

Psychological and Behavioral Approaches to Cancer Pain Management

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ABSTRACT

This review examines evidence for psychological factors that affect pain across the cancer continuum from diagnosis through treatment and long-term survivorship or end of life. Evidence is convincing that emotional distress, depression, anxiety, uncertainty, and hopelessness interact with pain. Unrelieved pain can increase a desire for hastened death. Patients with cancer use many strategies to manage pain, with catastrophizing associated with increased pain and self-efficacy associated with lower pain reports. A variety of psychological and cognitive behavioral treatments can reduce pain severity and interference with function, as indicated in multiple meta-analyses and high-quality randomized controlled trials. Effective methods include education (with coping skills training), hypnosis, cognitive behavioral approaches, and relaxation with imagery. Exercise has been tested extensively in patients with cancer and long-term survivors, but few exercise studies have evaluated pain outcomes. In survivors post-treatment, yoga and hypnosis as well as exercise show promise for controlling pain. Although some of these treatments effectively reduce pain for patients with advanced disease, few have been tested in patients at the end of life. Given the clear indicators that psychological factors affect cancer pain and that psychological and behavioral treatments are effective in reducing varying types of pain for patients with active disease, these methods need further testing in cancer survivors post-treatment and in patients with end-stage disease. Multidisciplinary teams are essential in oncology settings to integrate analgesic care and expertise in psychological and behavioral interventions in standard care for symptom management, including pain.

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INTRODUCTION

Psychological factors influence both the experience of pain and the response to pain treatment for patients with cancer. Evidence also indicates that across the cancer continuum, unrelieved pain increases the risk for psychological distress. The prevalence of pain averages 53% across the cancer continuum from diagnosis through survivorship or end of life¹; 38% of cancer survivors suffer from mood disorders,² and numerous other psychosocial responses are associated with cancer pain.^{3,4} Patients are often reluctant to raise concerns about their pain or to mention discomfort that is restricting function. Barriers to communication about pain have been extensively defined and include fear that pain indicates disease progression or recurrence, not wanting to seem weak or to have treatment reduced, not wishing to disappoint or distract their oncology provider, not liking the adverse effects of treatment, not wishing to appear to be seeking drugs, or not believing something can be done to relieve cancer pain. Thus, it is important to consider psychological factors as a component of pain management in patients

with cancer in any phase of care. Psychological and behavioral treatments for cancer pain need to be considered as additions and not as alternatives to biologic treatments for cancer pain.

Randomized controlled trials (RCTs) of psychological or behavioral interventions targeting cancer pain have demonstrated clinically meaningful effect sizes. A recent meta-analysis of psychosocial interventions for pain, for example, found 37 studies worthy of inclusion; half were education focused.⁵ Other meta-analyses and systematic reviews have examined evidence for psychosocial, mindfulness, or hypnosis interventions for cancer pain.⁶⁻⁹ Most treatment efficacy trials have focused on pain during cancer treatment, with few addressing pain during post-treatment survivorship or at the end of life.

In this article, we summarize findings relevant to the effects of psychological factors on pain as well as the psychological and behavioral interventions that have been tested to relieve cancer pain. Interventions were included if they had a psychological component about thoughts, feelings, or behaviors. Many included cognitive and behavioral elements. Cognitive behavioral therapy (CBT) includes a family

Table 1. Psychological Factors Related to Cancer Pain at Diagnosis and During Treatment

Psychological Factor	Key Findings	Design	Level of Evidence*
Depression	Depression aggravates physical symptoms of pain, fatigue, and sleep disruption Depression has stronger impact on pain in patients with cancer rather than vice versa	Prospective longitudinal, cross-sectional	Strong
Distress and anxiety	Clinically significant pain is strongly and independently associated with emotional distress in patients with cancer	Prospective longitudinal, cross-sectional	Strong
Uncertainty	Greater perceived illness uncertainty confers significant risk for negative outcomes, including pain, clinically relevant distress, intrusive thoughts, avoidance behaviors, and reduced quality of life Uncertainty increases when patients lack information or knowledge to understand their condition or symptoms or when outcomes are unpredictable and resources (eg, social support, medical care, education) are insufficient to provide patients with sense of control over their illness	Prospective longitudinal, cross-sectional	Moderate for direct association with pain
PTSD	When cancer-related PTSD is untreated, pain, treatment nonadherence, desire for hastened death, and disability increase	Prospective longitudinal, cross-sectional	Weak for direct association with pain

Abbreviation: PTSD, post-traumatic stress disorder.

*Strong evidence: meta-analysis or multiple studies across diagnoses and/or longitudinal studies indicating associations with pain outcomes. Moderate evidence: single diagnosis or study with longitudinal data or multiple diagnoses with cross-sectional studies indicating associations with pain outcomes. Weak evidence: single study, single diagnosis, or cross-sectional data only indicating associations with pain outcomes.

of interventions teaching patients to respond to pain awareness with a shift in their thoughts and/or coping behaviors. Cognitive training focuses on reframing pain-related catastrophic thoughts (eg, “It’s only going to get worse,” “I can’t stop thinking about it,” “I can’t stand this”)¹⁰ by preparing alternative and more adaptive thoughts (eg, “I can do this”). Behavioral training teaches patients to use adaptive behaviors including engaging in distracting activities, pacing activities, and appropriate use of medications or physical modalities such as heat, ice, or movement. Patients may be taught to observe what increases pain and to take a pain medication before that activity, or they may learn that their pain is less disruptive in the morning so that priority activities should be done early in the day. Behavioral approaches such as relaxation, imagery, exercise, or yoga not only provide physiologic benefits but also add competing sensory input to the brain, which can shift thoughts and emotional responses. Related strategies shift focus away from pain, as with hypnosis or meditation. Educational interventions often include CBT elements that provide adaptive coping skills and address barriers to use of treatments for pain, as well as increase understanding of how to use treatment options and how to communicate with health care providers about pain. Other psychosocial methods include a focus on partner/caregiver responses to pain or supportive-expressive or meaning-centered therapies that allow patients to explore their feelings, needs, and interpretation of their experiences with a supportive and facilitating therapist. To the extent these are used for patients with cancer with pain, we also consider these.

PAIN AND PSYCHOLOGICAL FACTORS DURING TREATMENT

Cancer-related distress, clinical depression, and other mood disorders are prevalent in patients with active cancer. Indeed, pain, fatigue, and emotional distress are the three most commonly co-occurring symptoms in patients with cancer, with pain occurring in approximately 59% during treatment.¹¹ Recent estimates indicate that approximately one sixth of patients with cancer have depression and approximately one quarter have other mood disorders while actively

receiving treatment.² Moreover, major depression is clearly associated not only with pain and other symptoms but also with a decrease in adherence to treatment, longer hospitalization, increased suicide rates, a heightened desire to die, and poorer quality of life in patients with cancer.¹²

Although the association between depression and pain is well established, most studies in cancer populations have been cross-sectional (Table 1). Therefore, the temporal relationship between psychological factors and pain remains unclear. A recent important contribution is a longitudinal study examining the depression-pain relationship in cancer populations. In this study, Wang et al¹³ conclude that improvement in depression has a stronger impact on pain than vice versa. Thus, effective management of comorbid depression in patients with cancer-related pain may be important in optimizing analgesic therapy and other pain-specific treatments. These findings support the importance of screening for, monitoring, and treating both pain and depressive symptoms concurrently in patients with cancer.¹³

The psychological and emotional impact of cancer diagnosis and related pain can be influenced by many factors, including the way in which clinicians impart a diagnosis, previous history of pain and psychological morbidity, and patient personal characteristics such as personal control over life, optimism, and personality style.^{14,15} Recurrence of disease is psychologically the most difficult point in the cancer continuum for many patients. Research indicates that middle-aged patients with recurrence report the highest levels of symptom distress, depression, and anxiety across time points.¹⁴

Although there is limited research supporting a direct association between cancer-related pain and illness uncertainty, numerous studies document that uncertainty is associated with how well patients cope with their cancer symptoms. Uncertainty increases when patients lack the information or knowledge to understand their condition, when their symptoms or outcomes are unpredictable, and when psychosocial resources (eg, social support, medical care, and education) are insufficient to provide patients with a sense of control over their illness. Uncertainty confers significant risk for negative

outcomes such as clinically relevant distress and reduced quality of life, including pain.¹⁶

A cancer diagnosis and invasive cancer treatments qualify as traumatic events that can predispose patients to post-traumatic distress. Up to one third of patients experience post-traumatic stress symptoms after a cancer diagnosis, and between 3% and 22% may develop post-traumatic stress disorder (PTSD).^{17,18} Moreover, cancer is not a discrete, time-limited stressor involving the threat of death or serious injury. Rather, cancer is associated with multiple and prolonged traumatic experiences, which distinguishes it from many other stressors leading to PTSD. Cancer also carries with it a constant threat of re-emergence. When cancer-related PTSD is untreated, pain reports are higher, and there may be an increase in treatment nonadherence, desire to die, and disability.¹⁹ Unfortunately, the identification of these symptoms is often limited by clinicians' lack of training to identify and address the trauma occurring with cancer diagnosis and treatment. Evidence of successful treatments for PTSD related to cancer is being published, although impact on pain has not been examined.²⁰

Psychological and Behavioral Interventions During Treatment

Strong and consistent evidence supports the efficacy of psychological interventions for alleviating pain during procedures and disease treatment for a variety of cancer diagnoses (Table 2).

Hypnosis. Hypnosis is an increasingly used approach to symptom management in patients with cancer. It typically involves the clinician inviting the patient to focus his or her awareness and use his or her imagination to experience beneficial changes in symptoms and emotional responses. In their thorough review of hypnosis for cancer care, Montgomery et al⁸ document evidence from multiple meta-analyses and individual RCTs and conclude that hypnosis has moderate to large effect sizes when used to improve pain and distress related

to numerous aspects of cancer treatment, in addition to improving cost outcomes. Hypnosis has large effect sizes in improving pain, distress, pace of recovery, and costs associated with diagnostic procedures for breast cancer, lumbar puncture, and bone marrow aspirations in both adults and children, as well as with surgical procedures.⁸ During treatment, hypnosis has beneficial effects in reducing pain from mucositis during hematopoietic cell transplantation and reduces pain, anxiety, and the need for medication during percutaneous treatment of tumors.^{8,21} Although usually provided to an individual, hypnosis for pain related to advanced breast cancer can be successfully delivered in a group therapy setting.²²⁻²⁴ In pediatric patients, hypnosis has been shown to reduce anticipatory anxiety, procedure-related pain, procedure-related anxiety, and behavioral distress during venipuncture.⁸

Relaxation with imagery and meditation training. Relaxation training involves asking a patient to focus on letting go of muscle tension through awareness and suggestion. When used for cancer pain, it usually includes imagery and suggestions for shifts in the perception and interpretation of pain signals, thereby directly targeting the reduction of pain. Thus, relaxation training is much like hypnosis, although labeling the treatment as hypnosis improves the effect size of the intervention. Consequently, effect sizes for hypnosis tend to be larger than those for relaxation with imagery.⁸ Meta-analyses and systematic reviews indicate that relaxation with imagery has small to moderate effect sizes in reducing pain related to breast cancer treatment⁶ or when examined across multiple cancer diagnoses and treatments.^{5,7} Mindfulness-based meditation strategies have been infrequently tested for pain reduction during treatment, and some efficacy has been demonstrated for sleep and distress, but studies do not support improvements in pain.⁷

CBT. CBT approaches have been widely tested in patients with cancer for managing depression, anxiety, and quality of life related to diagnosis and treatment, with generally moderate and sometimes

Table 2. Psychological and Behavioral Interventions for Reducing Cancer Pain at Diagnosis and During Treatment

Treatment	Key Findings	Design	Level of Evidence*
Hypnosis	Hypnosis reduces multiple types of pain, in multiple cancer diagnoses, during cancer treatment, including cancer diagnostic procedures, surgery, treatment-related procedures, and treatment-related pain such as mucositis Hypnosis improves other clinical and cost outcomes associated with cancer diagnosis, procedures, and treatment	Meta-analysis, high-quality RCTs	Strong
Relaxation with imagery	Relaxation with imagery reduces cancer treatment-related pain	Meta-analysis, systematic review, RCTs	Strong
Meditation training	Meditation training has not reduced cancer-related pain	Meta-analysis, systematic review, RCTs	No evidence supports meditation effect on cancer pain
CBT	CBT that includes relaxation and imagery reduces pain and distress when tested in patients with different cancer diagnoses and treatments Most CBT includes relaxation with imagery; when imagery is not included, effects on pain are not seen consistently for patients during treatment	Meta-analysis, systematic review, RCTs	Strong for CBT with relaxation and imagery
Education with CBT components	Education with CBT coping skills training improves pain during cancer treatment	Meta-analysis, high-quality RCTs	Strong

Abbreviations: CBT, cognitive behavioral therapy; RCT, randomized controlled trial.

*Strong evidence: demonstrated to reduce pain outcomes in patients with cancer during diagnosis and treatment based on meta-analysis or multiple high-quality RCTs. Moderate evidence: reduces pain outcomes in patients with cancer during diagnosis and treatment based on two or more RCTs. Weak evidence: reduces pain in patients with cancer during diagnosis and treatment based on single RCT or nonrandomized trials.

large effect sizes found.^{25,26} Fewer studies have directly targeted cancer pain reduction using CBT. A meta-analysis concluded that CBT techniques have beneficial effects on pain and distress in women with breast cancer, finding moderate effect sizes.⁹ Other meta-analyses have examined CBT for cancer pain, usually including relaxation with imagery training, and have found small to moderate effect sizes, although it is not clear that the effects extend beyond those seen with relaxation and imagery alone.^{5,6,27}

Educational and other psychosocial interventions for pain. Educational methods that address barriers to pain treatment and teach patients to understand and communicate their pain and medication needs have resulted in reduced pain, with generally small to moderate effect sizes in meta-analyses.^{5,28,29} An essential component needed for efficacy of educational methods for pain reduction seems to include enhancement of self-efficacy or confidence in one's ability to manage pain.²⁹ Other supportive interventions have been tested for reduction of symptoms including pain, with effect sizes generally smaller than those of the strategies reviewed in this article.⁵⁻⁷

Exercise. In a Cochrane review, Mishra et al³⁰ identified 56 articles testing exercise interventions with patients just before or during treatment. Remarkably, pain was not a reported outcome in most of these studies. One RCT evaluated the impact of a walking intervention on self-reported physical function and pain during chemotherapy or radiation therapy in patients with a variety of cancer diagnoses.³¹ This study found that increased doses of exercise were associated with decreased pain at the end of cancer treatment. A second longitudinal RCT found that exercisers during treatment reported lower fatigue and depression scores at completion of treatment, but not improved sleep disturbance or pain.³² Additional research on the impact of exercise on specific types of cancer- and treatment-related pain will add important information to this understudied yet important clinical issue.

Clinical Implications of Pain During Treatment

Psychological factors have major impacts on pain for patients with cancer at diagnosis and during treatment. Addressing depression,

anxiety, uncertainty, and hopelessness and providing psychological and behavioral strategies for pain management can help to relieve this pain and suffering. High-quality evidence indicates that education, hypnosis, relaxation, and imagery, as well as education that includes coping skills, can be effective in reducing pain when added to analgesic treatment. The effect sizes and stability of effects for these methods are substantial enough to support their inclusion in standard care for cancer pain during treatment.

PAIN AND PSYCHOLOGICAL FACTORS DURING SURVIVORSHIP

After the completion of treatment, pain commonly co-occurs with other symptoms such as fatigue, insomnia, chemotherapy-induced peripheral neuropathy, and emotional distress or depression.³³ Although the prevalence of pain in survivors varies widely with disease, type of treatment, and time since treatment, estimates range from 20% to 40% of survivors reporting pain.^{1,34} Importantly, although fatigue and distress are more prevalent in survivors, pain is more strongly associated with disability.³⁵ Until recently, there have been few standards for managing chronic pain in survivors, because guidelines have focused on pain during active treatment, where unrestricted opioid use has been the standard of care.³⁶ As patients transition into the post-treatment survivorship phase of care, their pain may continue as chronic syndromes such as neuropathy, lymphedema, myalgias, arthralgias, and genital pain.³⁷ Although opioids may be considered for some chronic pain syndromes, concerns such as adverse effects, tolerance, and addiction potential reduce their long-term suitability for many survivors.^{33,37-39} For these survivors, psychological aspects of their pain are particularly relevant.

Emotional distress, insomnia, fatigue, physical activity, and physical function are clearly associated with persistent pain after recovery from treatment (Table 3). Younger survivors seem to be particularly vulnerable to higher levels of pain after treatment.⁴⁰ Most research on pain in survivors has involved women who have completed treatment

Table 3. Psychological Factors Related to Cancer Pain in Survivors

Psychological Factor	Key Findings	Design	Level of Evidence*
Depression and anxiety	Depression and anxiety are associated with increased pain across ethnic groups Depression predicts long-term pain, including postmastectomy pain, after breast cancer	Longitudinal, cross-sectional	Strong
Loneliness	Loneliness is associated with greater pain and fatigue in breast and colorectal cancer survivors	Longitudinal	Moderate
Catastrophizing	Catastrophizing thoughts about pain are associated with increased postmastectomy pain in breast cancer survivors	Cross-sectional	Weak in survivors
Fear of recurrence	Pain is associated with increased fear of recurrence across racial and ethnic groups in breast cancer survivors	Cross-sectional	Weak
Fatigue	Pain and fatigue symptoms are associated across diagnoses in survivors and specifically after prostate and breast cancers in several racial groups	Cross-sectional	Moderate
Sleep	Sleep problems are greater in survivors of multiple diagnoses who also report more pain Association of sleep and pain continues long term in survivors of cancer	Cross-sectional	Moderate
Physical activity	Higher levels of physical activity are associated with lower pain levels	Longitudinal, cross-sectional	Strong

*Strong evidence: meta-analysis or multiple studies across diagnoses and/or longitudinal studies. Moderate evidence: single diagnosis or study with longitudinal data or multiple diagnoses with cross-sectional studies. Weak evidence: single study, single diagnosis, or cross-sectional data only.

for breast cancer. In these women, higher levels of pain catastrophizing and fear of recurrence are associated with increased pain, most notably for postmastectomy pain.⁴¹⁻⁴³ Depression is strongly associated with pain, even 4 years after breast cancer treatment,⁴ and is associated with suicidal ideation in adult survivors of childhood cancer.⁴⁴ Furthermore, pain predicts the later development of depression in breast cancer survivors.⁴⁵ A study that followed breast cancer survivors from 40 months after diagnosis to 10 years after diagnosis found that one third reported increased pain over time.⁴⁶ Women with weight gain > 5% and those not meeting physical activity guidelines were at greater risk for increased pain 10 years after diagnosis.

Psychological and Behavioral Interventions for Pain During Survivorship

Clinical trials of psychological and behavioral interventions to relieve pain in the survivorship phase of the cancer continuum have largely been tested among breast cancer survivors, and many of these interventions have involved exercise (Table 4).

Physical activity. Tested activity interventions vary from strength or resistance training to walking, cycling, yoga, Qigong, or Tai Chi. Findings of a meta-analysis and Cochrane review of cancer survivors indicate that structured activity programs reduce fatigue and anxiety and improve physical function, self-esteem, body image, emotional well-being, social functioning, sleep, and sexuality.^{47,48} Unfortunately, pain rarely has been a primary or secondary outcome in these survivorship studies. However, resistance training may be particularly beneficial for musculoskeletal pain. In an RCT of exercise for head and neck cancers, progressive resistance exercise reduced upper extremity pain and disability more than standard therapeutic exercise.⁴⁹ CBT and group support elements may also be valuable in enhancing the impact of exercise. An RCT of combined physical activity and CBT for breast cancer survivors reduced pain along with other quality-of-life

improvements.⁵⁰ Also, mixed diagnosis patients participating in a community-based strength training program reported reduced pain and improved function in a pre-post study design.⁵¹ Studies underway are testing telehealth and online strategies for reaching underserved cancer survivors with activating interventions, with pain as a secondary end point.⁵²

Yoga. The impact of yoga on pain in survivors has varied from having insignificant to large effect sizes.⁵³ Aromatase inhibitor-associated arthralgias may be especially responsive.^{54,55} Many yoga programs for cancer survivors include meditation and CBT components. For instance, a yoga of awareness program reported by Carson et al⁵⁴ included CBT elements along with meditation and breathing exercises and found improvements in joint pain in breast cancer survivors.

Meditation, hypnosis, and CBT. No RCTs have specifically tested CBT for pain in cancer survivors post-treatment, although a small study with a pre-post design suggests some promise for reducing chronic pain and improving pain coping success with CBT for survivors.⁵⁶ As with yoga and exercise, most studies of meditation for survivors have focused on improved sleep, fatigue, and stress rather than pain, and when pain has been assessed, it has generally not shown significant improvement with meditation.⁵⁷ In contrast, hypnosis research for reduction of pain in survivors has been minimal, but hypnosis may be promising. A small pre-post assessment of hypnosis for pain, fatigue, sleep, and hot flashes in breast cancer survivors found reduced pain and fatigue with improved sleep; a larger RCT is in process.⁵⁸

Clinical Implications of Pain During Survivorship

Psychological and behavioral aspects of pain have been remarkably underconsidered in cancer survivorship research. Only in breast cancer is there an adequate body of work to even begin to consider

Table 4. Psychological and Behavioral Interventions for Reducing Cancer Pain in Survivors

Treatment	Key Findings	Design	Level of Evidence*
Physical activity	Few exercise studies of survivors include pain as outcome; results range from no effect to large effect on pain Exercise programs combined with group support and CBT elements are effective for pain Progressive resistance exercise reduces musculoskeletal pain in survivors	Meta-analyses, systematic reviews, high-quality RCTs, nonrandomized trials	Moderate, given infrequent inclusion of pain as outcome in RCTs
Yoga	Yoga programs often include CBT and meditation Small studies suggest potential for improvement in pain severity, with fatigue and other quality-of-life outcomes more consistently measured and found	Combined intervention meta-analysis, single small RCT, pre-post test	Weak
CBT	Studies with survivors have tested CBT in RCTs only as a component with other treatments, such as exercise, yoga, or meditation Small studies of CBT alone or when combined with yoga or exercise suggest it may be helpful for managing chronic pain in survivors	Combined intervention meta-analysis, pre-post test for CBT alone	Weak
Meditation	Pain is rarely included as outcome in meditation studies; when it is included, no evidence is found for direct effects on pain outcomes	Combined intervention meta-analysis, one RCT, several pre-post tests	Weak
Hypnosis	Preliminary evidence suggests potential for reducing pain in breast cancer survivors	Pre-post test	Weak

Abbreviations: CBT, cognitive behavioral therapy; RCT, randomized controlled trial.

*Strong evidence: demonstrated to reduce pain outcomes in cancer survivors post-treatment based on meta-analysis or multiple high-quality RCTs. Moderate evidence: reduces pain outcomes in cancer survivors based on two or more RCTs. Weak evidence: reduces pain in cancer survivors based on single RCT or nonrandomized trials.

needs and interventions that may be effective. This may result from the diversity of pain syndromes in survivors and the lack of consistently effective medical treatments to drive research funding. Opioids, which are the mainstay of pain approaches during treatment, are of limited value for most chronic pain syndromes seen in long-term survivors.³⁶ Physical modalities, rehabilitation, and psychological or behavioral interventions hold promise but urgently need further study. At this point, research provides preliminary support for the benefits of physical activity, yoga, and hypnosis for pain reduction and related improvement in function for long-term cancer survivors. CBT and meditation, as with these other methods, require further investigation to determine whether there are syndromes that respond to these treatments.

PAIN AND PSYCHOLOGICAL FACTORS AT THE END OF LIFE

Unrelieved pain is one of the most feared and most frequently experienced symptoms that can occur in the last months of life.⁵⁹ Patients with advanced disease typically experience pain that is more severe and that occurs in more sites than patients with early-stage disease.⁶⁰ Although the severity and source of pain may vary, estimates indicate that pain occurs in up to 70% to 90% of patients with cancer at end of life (EOL).^{61,62} Individuals with advanced disease who have pain are more likely to experience problems with important daily activities such as eating, washing, transferring from one position to another, walking, and sleeping.⁶² In advanced cancer, pain is often viewed as a continuous reminder of disease progression, death, and uncertainty.⁶³

The context of pain at EOL is complex. Pain is usually one of numerous significant symptoms including fatigue, weakness, confusion, anorexia, constipation, weight loss, and urinary and bowel prob-

lems.^{64,65} Medications (nonopioids, opioids, adjuvant medications) are the mainstay of cancer pain treatment at EOL^{66,67}; however, problems common at EOL, such as confusion/dementia, physiological changes that modify the bioavailability of medications, and increased risk of adverse events, complicate pain assessment and management. Finally, even at EOL, patients may be reluctant to report pain, may be fatalistic about pain, or may be fearful of addiction.^{68,69} With recognition of the limitations of a strictly biomedical approach to pain at EOL has come increased interest in how psychological factors and interventions can influence the pain experience.

A growing number of studies have examined psychological factors that influence pain in patients at EOL or who have advanced disease (Table 5). Zaza and Baine⁷⁰ conducted a meta-analysis examining how anxiety, depression, emotional distress, fear, and worry were related to cancer pain. Of the 14 studies reviewed, nine included terminally ill patients or patients with advanced cancer. Results provided strong evidence that high levels of psychological distress were related to more severe pain, although most studies were cross-sectional.

Among patients with pain at various stages of their disease, desire for a hastened death (DHD) has been found in 32%.⁷¹ At EOL, patients vary in their will to live, and some report DHD.⁷² Both pain and functional impairment caused by pain predict DHD.⁷²⁻⁷⁴ As in other populations, hopelessness and the severity of depression also are strong predictors of DHD.

Confronted with pain, most patients develop ways to deal with it. Among strategies used to cope with pain at EOL are distraction, imagery, relaxation, changing activity patterns, and prayer.⁶⁰ There is little evidence that any one of these strategies is consistently related to pain severity. However, there is evidence among patients with

Table 5. Psychological Factors Related to Cancer Pain in Patients With Advanced Disease or at End of Life

Psychological Factor	Key Findings	Design	Level of Evidence*
Psychological distress	In patients with advanced disease, pain severity and interference are associated with emotional distress, depression, anxiety, and hopelessness Patients who report high level of spiritual pain report higher levels of depression, but not physical pain	Cross-sectional, longitudinal	Strong
DHD	Pain severity in patients with advanced cancer is not consistently associated with DHD Functional impairment caused by pain, severe depression, or hopelessness is consistent predictor of DHD	Cross-sectional, longitudinal	Moderate
Pain coping and appraisal	Patients with advanced cancer use wide variety of pain coping behaviors, including religious practices, positive self-statements, distraction, pleasant imagery, expression of feelings, avoidance of movement, repression, catastrophizing, and crying/moaning Patients who use catastrophizing as coping style or feel more helpless report more severe pain as well as symptom distress and engage in higher level of pain behavior Self-efficacy related to pain control is associated with lower pain severity and interference and higher quality of life	Cross-sectional, longitudinal	Strong
Caregiver response and pain level	Pain can disrupt relationships at end of life Concerns about pain are second most frequent problem reported by relatives caring for patients with advanced cancer in home Patients report higher levels of pain and pain behavior when their caregiver partners are ambivalent about expressing their own emotions; caregiver partners indicate more relationship interference when patients report more pain	Cross-sectional	Weak

Abbreviation: DHD, desire for hastened death.
*Strong evidence: meta-analysis or multiple studies across diagnoses and/or longitudinal studies. Moderate evidence: single diagnosis or study with longitudinal data or multiple diagnoses with cross-sectional studies. Weak evidence: single study, single diagnosis, or cross-sectional data only.

advanced cancer that beliefs about pain coping abilities are related to pain. For example, patients who engage in pain catastrophizing report much higher pain, whereas those reporting high self-efficacy, lower helplessness, and high perceived ability to control pain report much lower pain.⁷⁵⁻⁷⁷ Patients with advanced cancer who spend time in private religious activities before their diagnosis report higher quality of life, including symptoms such as pain.⁷⁸

Caring for a loved one who is dying and in pain is one of the most stressful experiences that one can go through.⁷⁹ Concern about pain is the second most frequent problem reported by relatives caring for patients with advanced cancer in the home.⁸⁰ When patients with metastatic disease report more pain, their partners report more relationship disruption.⁶⁸ Caregivers who are confident they can help their loved one manage pain at EOL report lower caregiver strain and better mood.⁷⁵ Patients are also influenced by their caregivers' reactions. When caregivers have difficulty expressing their emotions, patients are more likely to report higher levels of pain and pain behavior.⁷⁵ However, although encouraging patients to express cancer-related emotions to their partner has demonstrated value to couples' relationships, it has not directly affected pain.⁸¹

Psychological Interventions for Managing Cancer Pain at EOL

Few interventions have focused on patients specifically at EOL, although numerous clinical trials have enrolled patients with metastatic disease (Table 6). No differences in the effects of these interventions have been detected when used for patients with versus without metastases.⁹

Training in pain coping skills. Education-oriented interventions that include CBT components and often relaxation with imagery have been used effectively to teach patients skills for managing pain at EOL. A meta-analysis of 37 studies (26 of which included samples where > half of patients had advanced disease) found that such skills-based interventions improved pain severity and pain interference.⁵

Hypnosis. In several RCT replications, when self-hypnosis training is included with supportive-expressive group therapy for women with metastatic breast cancer, pain increases are less over the year of therapy.^{6,22-24} Further research is needed to clarify whether these effects extend to patients with other advanced cancers and whether the effects can be attributed to the hypnosis or the year-long group therapy.

Clinical Implications of Pain During Advanced Disease and EOL

There is growing evidence that psychological factors such as high levels of distress or pain catastrophizing can heighten the severity and impact of pain in patients with advanced disease. Unfortunately, most studies rely on cross-sectional designs, making it difficult to determine if psychological factors lead to increased pain or vice versa. Nevertheless, with mounting evidence on the effects of psychological factors on pain has come increased interest in psychological interventions that reduce pain experienced by patients with advanced disease. Although there is strong evidence from RCTs that skills-based training in pain coping strategies and hypnosis can reduce pain in patients with advanced disease, relatively few treatment studies have specifically focused on patients at EOL. For skills training, little information is available on which patients and caregivers are likely to respond best to these interventions or how comorbid conditions common at EOL can affect response to training.

DISCUSSION

Evidence is irrefutable that psychological factors contribute to increased pain and suffering among patients with cancer and their families across the cancer continuum. As reviewed here, psychological and behavioral interventions have clinically meaningful impacts on this pain and suffering, with effect sizes that range from large to small. However, numerous gaps exist in knowledge regarding which strategies are effective for which pain syndromes during which phases of care. Hypnosis and educational strategies that include cognitive behavioral coping skills to enhance self-efficacy have the strongest evidence of high-quality RCT support, with hypnosis demonstrating large effect sizes and education demonstrating small to moderate effect sizes. Studies indicate that patients with diverse racial, ethnic, and socioeconomic status respond equally well to these interventions, although when pain is the primary focus rather than a secondary target of the intervention, effect sizes are larger.⁵ On the basis of the findings that psychological and behavioral interventions reduce pain in patients and long-term survivors, access to these treatments and integration of providers with expertise in these methods need to be standards of care for oncology programs.

Table 6. Psychological and Behavioral Interventions for Reducing Cancer Pain in Patients With Advanced Disease or at End of Life

Treatment	Key Findings	Design	Level of Evidence*
Training in pain coping skills	Coping skills for managing pain (eg, education with CBT and relaxation with imagery) improve pain severity and interference for patients across disease stage, including advanced disease Results specific to coping skills training or other psychological or behavioral strategies for pain in patients with end-stage disease are small and inconclusive	Meta-analysis, high-quality RCTs	Strong
Hypnosis	Hypnosis in support-group format improves pain in women with metastatic breast cancer, including some who are at end of life	Replicated high-quality RCTs	Strong

Abbreviations: CBT, cognitive behavioral therapy; RCT, randomized controlled trial.
 *Strong evidence: demonstrated to reduce pain outcomes in patients with cancer with advanced disease or at end of life based on meta-analysis or multiple RCTs. Moderate evidence: reduces pain outcomes in patients with cancer with advanced disease or at end of life based on ≥ two RCTs. Weak evidence: reduces pain outcomes in patients with cancer with advanced disease or at end of life based on single RCT or nonrandomized trials.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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