

Review

## Addressing Symptom Clusters with Complementary and Integrative Health Therapies in Palliative Care Populations: A Narrative Review.

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### Abstract

Both palliative care (PC) and integrative medicine (IM) focus on the whole person to optimize wellbeing. Integrative palliative care combines the best of both approaches in relieving the distressing symptoms of serious illness and its treatment by combining evidence informed, pharmacological and nonpharmacological modalities that are aligned with the person's goals, values and preferences. Healing is valued, as well as symptom relief, shared decisionmaking, person empowerment, compassionate care, and nurturing of hope. Increasingly, symptom clusters in serious illness are being recognized and addressed in both PC and IM. Symptom clusters arise from the complexity of the physical, psychological, social and spiritual aspects of a person interacting with serious illness. Many complementary and integrative health (CIH) modalities address symptom clusters effectively, and may allow for reduced doses of medication and their resulting side effects, or help alleviate the need for medication altogether, and increase



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health, healing and well being. Research reveals that the public desires more access to CIH including palliative care settings although actual delivery of these services in health care settings remains limited. This review explores the evidence for a combined palliative care and integrative medicine approach to symptom clusters experienced by people with serious illness through increased access and funding of these services in the community and health care settings with quality practitioners.

### **Keywords**

Integrative medicine; palliative care; symptom clusters; integrative palliative care

## **1. Introduction**

Palliative care (PC) is a medical specialty that focuses on addressing symptoms in advanced, chronic and life-limiting illnesses. PC in the last months of life is referred to as hospice care. PC draws from interprofessional teamwork, communication skills that clarify a person's values and preferences, empowerment of people with serious illness to join with their clinicians and interprofessional care teams in shared decision-making, support of caregivers, and advance care planning [1]. Primary palliative care includes the palliative care skills of symptom management, advance care planning and communication that are within the clinical toolbox of all health care practitioners.

Integrative medicine (IM) broadens the interprofessional team approach to include other modalities and practitioners that are often outside of mainstream, conventional care, and referred to as complementary and integrative health (CIH) practitioners. Examples of CIH therapies include supplements, acupuncture, yoga, energy healing, etc. Integrative therapies, integrative medicine and integrative practitioners combine the best of conventional medicine with evidence informed therapies outside of mainstream, conventional medicine to achieve health, wellbeing and relief of distressing physical, psychological and spiritual symptoms. Integrative medicine highlights the empowerment of people taking charge of their health, and the integration of strategies for promotion of optimal health and healing including pharmacological and non-pharmacological means, and whole person care [2]. In palliative care populations, this translates to optimal symptom management resulting in best possible function and quality of life (QOL).

Palliative care and integrative medicine/CIH and their interventions are evidence-informed, and tailored to the person's goals, values and preferences [2]. Serious illness is often a strong motivator for people to reassess their health goals, and incorporate changes to their lifestyle that optimize well-being, slow the progression of disease, reduce symptom burden of the illness and treatments, and generally promote healing, meaning and purpose in living fully [3]. When a serious illness is diagnosed, people often reassess their lifestyle choices, and reach out to a variety of practitioners to support them through this illness trajectory. At this point, both integrative medicine and palliative care are appropriate and often desired to decrease fear, increase control, foster hope, and move forward in wellness through serious illness treatment and living fully[1-3].

Symptoms of serious, chronic illness are increasingly recognized as occurring in clusters rather than isolated symptoms treated one at a time. Integrative approaches generally address the whole person and clusters of symptoms or distress. Symptom clusters in cancer, renal disease, HIV disease, heart disease, etc, are increasingly being recognized [4]. Advanced renal disease, for example, includes the symptom cluster of fatigue, pain and depression [5]. Anticipated symptom clusters can often be treated proactively with an integrative strategy [6]. Research by Avis et al, found that high symptom burden profiles in women with breast cancer significantly decrease quality of life (QOL), and that QOL was more affected negatively with high psychological symptom burden as opposed to high pain burden [7]. Many CIH modalities promote emotional/psychological wellbeing while decreasing physical symptoms.

In December 2012 through March 2016, the Palliative Care Quality Network analyzed symptom assessment data from 38 inpatient palliative care teams nationally. They found that symptoms are related to others, and that the relief of one symptom is often associated with the improvement of another. Improvements in pain were correlated with relief of anxiety, nausea and dyspnea. Improving anxiety improved pain by a factor of 2.9, and dyspnea by 1.4. Comfort focused care improved pain significantly, and relief of pain, anxiety and dyspnea reduced hospital length of stay. Those with moderate to severe nausea were 3.7 times more likely to have pain as compared to patients with little to no nausea. These findings reveal that a symptom does not occur in a vacuum, but interdependent with other symptoms including their degree of severity and relief. The conventional strategy of symptom control typically addresses one symptom at a time, as though symptoms occur independently from others [8].

CIH modalities ideally reduce the need for medication to control symptoms. Drug side effects and drug-drug interactions can increase symptom burden. The drugs that are the most serious offenders are antiepileptics, antidepressants, corticosteroids, and opioid and nonopioid analgesics. Serious side effects such as liver and renal toxicity, sedation, delirium, etc. can occur. But less serious side effects of opioids alone can add to symptom clusters and symptom burden. Opioids can cause pruritus, nausea and vomiting, sedation, myoclonus, constipation, etc. If opioids for pain can be minimized with nonpharmacological means, the patient has improved QOL and fewer iatrogenic symptoms [9].

In this review, we will describe what are the most common complementary and integrative therapies used in PC, the common symptom clusters addressed by CIH therapies in PC settings, and the state of the delivery of CIH therapies in PC settings.

## **2. Most Common CIH Therapies Used in PC**

In both PC and IM, a variety of conventional and CAM modalities can be used synergistically to avoid over-reliance on drug therapies to address symptom clusters. They also address symptoms in their complexity on all levels of wellness and distress including social, physical, emotional and spiritual aspects of whole person care. CIH modalities promote wellness, healing and symptom relief. Patient values and preferences must be elicited with attentive listening, presence, putting aside clinician agendas, and asking about therapies that the patient already finds essential to promoting health [10].

## **2.1 Mindful Movement**

Many of the investigations on exercise improving symptom clusters are in advanced cancer research. Exercise improves fatigue, pain, functional capacity, mood, and QOL. Often, seriously ill patients are discouraged from movement due to concerns that movement will cause them more fatigue. Movement must be consistent with the functional capacities and desires of the person. In a review of 15 RTC's, exercise in advanced stage cancer improved QOL, fatigue, insomnia, physical function, social function and dyspnea reduction [11]. In another meta-analysis of RTC studies of people with advanced solid tumor cancers, exercise improved QOL and fatigue [12].

There is evidence for exercise and yoga improving anxiety and depression [13]. Tai Chi improves cancer related fatigue, and a reduced effect on physical and emotional fatigue. Yoga improves QOL, decreases fatigue and improves sleep in a recent Cochrane Review [14]. Qigong can improve QOL, fatigue, depression and anxiety, and reduce inflammation (C reactive protein measure) in cancer patients [15]. In people with Parkinson's Disease, a RCT of yoga versus stretching and resistance training improved anxiety and depression, and improved motor function [16].

## **2.2 Supplements**

The use of nutraceuticals in the US is ubiquitous. It is estimated that 3 out of 4 adults consume supplements and botanicals [17]. In integrative palliative care (IPC), polypharmacy with nutritional supplements and pharmaceuticals at end-of-life (EOL) in particular, are ideally reduced with a careful assessment of risk/benefits of each entity, and open, nonjudgmental discussion about a person's choices, thoughts of benefit, and practitioners knowledge of potential harm or drug/drug/nutraceutical interactions. Too many supplements (or drugs) with minimal benefit can increase the burden on the patient financially and physically, and should be avoided. Each supplement and medication that is deprescribed should be fully discussed with the patient in shared decisionmaking, with the clinician being aware of the reasons why the patient has chosen to take that supplement and a fully informed discussion and education about benefits and potential harm or burden to the patient of continuing that supplement. Patients and families might hold strong beliefs about certain supplements, and those should be continued unless there is a potential harmful effect or the person is no longer able to swallow them [3]. Medications should be de-prescribed only after discussion with the primary clinician prescriber and the patient.

Vitamin D is essential for health, and a deficiency state is common in seriously ill patients who have limited sun exposure. Sources of vitamin D in food are limited. Supplementation with vitamin D3 can prevent deficiency states that could lead to fatigue, myalgias, and vague not feeling well states, increased mortality and decreased immune function [18].

Cannabis is a substance that can help with chronic pain, anxiety, appetite, depression, and fatigue. Although currently legal in 33 states and the District of Columbia, it remains a controlled substance (Schedule 1) on the federal level with no therapeutic benefits recognized [19]. Despite federal regulations, research continues on the uses of cannabis for a variety of symptoms associated with serious illness. In 2017, the National Academy of Sciences, Engineering and Medicine published a report

on the evidence supporting the use of cannabis in medicine. The reviewers found strong evidence for the use of cannabis for chronic pain, patient reported muscle spasticity in multiple sclerosis (MS), and chemotherapy induced nausea and vomiting. Limited evidence exists for improvement of insomnia due to sleep apnea, fibromyalgia, chronic pain and MS. There was insufficient evidence to support cannabis use for cancer related cachexia and anorexia [20]. Karim et al found that authorizations for cannabis use in Canada between 2014 and 2016 in people with a cancer diagnosis were associated with younger age, active cancer treatment and more serious illness[21].

The cannabis plant has more than 100 different components, including cannabinoids, flavonoids and terpenoids, with delta-9-THC being the most psychoactive component. Cannabidiol (CBD) also has powerful therapeutic effects, but without psychoactive side effects, and can help modulate and enhance the central nervous system effects of THC (called the “Entourage Effect”) [22]. Cannabinoid receptors are located in the central and peripheral nervous system (CB1) and the immune system (CB2) [23]. A great deal more research is needed to understand the full breadth and applications for this plant and its components in improving well-being [22].

Medical cannabis has a potential role in PC for the relief of anorexia, pain, nausea, insomnia, depression, pain, and anxiety according to Abrams and Guzman. Oral forms are longer acting but have variable bioavailability in the GI tract. Inhaled or vaporized forms are shorter acting, and more immediate in effect. The cytochrome P450 enzymes in the liver are affected by cannabis, which can affect the metabolism of other drugs [24].

In a review of 165 studies on medical marijuana use, less than 7 mg of THC is considered as low dose, 7–18 mg as medium dose, and greater than 18 mg as high dose. Tolerance occurs generally in a few days through downregulation of cannabis receptors [25]. Most side effects of cannabis are due to THC and include dizziness, dry mouth, sedation, fatigue, headache, hypotension, irritability, and poor memory or concentration. More serious side effects include paranoia, psychosis, and disorientation [26]. Psychoactive side effects can worsen mental illness, psychotic illness, dementia, or delirium. Addiction potential is much less than alcohol, opioids and other drugs of addiction, but higher in heavy chronic users and adolescents. Cannabis intoxication can cause transient psychosis. Cannabinoids can inhibit hepatic enzymes and interfere with drug concentrations of antiviral medications and warfarin [20, 27].

### **2.3 Mind-Body Therapies**

Because each individual experiences symptoms uniquely, it is useful to utilize a variety of different mind-body therapies to address chronic pain, fatigue, anxiety, depression and insomnia. These symptoms, which typically occur in clusters, are experienced on a subjective level, and therefore using techniques that help to alter the way in which the symptoms are experienced can assist in the decreasing that symptom or cluster of symptoms. For example, physical pain is modulated by the mind in perceiving and interpreting the stimulus of symptoms such as pain (in chronic pain, stimulus is no longer able to be identified) [28]. Mind body therapies work on chronic pain by activating modulating areas of the brain, decrease sympathetic nervous system (SNS) activation, activates the

parasympathetic nervous system (PNS), and hormones released, and regenerates neuronal tissue. By activating the PNS and decreasing SNS, anxiety and stress are decreased as well [29].

#### **2.4 Mindfulness-Based Stress Reduction**

Mindfulness-based stress reduction (MBSR), developed by Jon Kabat-Zinn and having its basis in vipassana meditation, incorporates several modalities that can be used with PC patients. These include walking, sitting, or lying meditation, body scan meditation, gentle movement and Hatha yoga, and breath awareness [30]. MBSR is typically taught in an eight-week program and a meta-analytic review of MBSR found that participants who completed this program experienced reductions in chronic pain, depression, anxiety and stress. These types of symptoms are often experienced by patients facing serious disease or at the end of life [31, 32]. Using the techniques of MBSR can also increase calmness and peace, quality of life, and well-being [22, 33]. Even a single class in MBSR was found by one study to increase well-being and reduce symptoms of anxiety, fatigue and dyspnea. (38) One large meta-analysis from Boston University [33] found that mindfulness had a moderate effect size in improving anxiety and depressive symptoms. For patients with both anxiety and mood issues, mindfulness training had a larger effect size. These changes were robust and maintained over time. Another meta-analysis showed improvements in depression, anxiety, and pain from mindfulness [34].

Mindfulness has also been effective in addressing the psychological stressors and coping with chronic and life-threatening illnesses [35]. In cancer patients, studies have shown mindfulness is associated with improvements in mood and a reduction of stress [36] and improvements in quality of life [37]. Research also supports mindfulness for coping with rheumatoid arthritis, cardiovascular disease, diabetes, HIV/AIDs, irritable bowel syndrome, organ transplant, chronic pain, and fibromyalgia [35].

#### **2.5 Hypnosis and Guided Imagery**

Similar to MBSR, hypnosis and guided imagery can help to reduce pain, stress and anxiety. They can also help to attenuate nausea and vomiting in patients undergoing chemotherapy. (41) A study of clinical and self-hypnosis found that PC patients receiving hypnosis as an adjuvant therapy experienced significantly less anxiety and pain and received less pain medications up to two years after the intervention. The control group were 4 times more likely to need an escalation in analgesic medication [38]. Hypnosis promotes relaxation and helps to focus attention, which has been shown to improve well-being and resilience when facing death [39, 40]. It was found that nurse led guided imagery in an inpatient PC unit, decreased pain, heart rate, respiratory rate and increased comfort for patients [41].

#### **2.6 Music Therapy**

Music therapy consists of many therapeutic approaches that range from listening to music that a person finds enjoyable, relaxing and uplifting or music that is created or played for a therapeutic purpose generally delivered by a music therapist. The former intention of this modality is passive, and the latter form is more active and prescriptive. In a meta-analysis and systematic review of music

therapy in terminally ill patients, Yinyan et al. found that this CIH modality significantly reduced anxiety, depression, pain and insomnia, and improved mood and QOL. It did not seem to have an effect on fatigue [42]. Gao et al. also performed a similar analysis of 11 RCT's and found that music therapy significantly reduced pain, anxiety, depression, and improved emotional function and QOL [42]. The duration of the music therapy does not have to be long, and in a review of 18 RCT's in ICU's, music therapy for 20-30 minutes reduced pain scores by about 1.06 on a 10 point scale [43]. In another study, prescribed music sessions for 30 minutes five times a week compared to ambient music relieved pain and fatigue [44, 45]. Harp music therapy in one study relieved anxiety, fear, dyspnea, nausea, and pain, and helped 77% of patients [46]. Music therapy can help relieve depression, and in one study reduced pain intensity by 70%, and decreased opioid requirements [47, 48].

## **2.7 Massage**

Many forms of massage therapy can have a therapeutic effect on symptom clusters. Multiple studies have shown efficacy for relief of pain, anxiety, depression, and insomnia [49-58]. In a large study of cancer patients, massage relieved pain, fatigue, anxiety and nausea by 50% [59, 60]. Hand massage can help with dementia related agitation by promoting relaxation [61]. Massage therapy is offered frequently in hospice settings due to benefits of touch, and relaxation[62-64].

## **2.8 Aromatherapy**

Aromatherapy is often combined with massage therapy, but can also be used alone in a diffuser or on a cotton ball attached to the patient's garments. Small studies that used aromatherapy alone found that lavender can help decrease anxiety, rosemary oil can increase alertness and reduce anxiety, and spearmint and peppermint oils can help relieve nausea due to chemotherapy [65-67]. In a systematic review of aromatherapy, massage and reflexology studies, these modalities were reported as frequently used in PC and hospice settings, but with limited quality evidence for positive outcomes[68]. In another systematic review, aromatherapy massage showed benefit for psychological well-being and anxiety. Limited evidence existed for benefits in nausea, pain, and depression [69].

## **2.9 Healing Touch, Therapeutic Touch and Reiki Therapy**

Reiki, healing touch and therapeutic touch are considered biofield therapies. Healing touch and therapeutic touch include a focus on the part of the practitioner to heal the patient through a transfer of energy from the environment, through the practitioner to the patient without actually touching the patient. In a systematic review and a study of hospital inpatients, these healing modalities reduced pain, anxiety and increased relaxation [70-72]. Reiki therapy balances energy fields of the patient. Here a light touch is often used. Reiki may reduce pain and anxiety [73]. In one review of biofield therapies, Hanneghan and Schnyder found that these therapies can relieve pain, improve QOL and wellbeing, and reduce stress [70]. Results of another study were inconclusive [74].

## **2.10 Acupuncture and Traditional Chinese Medicine**

Acupuncture is a complex CIH modality that addresses the whole person and not just a specific symptom. This is one reason acupuncture is an ideal modality to treat symptom clusters. Evidence shows that it can effectively treat nausea, pain (both nociceptive and neuropathic), anxiety, fatigue, and increase well being. Other studies also shows a positive effect on insomnia, depression, vasomotor instability, and xerostomia [75-82]. At a National Cancer Institute's conference on acupuncture, this modality was found to be safe and effective. They expressed caution with acupuncture for those patients who are neutropenic, and thrombocytopenic. In a meta-analysis of 20 RCT's of acupuncture in oncology patients, they found that acupuncture combined with analgesics provided faster pain relief with improved QOL [83].

## **3. Delivery of CIH Therapies in PC Settings**

CIH use in hospice and palliative care settings is popular, yet accessibility of these services is challenging. For profit hospices in a survey of hospices in Texas were 4 times less likely to offer CIH services [84]. Larger hospices and non-profit hospices located in the Northwest regions of the US were more likely to employ a CIH practitioner [85]. Kozak et al. found that 86% of hospices in Washington state offered CIH therapies, but practitioners were largely volunteer and CIH services were not covered by the Medicare hospice benefit [63]. In a Nevada and Montana hospice survey of CIH services, 70% of hospices provided these services, but less than 25% of patients received them [86]. In another hospice survey, 60% of these hospices provided CIH services, but less than 25% of patients received them [62]. A national survey of hospices funded by US Department of Human Services, the Center for Disease Control and National Center for Health Statistics found that 42% of hospices offered CIH services [64]. In another national survey of hospices in the US, 29% employed a CHI therapist, which included a massage therapist 74% of the time, 53% music and 22% art [85].

CIH therapies are commonly used by oncology patients for symptom control, well-being and healing. From 1997 to 2005, Sirios notes that motivation to seek CIH therapies changed from predominantly using them as an alternative to conventional care, to a more empowered, positive integrative approach using CIH therapies to augment conventional therapies. (97) In a Swedish study of cancer patients, 26% reported use of CIH therapies to optimize health, fight disease, and increase physical and emotional wellbeing [87]. In many surveys, satisfaction with CIH is high, and satisfaction with hospice services is increased with CIH use [87, 88]. Barriers identified that negatively impact patient disclosure of CIH use to oncologists include: physician did not ask or that they felt their physician did not want to know. In one study, only 26% of patients disclosed CIH use to their oncologists [87, 89]. Barriers to CIH use in hospices include lack of funding/reimbursement, lack of CIH providers, resistance to CIH modalities by staff and patients, and lack of knowledge about benefits of CIH [62].

The most common CIH modalities offered by hospices include massage therapy, music therapy, pet therapy, guided imagery, reiki, aromatherapy, harp music, reflexology, hypnosis, acupuncture and art therapy. Less offered modalities included movement therapies [62-64]. In oncology patients, supplements and osteopathic and chiropractic manipulation use was 36% and 25% respectively, with

less frequent use of massage, movement therapies, and mindfulness meditation [89]. In a Canadian PC unit study, CIH modalities contributed to a decrease in intensity of pain, restlessness, low mood, and anxiety and increased a sense of peace [90]. CIH are considered generally safe, well tolerated. In their systematic review of CAM in hospice and palliative care, Zeng et al. discovered many barriers to research of CIH in this population, but also found that reiki, music and massage therapy had the highest potential benefits [91].

#### **4. Discussion**

The skills required to provide integrative palliative care are not currently taught in most health science professional training programs, but many of the core concepts and skill set taught in PC are in alignment with CIH care. As we have addressed above, CIH modalities are a valuable resource to address symptom clusters in palliative care patients. IPC calls on us to be creative and innovative in the care of seriously ill patients, expanding options to enhance healing, maintain hope, and improve well-being in a unique way for each person

PC can occur together with life-prolonging measures, and with the relief of symptoms and improvements in quality of life (QOL), PC may actually prolong life [1].

Pharmaceuticals are widely available for symptom cluster management, but with significant side effects and risk of harm[9]. They seldom treat the root cause of symptoms, and provide limited symptom relief. Pharmaceuticals can be effective, but CIH modalities allow for the possibility of reducing the need for medications with challenging and harmful side effects, and increase wellbeing, healing and health in serious illness and at end of life [9]. Optimally, medications are used safely, monitored closely and used in the lowest effective dose. Nutraceutical and drug interactions are largely underappreciated, since conventional practitioners rarely ask their patients about their use, or without knowledgeable about supplements, dismiss them and discourage their use [89].

CIH continues to be available to people primarily in outpatient settings, and is an out of pocket expense limiting access unless services are affordable. Inpatient PC settings at times provide services such as music, art, limited massage and aromatherapy and pet therapy to patients [3]. Less available are acupuncture, biofield therapies and narrative interventions. Although cancer centers and hospices generally offer a wide array of CIH services, hospital-based PC settings may have a limited number of practitioners trained in CIH, despite high patient satisfaction with CIH modalities for overall comfort and wellness.

Few hospital-based PC practitioners ask their patients about CIH therapies, and few prescribe them or are knowledgeable about these therapies. Within hospices, CIH therapies and practitioners are generally underfunded, and facilities rely on volunteer services [63, 92].

Studies of IPC are often in PC inpatient units, hospices or oncology populations. There is a need for more study of symptom clusters across all advanced serious illnesses and the symptom clusters they produce and the therapies that are most effective in relieving them. In PC populations, patient often have more than one serious illness, therefore evidence based on a single disease entity in PC studies is challenging.

## 5. Conclusions

Surveys of people enduring serious illness reveal the use and significance of CIH in an overall strategy to reduce drug side effects, and support health and wellness [3, 9]. An integrative approach to palliative care allows for healing modalities that support overall wellness and reduce suffering from physical, emotional, and spiritual distress. Addressing palliative care symptoms from the perspective of symptom clusters allows for a more wholistic approach to PC. CIH modalities are important and effective in treating symptom clusters and there is a need to prioritize access to these modalities with well-trained clinicians from both, the conventional and CIH fields.

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## Author Contributions

LM: Most (80%) of the writing, editing, research, submission of manuscript. DL: Writing, Editing, research. LK: Writing, editing, research.

## Competing interests

The authors have declared that no competing interests exist.

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