospitalized patients receiving intensive chemotherapy and found no significant difference in fatigue between groups.

Discussion

A total of six mind-body interventions that had been studied for cancer-related pain, fatigue, or sleep disturbance were initially identified in this review; all interventions except virtual reality demonstrated beneficial effects on at least two of the symptoms and met criteria for review. Findings suggest there is at least some evidence to support the use of CBT / CST interventions and imagery / hypnosis interventions for all three symptoms. Relaxation has demonstrated efficacy in managing pain and sleep disturbance. Meditation has been supported in the treatment of both fatigue and sleep disturbance. And music has been efficacious in managing both pain and fatigue. This evidence suggests there is value in exploring these five mind-body interventions as potential crossover treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer.

Of the fifteen studies that measured multiple symptom outcomes, only six indicated improvement in more than one symptom from the single intervention being tested. In each of those cases, the two symptoms improved were fatigue and sleep disturbance. Three of six studies used pretest-posttest, within group designs. These studies don't control for the possibility of improvement simply due to passage of time rather than effects of the mind-body intervention. None of the studies demonstrated concurrent improvement in pain and fatigue or pain and sleep disturbance, and none demonstrated improvement in all three symptoms. It is important to note, however, that none of these studies specifically targeted a symptom cluster as their focus of treatment. They simply measured other concurrent symptoms in addition to the primary symptom of interest. Most importantly, none of the studies used inclusion criteria to select patients who were experiencing the pain-fatigue-sleep disturbance symptom cluster. Thus, baseline symptom status may not have been sufficient to demonstrate significant improvement across the symptom cluster.

Relaxation interventions demonstrated efficacy in four of six trials in which relaxation was the primary intervention, and one of two trials that used relaxation as a comparison condition. The greatest evidence was for its effect on cancer-related pain. No studies supported effects on fatigue, but one study did suggest improvement in sleep disturbance. Both inpatients and outpatients were included in the studies as well as patients on and off therapy (surgery, chemotherapy, radiation). The most frequently studied intervention was PMR delivered over three or more training sessions, facilitated with an audio-tape and

independent patient practice. Control conditions were most often described as treatment-as-usual. When more active comparison conditions were used (i.e., education and counseling, distracting activity, imagery) effects of relaxation did not differ significantly from those of the comparison group.

Imagery / hypnosis intervention demonstrated efficacy in five of six studies in which it was the primary treatment being tested, and three of four studies in which it was used as an active comparison condition. The majority of studies demonstrated support in relieving pain. Two studies documented improvement in sleep and one study documented improvement in fatigue with an imagery intervention. Most of these studies used randomized or crossover designs with treatment-as-usual control conditions. The imagery / hypnosis studies were conducted primarily with hospitalized patients experiencing cancer-related pain. Interventions ranged from a one-time 12 minute exercise to sessions of 50 minutes or more plus daily practice over several weeks.

CBT / CST interventions were efficacious in fourteen of twenty-one studies. Studies demonstrated improvement in all three symptoms, but the most support was demonstrated for fatigue and sleep disturbance. Nearly half of the studies involved women with breast cancer either during or after completing treatment. All of the studies that used experience of the symptom(s) of interest as an inclusion criteria demonstrated improvement in that symptom. Again, treatment-as-usual was the most frequent control condition, although some used active comparison conditions. Two studies compared CBT / CST interventions to education and found greater effect of the CBT / CST intervention in comparison (65,72); however, three studies that used imagery interventions as a comparison found similar or stronger effects in the imagery group (50–52).

Meditation interventions demonstrated efficacy in only one of the four studies, and those findings were within group differences in fatigue and sleep disturbance; a control or comparison condition was not included (77). Populations studied included only outpatients, most with early stage breast cancer and post-treatment. The relatively healthy samples may have precluded the ability to demonstrate improvement in symptoms. Both meditation studies that used control conditions failed to demonstrate significant effects of the mind-body intervention, regardless of whether the control was a wait list or an active comparison (patient-selected stress management techniques such as talking with a friend or exercising).

Music interventions demonstrated greater effects than control or comparison conditions in three of the six studies. Evidence was strongest for effects on pain. One study documented beneficial effects on fatigue. No studies evaluated the effect of music on sleep disturbance. Patients studied were both in- and outpatients, with most experiencing the symptom of interest as inclusion criteria for the study. The length of music interventions were typically brief, 30–45 minutes delivered either as a one-time intervention or twice a day over 2–3 days. Four trials used randomized controlled designs with treatment-as-usual or “rest” as control conditions. Two used an active comparison condition involving a distraction technique or white noise, which did not differ from the effects of music.

Few investigators used multi-symptom inventories in their studies, which could have provided useful leads in understanding the effects of mind-body interventions on co-occurring symptoms. Given that symptom cluster research is still a relatively new field, an ideal measure of the pain-fatigue-sleep disturbance symptom cluster has not yet been identified. Several scales used in the current studies appeared to have been sensitive to effects of the mind-body interventions. Those scales that most frequently detected changes in pain were the visual analog scale and the 0–10 numeric rating scale. Instruments that most frequently detected changes in fatigue included the visual analog scale, the fatigue and vigor

subscales from the Profile of Mood States (94), and the Multidimensional Fatigue Inventory (95). Measures most frequently sensitive to the effects of mind-body interventions on sleep disturbance included sleep diaries, the Pittsburg Sleep Quality Index (96), sleep subscale of the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (97), and the Insomnia Severity Index (98). Additional research is necessary to identify the items and scales most useful in measuring symptom clusters. The optimal measure would be sensitive to clinically relevant changes in each symptom, but also brief and simple to complete given the symptom burden experienced by the cancer population.

The studies we reviewed have several strengths. Nearly all were randomized controlled trials, offering the highest level of evidence for the interventions tested. The specific content of interventions was fairly consistent within each category. Although breast cancer was a common study population, a wide variety of patients were studied, including inpatients and outpatients, persons receiving treatment and those who had completed it, as well as persons with various diagnoses and stages of disease. Some of the studies required the presence of symptoms as an inclusion criterion, reducing the possibility of floor effects in these trials.

The studies did, however, have some limitations. Sample sizes used in most trials were small to moderate ($N < 100$ in 35 of 43 trials). Specific doses (timing, frequency of practice) of CBT / CST interventions varied across studies. Relatively few studies tested meditation interventions. Most music interventions were fairly brief (1–6 sessions delivered over < 3 days) and few active comparison conditions were used in these studies. Several studies combined interventions and did not attempt to determine which intervention component actually produced the symptom improvement. Furthermore, most of the studies were efficacy trials, testing the mind-body interventions in a controlled, somewhat artificial context with a selected patient population. A few of the investigators described their studies as effectiveness trials, using clinic nurses (67) or social workers (61) to administer treatment in the clinical setting. As efficacy trials provide support for mind-body interventions in the context of treating a specific symptom cluster, effectiveness trials will need to be carried out to determine if the outcomes are reproducible in contemporary cancer care settings.

Limitations of this review must also be noted. The authors identified criteria used to categorize the mind-body interventions and some readers may disagree with our decisions. We focused this review on mind-body interventions that involved primarily mental activities. Other CAM strategies not addressed in this review may offer equally or more beneficial effects in treating the pain-fatigue-sleep disturbance symptom cluster. Our study inclusion criteria were meant to be liberal in identifying mind-body strategies that could hold promise in treating the symptom cluster, and as such, we did not evaluate or score study quality as part of this review. Thus, we may have erred on the side of being overly inclusive at this early stage. Similarly, we did not calculate effect sizes to identify relative strength of the mind-body interventions before they have been tested in treating the full symptom cluster.

Conclusions

Mind-body interventions such as relaxation, CBT / CST, mediation, music and imagery may offer benefit to patients with co-occurring pain, fatigue, and sleep disturbance related to cancer. Most patients are capable of using mind-body interventions. Age and advancing disease do not need to be barriers as the strategies reviewed here require some cognitive, but very little physical effort. Many of the mind-body interventions addressed in this review could be delivered by health care providers, as social workers, health psychologists, and oncology nurses receive training in cognitive-behavioral coping strategies as part of their educational preparation. Individualized training along with written or audiotaped

instructions could be used to evaluate effects on co-occurring symptoms or on a specific symptom cluster.

Although no studies tested mind-body interventions specifically for the pain-fatigue-sleep disturbance symptom cluster, there is sufficient evidence to suggest that relaxation, imagery / hypnosis, CBT / CST, meditation, and music interventions hold promise as crossover treatments, that may be efficacious for the full symptom cluster. Studies have shown that relaxation can improve pain and sleep disturbance, meditation can reduce fatigue and sleep disturbance, music can reduce pain and fatigue, and imagery / hypnosis and CBT / CST interventions can produce improvements in all three symptoms.

A number of unanswered questions about the effects of mind-body interventions on the pain-fatigue-sleep disturbance symptom cluster need to be investigated. To adequately determine if any of the mind-body interventions can be recommended as treatment for the symptom cluster, investigators need to design efficacy studies that select participants based on their experiences of these three symptoms. Researchers need to avoid floor effects by establishing inclusion criteria that allow room to demonstrate improvement in more than one clustered symptom. Studies need to move away from one-group pretest-posttest designs and enhance the quality of evidence by using randomized controlled designs. Because active comparison conditions provide a stringent test, and because patients are not likely to be content “doing nothing” about bothersome symptoms, comparison / control groups should be given careful thought. Eventually, effectiveness trials that make head-to-head comparisons among mind-body strategies will be necessary to determine if one treatment is more effective than another for a particular symptom cluster, or if one treatment can produce the same outcomes at a lesser cost.

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Mind-Body Intervention	Pain	Fatigue	Sleep Disturbance
CBT / Coping Skills Training	X	X	X
Guided Imagery or Hypnosis	X		X
Meditation		X	X
Music	X	X	
Relaxation	X		X
Virtual Reality		X	

X = Evidence of beneficial effects on the symptom.

Figure 1.
Evidence Supporting Effects of Mind-Body Interventions on Pain, Fatigue, and Sleep Disturbance

Table 1

Summary of Studies of Relaxation Interventions for Cancer-Related Pain, Fatigue, and Sleep Disturbance

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Anderson et al., 2006 (34)	57	Outpatients with chronic cancer-related pain	RCT	**Relaxation** 20-min PMR audiotape; practiced 5 × / week for 2 weeks.	**Positive Mood:** 20-min audiotape of positive mood statements and positive imagery; practiced 5 × / week for 2 weeks. **Distraction:** 20-min audiotape of a neutral topic (e.g., history, geography, vocabulary); practiced 5 × / week for 2 weeks. **Control:** Wait list.	Significantly lower pain in the relaxation and distraction groups compared to control immediately following the intervention, but no difference between groups at subsequent follow-ups. *0-10 Pain NRS*	Not measured.	Not measured.
Cannici, Malcolm & Peek, 1983 (38)	30	Cancer in- and out- patients with sleep onset insomnia	RCT	**Relaxation:** Three sessions of PMR training on 3 consecutive days + home practice twice per day.	**Control:** Treatment-as- usual.	Not measured.	Not measured.	Significant reduction in sleep onset latency in relaxation group. *Daily patient report*.
Decker & Cline-Elsen, 1992 (37)	82	Outpatients with cancer undergoing curative or palliative radiotherapy	RCT	**Relaxation:** Six 1-hr sessions of relaxation training + daily PMR practice with audiotape.	**Control:** Education and counseling about radiation therapy.	Not measured.	No significant differences in fatigue between groups. *POMS – Fatigue subscale*	Not Measured.
Domar, Noe & Benson, 1987 (36)	49	Patients scheduled for surgical resection of skin cancer	RCT	**Relaxation:** Recorded instructions for 20- min relaxation exercises practiced from time of cancer discovery to 1-week post surgery.	**Control:** 20-minutes of daily reading; practiced from time of cancer discovery to 1 week post surgery.	No significant differences in pain between groups. *McGill Melzack Pain Questionnaire*	Not measured.	Not measured.
Hernandez-Reif et al., 2005 (33)	58	Women with early-stage (I-III) breast cancer	RCT	**Relaxation:** 30-min audiotaped PMR 3 × / week for 5 weeks.	**Massage:** 30-min massage 3 x / week for 5 weeks. **Control:** Treatment-as- usual.	Significantly greater reduction in pain in PMR and massage groups compared to control. No difference between PMR and massage groups. *POMS State Anxiety Inventory* *McGill Pain Questionnaire (Short Form)*	Not measured.	Not measured.

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Tsai et al., 2007 (35)	37	Hospitalized patients with advanced cancer and pain rated ≥ 3.	RCT	**Biofeedback assisted Relaxation:** Six 45-minute training sessions using EMG biofeedback and diaphragmatic breathing, delivered over a 4-week period.	**Control:** Equal time spent with a nurse.	Significantly less pain in the relaxation group compared to the control. *Brief Pain Inventory*	Not measured.	Not measured.

Table 2

Summary of Studies of Guided Imagery / Hypnosis Interventions for Cancer-Related Pain, Fatigue, and Sleep Disturbance

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Ebell, 2008 (46)	32	Hospitalized patients with cancer- related pain	Crossover	**Self-Hypnosis:** Specific technique, duration, frequency not described	**Control:** Treatment-as-usual	Significant reduction in pain intensity and suffering from pain in hypnosis condition compared to control. *0–100 VAS*	Not measured.	Not measured.
Elkins et al., 2008 (48)	60	Women with non- metastatic breast cancer who had completed treatment and were having hot flashes.	RCT	**Hypnosis:** Suggestions for relaxation, mental images of coolness, dissociation from hot flashes, and other images; delivered in five 50-minute weekly sessions + audiotape for home practice.	**Control:** No treatment	Not measured.	Not measured.	Significant improvement in sleep scores in hypnosis group compared to control. *Medical Outcomes Study – Sleep Scale*.
Haase et al., 2005 (40)	60	Patients having curative surgery for colorectal cancer	RCT	**Guided Imagery:** 12 minute audiotape of imagined journey to a place of peace, comfort and safety; used 3 × /day for 2 days before surgery and until discharge.	**Relaxation:** 12 minute audiotape of passive PMR; used 3 x/ day for 2 days before surgery and until discharge. **Standard care:** No psychological intervention.	No significant differences in pain or analgesic use within groups or between groups. *0–100 Pain VAS*	No significant differences in fatigue within or between groups. *0–100 Fatigue VAS*	Not measured.
Kwekkeboo m, Kneip & Pearson, 2003 (45)	62	Hospitalized patients with cancer pain	One group pretest-posttest	**Guided Imagery:** Audiotape of 12-min pleasant nature imagery; used once.	**None**	Significant reduction in pain intensity. *0–10 Pain NRS*	Not measured.	Not measured.
Kwekkeboo m, Wanta & Bumpus, 2008 (39)	40	Hospitalized patients with cancer- related pain	Crossover trial	**Imagery:** 15-minute audiotaped analgesic imagery exercise; used 2 × / day for one day.	**Relaxation:** 15-minute audiotaped PMR exercise; used 2 × / day for one day. **Control:** 15-minute informational recording (attention control); used once / day for two days.	Significantly greater reduction in pain intensity and pain-related distress immediately post-treatment with imagery and PMR compared to control. (Imagery was not compared to PMR) *0–10 Pain NRS*	Not measured.	Not measured.
Sloman et al., 1994 (47)	67	Hospitalized patients with cancer pain	RCT	**Guided Imagery** (**Audiotaped**): 30-min audiotaped PMR and imagery of a peaceful scene; used 2 × / week for 2 weeks + practice twice a day for an additional week. **Guided Imagery (Live Guide):** Live nurse-guided	**Control:** Treatment as Usual	Significantly lower pain intensity, overall pain severity, and p.r.n. use of non-opiate analgesics in both the intervention groups compared to the control group.	Not measured.	Not measured.

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
				administration of PMR and imagery script as above; used 2 × / week for 3 weeks + practice twice a day for an additional week.		*McGill Pain Questionnaire (Short Form)* *Pain VAS*		

Table 3

Summary of Studies of CBT / Coping Skills Training Interventions for Cancer-Related Pain, Fatigue, and Sleep Disturbance

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Arathuzik, 1994 (49)	24	In- and Out-patients with pain from metastatic breast cancer	RCT	**CST:** 120 minutes of PMR, deep breathing, and images of inhaling energy, exhaling pain, and being in a comforting place + various distraction techniques and positive affirmations. Used one time.	**Relaxation and Imagery:** 75 minutes of PMR, deep breathing, and images of inhaling energy, exhaling pain, and being in a comforting place. Used one time. **Control:** Treatment-as-usual	No significant differences in pain intensity or pain distress between groups *0–10 VAS*	No significant differences in fatigue between groups *POMS – Fatigue subscale*	Not measured.
Armes et al., 2007 (56)	55	Adults with cancer-related fatigue receiving chemotherapy	RCT	**CBT:** Discussion of the meaning of cancer-related fatigue, aims and effects of coping strategies on fatigue, self-monitoring of fatigue and sleep disturbance, education and written information about fatigue management, goal setting, activity scheduling, graded task management, cognitive restructuring. Delivered in three individual 60-minute sessions, every 3–4 weeks.	**Control:** Treatment-as-usual	Measured, but not reported.	Trend toward lower fatigue rating in CBT group versus control. *100-mm VAS* Significant improvement in physical fatigue. *Multidimensional Fatigue Inventory – Physical Fatigue subscale* No difference in fatigue-related distress. *Fatigue Outcome Measure*	Measured, but not reported.
Arving et al., 2007 (71)	179	Patients with breast cancer starting adjuvant treatment	RCT	**Nurse-Delivered CBT:** Psychosocial support using cognitive- behavioral coping strategies delivered in 45–60 minute one- on-one sessions. Number of sessions were tailored to individual needs. **Psychologist-Delivered CBT:** Psychosocial support using cognitive-behavioral coping strategies delivered in 45–60 minute one- on-	**Control:** Treatment-as- usual.	No significant differences in pain between groups *EORTC-QLQ 30 Pain Subscale*	No significant differences in fatigue between groups *EORTC-QLQ 30 Fatigue Subscale*	Significantly less insomnia in nurse- led group than control. *EORTC-QLQ Insomnia Subscale*

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
				one sessions. Number of sessions were tailored to individual needs.				
Berger et al., 2002 & 2003 (68–69)	25	Women with early stage (I-II) breast cancer receiving chemotherapy.	One group repeated measured	**Sleep hygiene** Phase I: Individualized plan of relaxation exercises, sleep restriction, and stimulus control during 4 chemotherapy cycles. Phase II: Revised sleep hygiene activities at 30, 60, and 90 days after the last chemo treatment.	**None**	Not measured	PHASE I: No significant changes in fatigue. PHASE II: No significant changes in fatigue. *Piper Fatigue Scale*	PHASE I: No significant changes in sleep. PHASE II: Significant reduction in the number of nighttime awakenings and length of daytime naps over time. *Wrist actigraph Daily diary Pittsburgh Sleep Quality Index*.
Clark et al., 2006 (60)	63	Outpatients with cancer undergoing curative radiation therapy	RCT	**CST:** Personal preference of relaxing or distracting music plus training in PMR, imagery, and positive self-talk; 90-minute audiotape of music with instructions for use anytime except during radiation treatment.	**Control:** Treatment-as- usual.	No significant differences in pain between groups. *0–10 Pain NRS*	No significant differences in fatigue between groups. *POMS – Fatigue subscale*	Not measured.
Cohen & Fried, 2007 (52)	170	Women with early stage breast cancer; 2- 12 months post-treatment	RCT	**CBT:** Group training in reducing negative and automatic thoughts, positive reframing, distraction, problem- solving, decision- making, and activity scheduling. Met weekly for 90 min × 9 weeks + practice between meetings.	**Relaxation and Imagery:** Group training in deep breathing, autogenic relaxation, and imagery. Met weekly for 90 min × 9 weeks + practice between meetings. **Control:** Treatment-as-usual	Not measured.	Significantly greater decrease in fatigue in the relaxation and imagery group compared to CBT and control groups. *Fatigue Symptom Inventory*	Significantly greater decrease in sleep difficulty in the relaxation and imagery group compared to CBT and control groups. *Mini Sleep Questionnaire*
Dalton et al., 2004 (72)	131	Adults with chronic	RCT	**Tailored CBT (T CBT):** Elements of standard CBT matched	**Control:** Treatment-as- usual.	IMMED: Significantly greater	IMMED: No significant differences in	IMMED: No significant differences in

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Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
		cancer-related pain		to patient problems identified using a biobehavioral pain profile survey; met individually for 1 hour, once / week × 5 weeks. **Standard CBT (CBT)**: Counseling focused on thoughts and feelings related to pain plus training in 6–8 coping strategies; met individually for 1 hour, once / week × 5 weeks.		improvement in worst pain in T- CBT than standard CBT and control groups. 6-MONTHS: Significantly greater improvement in pain in standard CBT than T-CBT and control groups. *Brief Pain Inventory*	fatigue between groups 6-MONTHS: Significantly greater improvement in fatigue in the control group than PT-CBT. *Symptom Distress Scale*	sleep between groups. 6-MONTHS: No differences in sleep between groups. *Symptom Distress Scale*
Dalton, 1987 (55)	30	Adults with disease-related cancer pain	RCT	**Pain self-care program:** Education about pain physiology + training in 3 self-management methods: distraction, relaxation, and cutaneous stimulation. Met one time for individual training + recommendations to practice at home.	**Control:** (Not described)	No significant differences in pain between groups. *100-mm VAS*	Not measured.	Not measured.
Davidson et al., 2001 (70)	14	Adults with breast, GI, or GYN cancers with c/o insomnia	One group Pretest- posttest	**Sleep Therapy Program:** Stimulus control therapy + training in relaxation and other cognitive strategies; met in groups for 60- 90 minutes, once / week for the first 4 weeks and once again at week 8.	**None**	No significant reduction in pain. *EORTC QLQ C-30 Pain Scale*	Significant improvement in fatigue at 8 weeks. *EORTC QLQ C-30 Fatigue Scale*	Significant improvement in insomnia at 4 and 8 weeks. *Sleep Diary Sleep Impairment Index EORTC QLQ C-30 Insomnia Item*
Epstein & Dirksen, 2007; Dirksen & Epstein, 2008 (65℃ 66)	72	Women with stage I – III breast cancer, at least 3 months post-treatment with c/o sleep disturbance	RCT	**Cognitive Behavioral Training:** Stimulus control, sleep restriction, sleep hygiene, and sleep education for two group sessions and two phone interviews.	**Control:** Sleep hygiene and sleep education for two group sessions and two phone interviews.	Not measured	Trend toward greater reduction in fatigue among CBT participants. *POMS – Fatigue subscale*	Significantly less time in bed and greater improvement in sleep quality in CBT group, but no difference in insomnia severity.

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
								Daily sleep diary Sleep quality questionnaire Wrist actigraph Insomnia Severity Index
Espie et al., 2008 (67)	150	Adults with breast, prostate, colorectal or GYN cancers, at least 1 month post-treatment and with c/o chronic insomnia	RCT	**Nurse-led CBT:** Sleep information, sleep hygiene, sleep scheduling, relaxation, imagery, distraction and cognitive strategies to manage thoughts about sleep; met in groups for 50 minutes once / week x 5 weeks.	**Control:** Treatment-as-usual	Not measured	Significantly greater improvement in fatigue immediately post-treatment and at 6 months compared to control *Fatigue Symptom Inventory*	Significantly greater improvement in sleep immediately post-treatment and at 6 months compared to control. *Pittsburgh Sleep Quality Index Epworth Sleepiness Scale Sleep Diary Wrist actigraph*
Fawzy et al., 1990 (59)	80	Adults with early stage (I – II) malignant melanoma	RCT	**CBT:** Health education, illness-related problem-solving skills, stress management (relaxation techniques), and psychological support; met in groups for 90-minutes, once / week x 6 weeks.	**Control:** No treatment or therapist contact	Not measured.	No differences between groups in fatigue immediately post-treatment, but significantly less fatigue in the treatment group at 6 month follow-up. *POMS – Fatigue subscale*	Not measured.
Gaston- Johansson et al., 2000 (61)	128	Women with stage II-IV breast cancer undergoing autologous BMT	RCT	**Comprehensive coping strategy program (CCSP):** Preparatory info, avoiding negative coping strategies, using positive coping self-statements, relaxation + imagery; one time training, reinforced twice. Instructions to practice	**Control:** Treatment-as- usual.	No significant differences in pain between groups. *Pain-o-meter*	No significant differences in fatigue between groups. *100-mm Fatigue VAS*	Not measured.

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
				relaxation + imagery daily and as needed.				
Gielissen, Vehagen, & Bleijenberg, 2006; 2007 (57–58)	112 (N = 68 at follow-up)	Adults with complaints of severe fatigue, who had completed cancer treatment at least 1 year prior	RCT with follow-up after waitlist controls received treatment	**CBT:** Modules addressing: coping with cancer, fear of recurrence, dysfunctional thoughts about fatigue, dysregulated sleep, dysregulated activity, social support. Modules delivered one-on-one and based on individual need in three sessions over 9 – 12 weeks.	**Control:** Waitlist	Not measured.	IMMEDIATELY: Significantly lower fatigue severity in CBT group. FOLLOW-UP (1–4 YEARS): Significantly lower fatigue severity versus pre- treatment. *Checklist of Individual Strengths – Fatigue subscale*	Measured, but not reported.
Quesnel et al, 2003 (64)	10	Women with breast cancer, post-treatment, with chronic insomnia	Crossover	**CBT:** Training in stimulus control, sleep restriction strategies, fatigue management, cognitive reframing, and sleep hygiene. Met in groups for 90-minutes, once / week x 8 weeks.	**Control:** 3–10 week pre-CBT period of keeping a daily sleep diary.	Not measured.	Significant pre- to post-treatment improvement in general and physical fatigue. *Multidimensional Fatigue Inventory*	Significant pre-to post-treatment improvement in total wake time and sleep efficiency. *Sleep Diary Insomnia Severity Index*
Robb et al., 2006 (54)	13	Adults with chronic cancer-related pain	One-group pretest- posttest	**Pain Management Training Program:** Pain theory, goal setting, self-monitoring, exercise, relaxation, cognitive coping skills, and relapse prevention. Met individually for 60-minutes, once a week × 4 weeks, then once every 2–4 weeks × 3–6 mos.	**None**	Significant reductions in present pain, worst pain, and average pain. No change in least pain. *Brief Pain Status Questionnaire (present pain) 0–10 NRS (worst & average pain)*	Not measured.	Not measured.
Savard, et al., 2005 (63)	58	Women with stage I-III breast cancer post-treatment with chronic insomnia	RCT	**CBT:** Combined stimulus control therapy, sleep restriction, cognitive restructuring, sleep hygiene, and fatigue and stress management strategies; met in	**Control:** Wait list	Not measured.	No significant differences between groups. *Multidimensional Fatigue Inventory*	Significantly greater improvement in sleep efficiency, total wake time, sleep onset latency, and waking

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
				groups for 90- minutes, once / week x 8 weeks				after sleep onset in the treatment group. *Sleep Diary Insomnia Severity Index*
Syrjala, Cummings & Donaldson, 1992 (50)	67	Hospitalized patients with hematologic cancers having bone marrow transplant	RCT	**CBT:** Pain education and training in PMR, autogenic relaxation, cognitive restructuring, goal setting, and exploration of meaning with positive self-statements; met for two 90-minute sessions prior to hospital admission, then ten 30-minute booster sessions held twice weekly during hospitalization.	**Relaxation and Imagery:** Relaxation + imagery of the patient's preference; met for two 90-minute sessions prior to hospital admission, then ten 30-minute booster sessions held twice weekly during hospitalization. **Attention Control:** Equal time spent talking with a psychologist; no new coping skills introduced.	Significantly less pain in the hypnosis group compared to CBT training and attention control groups. No differences between CBT and control group. *100-mm Pain VAS*	Not measured.	Not measured.
Syrjala et al., 1995 (51)	94	Hospitalized patients with hematologic cancers having bone marrow transplant	RCT	**CBT:** Pain education and training in PMR, autogenic relaxation, pleasant and pain-transforming imagery, positive self-statements, distraction, and goal setting; met for two 90-minute sessions prior to hospital admission, then ten 30-minute booster sessions and ten 20- 40 minute practice sessions during hospitalization.	**Relaxation and Imagery:** Training in PMR, autogenic relaxation, pleasant and pain-transforming imagery; met for two 90-minute sessions prior to hospital admission, then ten 30-minute booster sessions and ten 20–40- minute practice sessions during hospitalization. **Attention Control:** Psychotherapeutic support. **Control:** Treatment-as- usual.	Significantly less pain in relaxation and imagery and CBT groups compared to control. No difference between CBT and Relaxation + Imagery *100-mm Pain VAS*	Not measured.	Not measured.
Vilela et al., 2006 (73)	138	Patients with head and neck cancer, post-treatment	Quasi-experimental (Controls matched by stage of disease and time since diagnosis)	**Nucare program:** Training in positive coping and ways of thinking, using social support, problem solving, goal setting, healthy lifestyle, and relaxation. Patient-choice of delivery format: group, one-on-one, or self-training.	**Control:** Not described	No significant differences in pain between groups. *EORTC-QLQ 30 Pain subscale*	No significant differences in fatigue between groups. *EORTC-QLQ 30 Fatigue subscale*	No significant differences in sleep between groups. *EORTC-QLQ 30 Sleep Disturbance item*

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Williams & Schreier, 2005 (62)	71	Women newly diagnosed with breast cancer starting chemotherapy	RCT	**Self-Care Behavior Training:** Treatment-as-usual + 20-min audiotape with education about relaxation and exercise, set to music; instructed to listen to the tape 12- 24 hours before each cycle of chemotherapy and as often as needed during treatment.	**Control:** Treatment-as- usual.	Not measured.	Lower incidence of fatigue in the Self- Care group. No difference between groups in fatigue severity or number of self-care behaviors used. *Self-Care Diary 1–5 Fatigue NRS*	Lower incidence of sleep disturbance in the Self-Care group. No difference between groups in sleep disturbance severity or number of self- care behaviors used. *Self-Care Diary 1–5 Sleep NRS*

Table 4

Summary of Studies of Meditation Interventions for Cancer-Related Pain, Fatigue, and Sleep Disturbance

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Carlson & Garland, 2005 (77)	63	Outpatients with cancer	One-group pretest posttest	**Mindfulness based stress reduction:** Mindfulness theory, meditation, and gentle yoga poses; met in groups for 90- minutes sessions, once / week × 8 weeks plus 45 minute home sessions 6 times a week for 8 weeks.	**None**	Not measured.	Significant improvement in fatigue pre- to post treatment. *POMS – Fatigue subscale*	Significant improvement in sleep disturbance pre- to post treatment. *Pittsburgh Sleep Quality Index*
Kieviet-Stijnen et al., 2008 (80)	47	Outpatients receiving treatment for cancer	One-group pretest posttest	**Mindfulness based stress reduction:** Training in meditation techniques, systematic body monitoring, shifting limits, recognizing thoughts, recognizing daily stresses, and techniques to relieve stress; met in groups for 150-minute sessions, once / week × 8 weeks plus 45 minute daily practice at home. One 8 hr day of silent meditation during week 6.	**None**	Measured, but not reported.	No significant changes in fatigue. *POMS, Short Form – Fatigue subscale*.	Not measured.
Moadel, et al., 2007 (81)	128	Women with stage I – III breast cancer	RCT	**Meditation:** Stretching, yoga poses, breathing, and meditation; delivered in 90- minute sessions once / week for 12 weeks plus audiotaped instructions for home practice.	**Control:** Waitlist.	Not Measured	No significant difference in fatigue between groups. *Functional Assessment of Chronic Illness Therapy-Fatigue*.	Not Measured
Shapiro et al., 2003 (82)	63	Women with Stage II breast cancer, in remission, within 2-years post- treatment	RCT	**Mindfulness based stress reduction**: Meditation techniques, body awareness, focused breathing, and gentle yoga poses delivered in 2-hour sessions, once / week × 6 weeks plus a 6-hour silent retreat.	**Control**: Free choice of stress management techniques (talking with a friend, exercising) plus workbook including support, community resources, poetry and diary for journaling. Once a week for 6 weeks.	Not measured.	Not measured.	No significant differences in sleep between groups. *Sleep Diary*

Table 5

Summary of Studies of Music Interventions for Cancer-Related Pain, Fatigue, and Sleep Disturbance

Author	N	Sample	Design	Treatment	Control / comparison	Pain Outcome	Fatigue Outcome	Sleep Disturbance Outcome
Beck, 1991 (90)	15	Outpatients with cancer- related pain	Crossover	**Music**: Personal preference of music style; listened for 45 minutes, twice a day x 3 days.	**Control**: 60-cycle hum; listened for 45 minutes, twice a day × 3 days.	Significant reduction in pain with both music and control, but no differences between groups. *McGill Pain Questionnaire Present Pain Intensity Scale Pain VAS*	Not measured.	Not measured.
Burns et al., 2008 (93)	49	Inpatients receiving intensive chemo-therapy for acute leukemia or high-grade lymphoma.	RCT	**Music**: Treatment as usual + 45-minute sessions with a music therapist twice a week × 4 weeks + recommendations to practice at least once / day with recordings of light classical or new age music.	**Control**: Treatment-as-usual	Not measured.	Fatigue scores decreased in both groups. No significant differences in fatigue between groups. *Functional Assessment of Chronic Illness Therapy-Fatigue*.	Not measured.
Cholburi, Hanucharur nkul & Waikakul, 2004 (88)	30	Hospitalized patients with cancer- related pain	Crossover	**Music**: Personal preference of music; listened for 30-minutes, twice a day × 2 days.	**Control**: Use of headphones without music; 30- minutes, twice a day × 2 days.	Significantly greater reduction in pain with music than control, but only during one trial. *Johnson Pain Scale*	Not measured.	Not measured.
Ferrer, 2007 (92)	50	Outpatients with cancer receiving chemothera py	RCT	**Music**: Personal preference of music style, played live (guitar and singing) for 20 minutes during one chemotherapy session.	**Control**: Treatment-as- usual.	Not measured.	Significantly greater reduction in fatigue in the music group. *8-cm VAS*	Not measured.
Kwekkeboo m, 2003 (91)	58	Outpatients with cancer undergoing noxious medical procedures	RCT	**Music**: Personal preference of music style played before and during the procedure.	**Distraction**: Personal preference of a book on tape played before and during the procedure. **Control**: Resting quietly before and during the procedure.	No significant differences in pain between groups. *0–10 Pain NRS*	Not measured.	Not measured.
Zimmerman et al., 1989 (89)	40	Hospitalized patients with chronic cancer pain	RCT	**Music** Preferred style of music played for one 30 minute session.	**Control**: Resting quietly for one 30 minute session.	Significantly greater reduction in pain in music group. *McGill Pain Questionnaire Pain VAS*	Not measured.	Not measured.