



Complementary Therapies and Integrative Medicine in Lung Cancer

Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

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Background: Physicians are often asked about complementary therapies by patients with cancer, and data show that the interest in and use of these therapies among patients with cancer is common. Therefore, it is important to assess the current evidence base on the benefits and risks of complementary therapies (modalities not historically used in modern Western medicine).

Methods: A systematic literature review was carried out and recommendations were made according to the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines development methodology.

Results: A large number of randomized controlled trials, systematic reviews, and meta-analyses, as well as a number of prospective cohort studies, met the predetermined inclusion criteria. These trials addressed many different issues pertaining to patients with lung cancer, such as symptoms of anxiety, mood disturbance, pain, quality of life, and treatment-related side effects. The available data cover a variety of interventions, including acupuncture, nutrition, mind-body therapies, exercise, and massage. The body of evidence supports a series of recommendations. An evidenced-based approach to modern cancer care should integrate complementary therapies with standard cancer therapies such as surgery, radiation, chemotherapy, and best supportive care measures.

Conclusions: Several complementary therapy modalities can be helpful in improving the overall care of patients with lung cancer.

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Abbreviations: ACCP = American College of Chest Physicians; CAM = complementary and alternative medicine; CIPN = chemotherapy-induced peripheral neuropathy; EPA = eicosapentaenoic acid; MBSR = mindfulness-based stress reduction; MeSH = Medical Subject Heading; NSCLC = non-small cell lung cancer; QOL = quality of life; RCT = randomized controlled trial

SUMMARY OF RECOMMENDATIONS

2.1.1.1. It is suggested that all lung cancer patients should be asked about their interest in and usage of complementary therapies. Counseling on the benefits and risks of those therapies should be provided (Grade 2C).

2.2.7.1. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce anxiety, mood disturbance, sleep

disturbance, and improve quality of life (QOL) (Grade 2B).

2.2.7.2. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce acute or chronic pain (Grade 2B).

2.2.7.3. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce anticipatory chemotherapy-induced nausea and vomiting (Grade 2B).

2.2.7.4. In lung cancer patients experiencing the symptoms, yoga, a movement-based mind-body modality is suggested as part of a multidisciplinary approach to reduce fatigue and sleep disturbance while improving mood and QOL (Grade 2B).

2.3.1.1. In lung cancer patients whose anxiety or pain is not adequately controlled by usual care, addition of massage therapy performed by trained professionals is suggested as part of a multi-modality cancer supportive care program (Grade 2B).

2.4.3.1. In patients awaiting pulmonary resection for suspected lung cancer with compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.4.3.2. In post-surgical lung cancer patients with compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.4.3.3. In advanced (inoperable) lung cancer patients receiving palliative anticancer therapy and compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.5.3.1. In patients having nausea and vomiting from either chemotherapy or radiation therapy, acupuncture or related techniques is suggested as an adjunct treatment option (Grade 2B).

2.5.3.2. In patients with cancer related pain and peripheral neuropathy, acupuncture is suggested as an adjunct treatment in patients with inadequate control of symptoms (Grade 2C).

2.6.3.1. In people who might develop lung cancer a diet rich in non-starchy vegetables and fruits is suggested to reduce the risk of lung cancer (Grade 2C).

2.6.3.2. In people who might develop lung cancer, limiting the consumption of a large amount of red meat and processed meat is suggested; lower meat consumption may reduce the risk of lung cancer (Grade 2C).

2.6.3.3. In patients undergoing treatment of lung cancer who have experienced weight loss, the addition of high calorie and protein supplements (1.5 kcal/mL) as a nutritional adjunct is suggested to achieve weight stabilization (Grade 2C).

2.6.3.4. In patients with lung cancer who have sarcopenia, oral nutritional supplementation with n-3 fatty acids is suggested in order to improve the nutritional status (Grade 2C).

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Integrative oncology refers to the study and use of complementary modalities that are not traditionally part of modern Western medical practices but can be used as adjuncts to mainstream medicine to control the symptoms associated with cancer and cancer treatment. Unfortunately, the term has been paired with “alternative medicine” to form the acronym CAM (for complementary and alternative medicine), thus blurring the critical distinctions between the two.

“Alternative medicine” refers to the use of unproven methods, most of which lack data to support the purported benefits and safety. These alternatives are often promoted for use as viable cancer treatments instead of mainstream cancer care, but they are typically fraudulent; deliver misleading pseudoscientific information with a heavy commercial bias²; endorse unproven, potentially harmful therapies³; and discourage conventional therapies such as surgery, chemotherapy, and radiotherapy, which are referred to as “cutting, poisoning, and burning.” Many so-called “alternative” cancer treatments are especially harmful to the patients with cancer who postpone needed and proper treatment and, thus, diminish the possibility of remission and cure.⁴

“Complementary therapies,” conversely, are rational, evidence-based techniques that alleviate physical and emotional symptoms, improve quality of life (QOL), and may improve adherence to oncology treatment regimens. “Integrative medicine” and “integrative oncology” are now widely accepted as the appropriate terms for describing the adjunctive role played by complementary therapies as part of multidisciplinary mainstream cancer care.⁵

Many patients with cancer use CAM therapies, but the effectiveness of many of these therapies has not been established. Physicians often face patients who are interested in CAM therapies and wonder if they can use them, but the physicians are ill equipped to answer the questions in a sensible and evidence-based manner. Rigorous research on these therapies has been lacking until recently. In the past decade, many randomized controlled trials (RCTs) have been conducted, and meta-analyses and systematic reviews have been published to summarize the findings from those trials. These publications form the evidence base from which specific recommendations can be made to guide clinical practice. In this article, we address such gaps in knowledge by reviewing the evidence on the following common complementary medicine modalities: mind-body modalities, massage, exercise, acupuncture, nutritional approaches, and dietary supplements.

Mind-body modalities are defined as those practices that focus on the interactions among the brain, mind, body, and behavior, with the intent of using the mind to affect physical functioning and promote health.¹⁵⁹ Several mind and body approaches ranked among the top 10 CAM practices reported by adults in the 2007 National Health Interview Survey.⁶ The most common symptoms for which people turned to these therapies were pain (55%), dyspnea (55%), and fatigue (37%).⁷ Here, we review the evidence supporting the application of mind-body techniques as an adjunct therapy across the lung cancer continuum (ie, from prevention to palliation).

Massage therapy involves applying pressure to muscle and connective tissue to reduce tension and pain, improve circulation, and encourage relaxation. The massage techniques most commonly used in oncology include Swedish massage, aromatherapy massage, reflexology, and acupressure. All involve manual manipulation of the soft tissues of the body by the therapist. However, the methods of applying touch, the degree of educational preparation, the regulatory requirements, and the underlying theoretic frameworks vary widely among these modalities. Massage therapy is usually used to reduce muscle tension and soreness. Clinical studies of massage therapy in patients with cancer tend to focus on symptom control, especially for anxiety, depression, and pain.

There is growing interest in and recognition of the potential role of exercise therapy across the entire lung cancer continuum. The key issues in exercise therapy are the safety and feasibility in a particular patient population (eg, those with inoperable disease); the kind of benefits, if any, that can be expected; the optimal type and amount of exercise; and the identification of the biologic mechanisms underlying the effects of the exercise. The current evidence base is reviewed.

Acupuncture’s traditional philosophy arises from Eastern Asia, and although its origin is a matter of scholarly debate, acupuncture was codified >2000 years ago.⁸ Basic techniques of acupuncture have been used in all forms of medicinal healing in Chinese medicine. Although distinct versions of acupuncture (Japanese, Korean, French, and so forth) have developed over the years, the essential theory of harmonizing imbalances in the body remains.⁸ Offshoots of acupuncture include acupressure techniques, auricular and scalp acupuncture, and electroacupuncture; each of these modalities is evaluated in the analysis.⁹ Since the 1970s, a significant body of research has developed to evaluate their efficacy and safety, with many RCTs comparing acupuncture with other modalities used to treat pain, nausea, and vomiting.⁸ We review the evidence for using acupuncture (and associated techniques) in the treatment of cancer and treatment-related nausea/vomiting and pain, where the evidence is the strongest.

Many studies have investigated the role that diet and nutrition play in lung cancer prevention. Malnutrition is a common problem in patients with lung cancer who are undergoing treatment. It has been recognized as an important component of adverse outcomes, including decreased QOL and increased morbidity and mortality.¹⁰⁻¹² The cause of the nutritional disorders and related symptoms observed in patients with lung cancer or other cancers can be attributed to the tumor and its psychologic, physiologic, and treatment-related effects. It has been shown that at the time of diagnosis, 60% of patients with lung cancer have already experienced a significant weight loss,¹³ generally defined as at least a 10% loss of body weight in 6 months’ time.¹⁴ It is estimated that >50% of patients with newly diagnosed advanced lung cancer have severe sarcopenia (loss of muscle mass).¹⁴ Nutrition is also an important issue in survivors of lung cancer. Here we review the literature on nutrition in the context of lung cancer prevention, treatment, and survivorship.

A dietary supplement is a product taken by mouth that contains a “dietary ingredient” intended to supplement the diet. The “dietary ingredients” in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and substances such as

enzymes, organ tissues, glandulars, and metabolites. Dietary supplements are very popular among patients with cancer, who take them hoping to prevent the spread of the cancer, alleviate symptoms, improve the immune system, and reduce the risk of recurrence. However, in studies looking at dietary supplements, the jury is still out on any potential protective benefits. In fact, there is some evidence that some supplements may increase the risk of lung cancer. For example, supplemental vitamin A and its derivatives (including the carotenoids) may be associated with a higher incidence of and mortality from lung cancer.^{15,16} Therefore, it is important to advise patients of the existing evidence. However, it is also important to apprise them as to what they can take to improve their QOL and other parameters during their medical treatment. For example, some researchers have found that certain herbs such as astragalus can actually improve the effectiveness of chemotherapy treatments.¹⁷ The use of dietary supplements for cancer prevention is reviewed by Szabo et al,¹⁸ "Chemoprevention of Lung Cancer," in the American College of Chest Physicians (ACCP) Lung Cancer Guidelines.¹⁸ Current literature is insufficient to support a specific recommendation on the use of dietary supplements during cancer treatment; therefore, we do not discuss this topic in this article, even though it is an important area and is asked about frequently by patients with cancer.

Compared with the diagnostic and therapeutic recommendations in other articles, most of the recommendations in this article deal with symptoms (anxiety, nausea, vomiting, pain, and other symptoms) shared by all patients with cancer rather than those limited to patients with lung cancer. Therefore, the literature reviewed in general is not limited to patients with lung cancer, except when the disease has a material impact on the intervention, such as is the case with exercise therapy, in which reduced pulmonary function may make the exercise intolerable or unsafe.

1.0 METHODS

In general, literature searches of major databases were carried out using keywords related to intervention modalities, symptom end points, cancer, or lung cancer. Searches were limited to meta-analyses, systematic reviews, and RCTs. Narrative reviews and single-arm studies were excluded. There was no exclusion based on sample size. The resultant reference lists were searched manually to exclude entries that were obviously irrelevant to the topics. Specific search strategies are described below and full descriptions are available on request. The searches were structured around the following patient, intervention, comparison, outcomes (PICO) questions:

1. In patients with lung cancer, do discussions about complementary therapies, their benefits, and risks improve the patients' understanding of how to take advantage of the

therapies that are helpful and how to reduce exposure to potential harm?

2. In patients with lung cancer experiencing symptoms, do mind-body modalities as part of a multidisciplinary approach help reduce anxiety, mood disturbance, pain, nausea, vomiting, and sleep disturbance?
3. In patients with lung cancer whose anxiety or pain is not adequately controlled by usual care, does massage therapy help reduce the symptoms?
4. In patients with lung cancer with compromised lung function awaiting or following surgical resection of lung lesions, does supervised exercise-based pulmonary rehabilitation improve cardiorespiratory fitness and functional capacity?
5. In patients with lung cancer with compromised lung function and inoperable disease, does supervised exercise-based pulmonary rehabilitation improve cardiorespiratory fitness and functional capacity?
6. In patients experiencing nausea and vomiting from chemotherapy or radiotherapy, does acupuncture as an adjunct treatment option reduce the symptoms?
7. In patients with lung cancer whose cancer-related pain and peripheral neuropathy is not controlled adequately, does acupuncture as an adjunct treatment help reduce the symptoms?
8. In people at risk of lung cancer, do certain dietary regimens help reduce the risk?
9. In patients with lung cancer, does nutritional intake of protein-energy-dense foods beneficially affect nutritional status compared with usual care?
10. In patients with lung cancer who have sarcopenia, does oral nutritional supplementation with n-3 fatty acids beneficially affect nutritional status compared with usual care with other nutritional supplements?

To investigate mind-body modalities in patients with lung cancer, a comprehensive literature review was conducted using Ovid MEDLINE, PubMed, and Web of Science (2000 to 2011) using the following Medical Subject Heading (MeSH) terms and text words: "lung cancer," "cancer meditation," "mind body," "yoga cancer," "hypnosis cancer," "visualization cancer," "relaxation cancer," "anxiety cancer," "dyspnea cancer," "fatigue cancer," and "depression cancer." Relevant reference lists were also searched manually. Studies exclusively involving adult patients with cancer that provided subjects with mind-body interventions were deemed eligible. Mind-body modalities were defined according to the National Institutes of Health/the National Center for Complementary and Alternative Medicine (NCCAM) definition: "Mind and body practices focus on the interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote health."¹⁵⁹ Many approaches embody this concept, and we included in our review interventions consisting of meditation/mindfulness-based stress reduction (MBSR); yoga; tai chi; qigong; and psychosocial, hypnosis, and mind-body relaxation techniques. Studies involving adult cancer were deemed eligible. Included studies could test the independent effects of the mind-body modality intervention. Studies with a participant mean age below 18 years or that were non-English were excluded.

To investigate massage therapy in patients with lung cancer, the PubMed database was searched from its beginning to December 2011, using the following search terms: ("massage" AND "depression" AND "cancer") OR ("massage" AND "anxiety" AND "cancer") for the effect of massage therapy on anxiety and depression; "massage"[ti] AND "pain" for the effect of massage therapy on pain; or "massage"[ti] AND "safety"[ti] for the safety of massage therapy. The research results were limited to "meta-analysis" or "reviews" and there was no language restriction.

To investigate exercise in patients with lung cancer, Ovid MEDLINE (1950-2011), PubMed (1966-2011), and Web of Science (1950-2011) were searched using the following MeSH terms and text words: "lung cancer," "non-small cell lung cancer," "thoracic malignancies," "exercise," "exercise therapy and exercise training," "aerobic training," "resistance training," and "rehabilitation." Relevant reference lists were also searched manually. Studies exclusively involving adult patients with histologically confirmed lung cancer who were provided with supervised exercise training programs were deemed eligible. Supervised exercise training was defined as interventions consisting of aerobic, resistance, or the combination of aerobic and resistance training as opposed to unsupervised or home-based interventions. Included studies could test the independent effects of exercise training or the effects of exercise training as part of a multidisciplinary rehabilitation program. Studies with a participant mean age below 18 years or that were non-English were excluded.

To investigate acupuncture in patients with lung cancer, Ovid MEDLINE (1950-2011), PubMed (1966-2011), Web of Science (2000-2011), and lists of related references in reviewed journal articles were searched using the following MeSH terms and text words: "lung cancer," "cancer," "thoracotomy," "acupuncture," "acupressure," "electro acupuncture," "auricular acupuncture," "nausea," "vomiting," "chemotherapy induced peripheral neuropathy," "cancer pain," "smoking cessation," "safety," and "efficacy." Relevant reference lists were also searched manually. Studies exclusively involving either pediatric or adult patients with a history of cancer who were provided with acupuncture or its variations for treatment were evaluated. Included studies involved using acupuncture as a treatment modality for nausea and vomiting, cancer pain, chemotherapy-induced peripheral neuropathy (CIPN), and smoking cessation; studies examining the safety of acupuncture were also included. Trials that were in non-English languages were included because a fair number of acupuncture studies are published in non-English journals. The abstracts were evaluated and this is specified in the review tables. The evaluations for pain and nausea were limited to patients who had a diagnosis of cancer.

To investigate nutrition in patients with lung cancer, Ovid MEDLINE (2005-2012) and PubMed (2005-2012) were searched using the following nested search terms and text words: "lung cancer," "non-small cell lung cancer," "thoracic malignancies and nutrition," "nutrition and lung cancer prevention," "nutritional therapy and lung cancer treatment," "nutritional management of lung cancer," and "nutrition and lung cancer survivorship." Relevant reference lists were also searched. Research involving adult patients over age 18, published in the English language or fully translated, including meta-analyses, epidemiologic studies of nutritional intake to prevent progression from high-risk histology to lung cancer, clinical trials testing specific individual or combination nutrients to improve prognosis and/or QOL or to alleviate symptoms of lung cancer treatment, and studies examining survivorship were included. The study population included the entire continuum of cancer, targeting individuals and populations at high risk of lung cancer and those with histologically confirmed lung cancer. Studies involving nutritional interventions for survivorship from lung cancer were also deemed eligible, but those with a participant mean age below 18 years or that were non-English were excluded.

2.0 CONTENT SECTIONS BASED ON THE RESEARCH (PICO) QUESTIONS

2.1 Usage of Complementary Therapies and Approaches in Addressing Patient's Needs

PICO question: In patients with lung cancer, do discussions about complementary therapies, their benefits,

and risks improve the patients' understanding of how to take advantage of the therapies that are helpful and how to reduce exposure to potential harm?

A National Health Interview Survey conducted in 2007 showed that the overall prevalence of CAM usage was estimated at four in 10 adults (38.3%; 83 million) and one in nine children (11.8%; 8.5 million under age 18 years).^{6,19} In patients with cancer, the usage prevalence varies from 10% to >60%, depending on the definitions of CAM that are applied.²⁰⁻²⁵ When stratified by cancer diagnoses, the prevalence of use was the highest in patients with lung cancer (53%), according to a nationwide survey in Japan.²⁶ A European survey reported greater complementary therapy use among those diagnosed with pancreatic, liver, bone/spinal, and brain cancers.²⁷ A more recent survey found that in the United States, up to 40% of patients with cancer use complementary modalities during the survivorship period following acute cancer therapies.²⁸

A common finding in these surveys is that patients who seek these modalities tend to be younger, more educated, and more affluent, representing a health-conscious segment of the population that is more proactive in finding health information, takes initiative regarding their health care, and can afford to pay for typically uncovered services. Patients may also seek out these therapies because of a poor prognosis even if receiving standard of care, a fear of adverse effects from conventional treatment, a lack of a sense of control in the complicated health-care system, a cultural and social affinity to therapies of natural origin, and the belief that unfamiliar therapies may yet hold surprising benefit.²⁹⁻³³ These unmet physical and psychosocial needs of patients require attention from health-care professionals. An open, receptive, and evidence-based discussion with the patient on the use of complementary therapies, with the patient's value system taken into consideration, builds trust and enhances the therapeutic relationship between the patient and his or her physician and other health-care providers.

2.1.1 Recommendation

2.1.1.1. It is suggested that all lung cancer patients should be asked about their interest in and usage of complementary therapies. Counseling on the benefits and risks of those therapies should be provided (Grade 2C).

2.2 Mind-Body Modalities

PICO question: In patients with lung cancer experiencing symptoms, do mind-body modalities as part of a multidisciplinary approach help reduce anxiety, mood disturbance, pain, nausea, vomiting, and sleep disturbance?

A total of 2,559 hits from January 2000 to December 2011 search criteria yielded 210 unique potential citations, and after initial review, 34 studies (four meta-analyses, 14 systematic reviews, and 16 RCTs) were deemed eligible. Specific recommendations were made on the basis of the strength of the evidence from these 31 studies. For the purpose of the clinical guidelines herein, we present empirical evidence for each mind-body modality reviewed. When available, a meta-analysis or systematic review is presented, and if not, individual RCTs are presented. Pilot and feasibility studies were not included. If a systematic review or meta-analysis was available, individual studies were not included, to prevent duplication, unless recent RCTs presented new findings different from those of the review or meta-analysis. If recent RCTs using the same dataset were published in more than one publication, the results were reported only once. Two RCTs were excluded because the primary outcomes were hot flashes and menopausal symptoms in breast cancer survivors. Of these 31 studies, those relevant to a specific modality (eg, meditation, yoga, and so forth) are included in the review of evidence for that particular modality. The results are summarized in the paragraphs that follow and the evidence in Tables S1 to S5.

2.2.1 Meditation/MBSR: One meta-analysis, three systematic reviews, and one RCT comprising 2,553 patients were reviewed. Although there are several forms of meditation, involving becoming aware, paying attention, or inward focusing, MBSR programs have the most empirical evidence in cancer populations. Mindfulness-based meditation strives to develop an objective “observer role” of the practitioner for emotions, feelings, and perceptions, and create a nonjudgmental “mindful state” of conscious awareness.³⁴ MBSR consists of several meditative components, including body scan, sitting meditation, and mindful movement, and is taught over a period of 6 to 8 weeks. Studies of MBSR in patients with cancer suggest benefits for mental health (QOL, mood stress, anxiety, depression),³⁵⁻³⁸ spirituality,³⁶ fatigue,³⁶ sleep,³⁶⁻³⁸ and self-rated physical health,³⁶ and reports show some promise for immune measures.³⁶ Although other forms of meditation have shown consistently to be beneficial in other illness populations,^{39,40} there are few studies in cancer populations. However, meditation is safe, and its clinical effects have been shown to impact a broad spectrum of physical and psychologic symptoms and syndromes, including reducing anxiety, pain, and depression; enhancing mood and self-esteem; and decreasing stress.^{41,42}

2.2.2 Yoga: Yoga is a unique mind-body therapy because it involves physical movement, breath control, and meditation components. There are many different styles of yoga. Our recommendations are based on

five RCTs, one meta-analysis, and one systematic review, for a total of 25 studies in 1,966 patients. Areas that benefit from yoga include mood,^{41,43-48} (anxiety, depression, distress), stress,^{45,46,48} QOL,^{43,46-48} and sleep. Some well-controlled trials confirm these findings and also suggest yoga is beneficial for chemotherapy-induced nausea and anticipatory nausea frequency and intensity,⁴⁹ pain,⁵⁰ invigoration and acceptance,⁵¹ fatigue,^{41,43,46} appetite loss,⁴⁶ benefit finding (finding meaning in the cancer experience),⁴⁴ and salivary cortisol levels,^{41,46} and investigators report a dose-response relationship.⁵¹

2.2.3 Tai Chi/Qigong: Our recommendations are based on one systematic review of 23 qigong studies and two RCTs on tai chi, for a total of 2,086 patients. Although the benefits of tai chi have been reported for several other chronic health conditions,⁵² little systematic controlled research has been conducted on its benefit for patients with cancer. Similarly, there are several reports of qigong with other populations, and several published case studies; however, evidence is lacking to critically evaluate specific benefits in cancer populations. Both tai chi and qigong appear safe and beneficial for patients with cancer; however, because of the limited number of controlled studies in oncology populations, no conclusions can be drawn. The few published trials appear to show promising effects on the immune system, health-related QOL, functional capacity, and mood.⁵³⁻⁵⁵

2.2.4 Hypnosis: Hypnosis is a state of focused attention or altered consciousness between wakefulness and sleep in which distractions are blocked, allowing a person to concentrate intently on a particular subject, memory, sensation, or problem. Our recommendations are based on two meta-analyses, one systematic review, and six RCTs, for a total of 69 studies with 2,831 patients. Hypnosis has been studied extensively and has been consistently found to be effective for a wide range of symptoms in cancer care, including pain (pain medication, pain intensity, procedural pain, postsurgical pain),⁵⁶⁻⁵⁹ fatigue,^{56,60} anticipatory and chemotherapy-related nausea and vomiting,^{58,61} mood (anxiety, depression),^{57,58,62,63} and mental and overall well-being.⁶³ Effects have been reported with just one brief session.^{56,58,62} One hypnosis study reported more emotional upset in three participants after hypnosis (although participants continued after these reports).⁶⁴ The World Health Organization cautions that hypnosis should not be performed on those with psychosis or certain personality disorders. A small percentage of patients may experience dizziness, nausea, or headache. These symptoms usually result from patients being brought out of trances by inexperienced hypnotherapists.⁶⁵

2.2.5 Music Therapy: Music therapy is provided by trained musicians who hold professional degrees in music therapy. One systematic review of 11 studies (three RCTs) with 419 patients does not provide sufficient evidence to provide strong recommendations for music therapy. A large number of qualitative studies describe emotional and physiologic benefits, with improvements in pain, anxiety, stress, depression, relaxation, mood, comfort, and fatigue. A review of the empirical data suggests a benefit on anxiety as well as cancer pain based on three controlled clinical trials.⁶⁶ Postoperative music reduces anxiety, pain, and morphine consumption.⁶⁷ Although there appears to be benefit, and no risk or harmful side effects, no recommendations specific to music therapy can be provided at this time because of the limited number of controlled studies.

2.2.6 Psychosocial Approaches/Relaxation: Psychosocial approaches, including cognitive behavioral therapy, relaxation training, imagery/visualization, psychoeducation, and behavioral approaches have been studied extensively in patients with cancer. Recommendations are based on six systematic reviews and one meta-analysis, with 178 studies and > 20,000 patients. Cognitive behavioral therapy is effective for improving QOL, depression, anxiety, pain, fatigue, and distress.⁶⁸ Behavioral approaches are effective for improving pain, nausea, vomiting, anticipatory nausea and vomiting, anxiety, and depression.⁶⁹ Relaxation training is effective for improving tension, anxiety, and mood and decreasing hostility, BP, pulse rate, nausea, sleep disturbance, and pain.⁷⁰ Psychosocial interventions do not prolong survival, but limitations in the studies make it difficult to ascertain whether there is a small effect. Results regarding physical outcomes are sparse and mixed, and individual interventions are more effective than group interventions.

2.2.7 Recommendations

2.2.7.1. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce anxiety, mood disturbance, sleep disturbance, and improve QOL (Grade 2B).

2.2.7.2. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce acute or chronic pain (Grade 2B).

2.2.7.3. In lung cancer patients experiencing the symptoms, mind-body modalities are suggested as part of a multidisciplinary approach to reduce anticipatory chemotherapy-induced nausea and vomiting (Grade 2B).

2.2.7.4. In lung cancer patients experiencing the symptoms, yoga, a movement-based mind-body modality is suggested as part of a multidisciplinary approach to reduce fatigue and sleep disturbance while improving mood and QOL (Grade 2B).

2.3 Massage Therapy

PICO question: In patients with lung cancer whose anxiety or pain is not adequately controlled by usual care, does massage therapy help reduce the symptoms?

To determine the effect of massage therapy on symptom control in patients with cancer, our search produced 38 publications on its effect on anxiety or depression and 14 publications on its effect on pain. Nonsystematic reviews and reviews focusing on patients with non-lung cancer (eg, patients with breast cancer), and reviews focusing on nonclinical end points, were excluded; the resulting two systematic reviews serve as the evidence base. The 2009 review, "Massage Therapy for Cancer Palliation and Supportive Care: A Systematic Review of Randomised Clinical Trials," included 14 RCTs, among which seven had anxiety, three had depression, and six had pain as an end point.⁷¹ A total of 514 patients were evaluated for anxiety, 107 patients for depression, and 718 patients for pain. The 2008 review, "Massage for Symptom Relief in Patients With Cancer: Systematic Review," included 12 RCTs, among which five had anxiety, two had depression, and three had pain as an end point.⁷² A total of 236 patients were evaluated for anxiety, 63 for depression, and 144 for pain. The control interventions in those trials were usual care, attention, or low-intensity body work. There is some overlap between the two systematic reviews, with six clinical trials included in both publications.

The reviewers concluded that the data support massage therapy as an effective adjunct in cancer supportive care to reduce anxiety, depression, and pain. The evidence supporting its effect on anxiety is stronger than that on depression. The limitation of the systematic reviews is that the methodologic quality of most of the included trials was poor (Table S6).

When examining the safety of massage therapy, the search produced three publications. One focused on back pain only, and thus was excluded.⁷³ The other two, focusing on the safety of massage therapy for patients with cancer⁷⁴ and on the safety of massage therapy in general,⁷⁵ are included. In "The Safety of Massage Therapy," a systematic review published in 2003, a computerized literature search located 16 case reports and four case series of adverse events related to massage therapy published from January 1995 to December 2001. The reported adverse events included cerebrovascular accidents, displacement of a ureteral stent, embolization of a kidney, hematoma,

leg ulcers, nerve damage, posterior interosseous syndrome, pseudoaneurysm, pulmonary embolism, ruptured uterus, strangulation of the neck, thyrotoxicosis, and various pain syndromes. Most adverse effects were associated with exotic types of manual massage or massage delivered by laymen, whereas massage therapists were rarely implicated.⁷⁵ In “Safety and Efficacy of Massage Therapy for Patients With Cancer,” a nonsystematic review published in 2005, the author presented a narrative description of three case reports.⁷⁴ The evidence consisted of case reports and case series, with their inherent risk of reporting bias. Given the frequency of reports of adverse events and the large number of massage therapies being delivered over the time frame, the authors concluded that massage therapy is not entirely risk free, but serious adverse events are probably a true rarity, especially when the massage therapy is performed by trained professionals.

Some moderate-strength data from RCTs support the premise that massage therapy can be an effective adjunct in cancer supportive care to reduce anxiety and pain. Data supporting its effect on depression are not as strong. Serious adverse events associated with massage therapy are extremely rare, especially when performed by trained professionals. In light of the limitations of current interventions in reducing anxiety and pain in patients with cancer and the low risk of professional massage therapy, we make the following recommendation.

2.3.1 Recommendation

2.3.1.1. In lung cancer patients whose anxiety or pain is not adequately controlled by usual care, addition of massage therapy performed by trained professionals is suggested as part of a multi-modality cancer supportive care program (Grade 2B).

2.4 Exercise

Patients with operable and inoperable lung cancer represent two distinct populations in which the benefits of exercise differ. Evidence for these two populations is reviewed and discussed separately as follows.

2.4.1 Exercise Training in Patients With Operable Non-small Cell Lung Cancer Before and After Surgical Resection: PICO question: In patients with lung cancer with compromised lung function awaiting or following surgical resection of lung lesions, does supervised exercise-based pulmonary rehabilitation improve cardiorespiratory fitness and functional capacity?

A total of 563 potential citations were identified and, after initial review, nine unique studies were

deemed eligible: eight original articles⁷⁶⁻⁸³ and one systematic review.⁸⁴ Of the original articles, all studies were cohort studies (single group, pre-post design) except one, which was a two-arm RCT. (Table S7)⁷⁶ Three studies were conducted on patients before their surgical resection,⁷⁸⁻⁸⁰ with the remaining studies conducted after surgical resection^{76,77,81-83}; two of these recruited patients receiving adjuvant therapy.^{77,83} The mean sample size was 24 (range, 10-51). Most studies tested the effects of a multidisciplinary intervention program (aerobic, resistance, and education or relaxation),^{78,80-83} two used aerobic training only,^{77,79} and one used aerobic and resistance training.⁷⁶ The intervention length ranged from 4 to 14 weeks, and study end points were varied and were not standardized among studies, and included exercise tolerance, muscle strength, and QOL. Only two studies reported adherence to the exercise program.^{77,79}

2.4.1.1 Preoperative Exercise Interventions—Overall, the three studies published to date⁷⁸⁻⁸⁰ suggest that short-term (about 4 weeks) multidisciplinary inpatient rehabilitation or supervised aerobic training is a safe and well-tolerated intervention associated with significant improvements in cardiorespiratory fitness (peak oxygen consumption) and functional capacity (6-min walk distance) prior to surgical resection (Table S8). No randomized trials of presurgical rehabilitation in lung cancer have been reported, although one such study was conducted in patients with coronary artery disease, with positive results.⁸⁵ Because published studies have important methodologic limitations, adequately powered, prospective trials with appropriate control groups are warranted.

2.4.1.2 Postoperative Exercise Interventions—Overall, the five studies published to date^{76,77,81-83} suggest that short-term (4-14 weeks) multidisciplinary inpatient rehabilitation or supervised aerobic training is a safe and well-tolerated intervention associated with modest improvements in exercise capacity and QOL end points following surgical resection for lung cancer. Only one randomized trial has been published to date (Table S9). Published studies have important methodologic limitations. Adequately powered, prospective trials with appropriate control groups are warranted.

2.4.2 Exercise Training in Patients With Inoperable Non-small Cell Lung Cancer: PICO question: In patients with lung cancer with compromised lung function and inoperable disease, does supervised exercise-based pulmonary rehabilitation improve cardiorespiratory fitness and functional capacity?

A total of 563 potential citations were identified and, after initial review, three unique studies were deemed eligible: two original articles^{86,87} and one systematic review.⁸⁴ Of the original articles, both were cohort

studies (single group, pre-post design) (Table S10). The mean sample size was 24 (range, 20-29) and both tested the effects of either a multidisciplinary intervention program (aerobic, resistance, and education or relaxation)⁸⁶ or aerobic and resistance training.⁸⁷ The intervention length ranged from 6 to 8 weeks. Study end points were varied and included exercise capacity, functional capacity, muscle strength, and QOL. Exercise adherence was reported in both studies.

Overall, the two studies published to date suggest that short-term (6-8 weeks), low-intensity, multidisciplinary, exercise-based rehabilitation is potentially feasible and safe for select patients with inoperable non-small cell lung cancer (NSCLC). The preliminary data further suggest that low-intensity, multidisciplinary, exercise-based rehabilitation may be associated with modest improvements in exercise tolerance and functional capacity end points in those select patients able to tolerate and achieve reasonable adherence. Published studies have important methodologic limitations, and further carefully designed studies in select populations appear warranted.

2.4.3 Recommendations

2.4.3.1. In patients awaiting pulmonary resection for suspected lung cancer with compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.4.3.2. In post-surgical lung cancer patients with compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.4.3.3. In advanced (inoperable) lung cancer patients receiving palliative anticancer therapy and compromised lung function, supervised exercise-based pulmonary rehabilitation is suggested to improve cardiorespiratory fitness and functional capacity (Grade 2C).

2.5 Acupuncture

2.5.1 Acupuncture for Chemotherapy- or Radiotherapy-induced Nausea and Vomiting: PICO question: In cancer patients experiencing nausea and vomiting from chemotherapy or radiotherapy, does acupuncture as an adjunct treatment option reduce the symptoms?

After initial review of potential articles, 16 unique studies were deemed eligible, 15 of which were original articles, with one systemic review. A high-quality Cochrane systematic review of 11 trials (total N = 1,247) concluded that

Electroacupuncture has demonstrated benefit for chemotherapy-induced acute vomiting, but studies combining electroacupuncture with state-of-the-art antiemetics and in patients with refractory symptoms are needed to determine clinical relevance. Self-administered acupressure appears to have a protective effect for acute nausea and can readily be taught to patients though studies did not involve placebo control. Noninvasive electrostimulation appears unlikely to have a clinically relevant impact when patients are given state-of-the-art pharmacologic antiemetic therapy.⁸⁸

Another systematic review of >40 RCTs in nonchemotherapy settings supports the role of acupuncture in preventing or attenuating nausea and vomiting (Table S11).⁸⁹ Studies published since the Cochrane review are, in general, consistent with these findings.⁹⁰⁻⁹⁸

2.5.2 Acupuncture for CIPN and Cancer-Related Pain: PICO question: In cancer patients whose lung cancer whose cancer-related pain and peripheral neuropathy is not controlled adequately, does acupuncture as an adjunct treatment help reduce the symptoms?

After initial review for CIPN articles, five were selected: one RCT, three prospective case series or reports, and one retrospective review.⁹⁹⁻¹⁰³ The RCT compared acupuncture with vitamin B12, but only the abstract was evaluated.¹⁰¹ The prospective trials may lend themselves to potentially larger trials that may evaluate efficacy; however, the data given were inconclusive.^{102,103}

After our initial search for articles on cancer-related pain and acupuncture, 19 were selected, 12 of which were RCTs, one a prospective trial, and six case series trials. The RCTs involving head and neck cancer- and breast cancer-related pain showed improvement in pain scores (Brief Pain Inventory).¹⁰⁴⁻¹⁰⁷ No difference was seen for postthoracotomy pain vs sham acupuncture.¹⁰⁸⁻¹¹⁰ The case series trials suggested improvement in pain scale scores (Brief Pain Inventory and numerical rating measurements) and symptoms related to pain.¹¹¹⁻¹¹⁵

Overall, there is a paucity of data on whether acupuncture could be useful in the treatment of CIPN. Small case series show some improvement in visual analog pain scale and neuropathy symptoms.^{102,103} Although data for cancer-related pain are more abundant, the data only support potential benefit in breast and head and neck cancer.^{104-107,116} There does not seem to be an improvement in pain control for post-surgical patients.^{108-110,117}

2.5.3 Recommendations

2.5.3.1. In patients having nausea and vomiting from either chemotherapy or radiation therapy, acupuncture or related techniques is suggested as an adjunct treatment option (Grade 2B).

2.5.3.2. In patients with cancer related pain and peripheral neuropathy, acupuncture is suggested as an adjunct treatment in patients with inadequate control of symptoms (Grade 2C).

2.5.4 Safety Issues, Morbidity, and Mortality Associated With Acupuncture Treatments: After initial review of safety-related articles for acupuncture treatments, nine articles, none of which were specific to patients with cancer, were included for discussion, and all were review articles. Two articles reviewed acupuncture treatments in the pediatric population.^{118,119} Two reviews are presented that are meta-analyses of review articles,^{120,121} and two reviews evaluated prospective trials and case reports in the literature.^{122,123} The remaining three reviews evaluated responses from practitioners with regard to adverse events.¹²⁴⁻¹²⁶ The rate of pneumothorax was reported as one in 150,000.^{121,123} In the prospective responder studies, no severe events were noted^{124,126}; however, the retrospective review showed numerous pneumothorax, hepatitis, and spinal cord injury.¹²⁵ Mild adverse event rates are reported as 1% to 10% in the pediatric population.^{118,119}

Therefore, acupuncture is generally safe when performed by qualified professional practitioners. Serious adverse events from acupuncture have been reported in the literature but appear to be rare. Precautions, including follow-up and infectious precautions, should be taken to reduce the rates of serious events.

2.6 Nutrition

The evidence for nutrition and cancer was evaluated in three distinct parts of the lung cancer continuum: (1) nutrition and lung cancer prevention; (2) nutrition during lung cancer treatment; and (3) nutrition in cancer survivors. A total of 24 potential citations relating to nutrition and lung cancer prevention were identified, nine pertaining to nutrition and lung cancer treatment but none for nutrition and lung cancer survivors. Specific recommendations were made on the basis of the strength of the evidence from these studies. There are a limited number of clinical trials examining the specific role of nutritional intervention during lung cancer treatment or in survivorship after lung cancer treatment, and recommendations are based on these studies, in addition to extrapolation of evidence from nutrition and cancer studies in other cancer sites with disease pathophysiology and symptoms similar to those of a patient with lung cancer. In addition, based on the contradictory findings in the literature with regard to nutrition and lung cancer prevention, this section of the recommendations is based on the source-specific effects of nutrients in lung cancer, namely dietary source and not supplement

as source. The data on specific supplements are discussed by Szabo et al¹⁸ in the ACCP Lung Cancer Guidelines.

2.6.1 Nutrition and Cancer Prevention: PICO question: In people at risk of lung cancer, do certain dietary regimens help reduce the risk?

Specifically, a common question asked by patients and health-care professionals is, “Does consumption of a diet rich in nonstarchy vegetables and fruits reduce the risk of lung cancer?” Several cohort, case-control studies, ecologic studies, and meta analyses have examined total intake of vegetables and fruits, other than those considered starchy (root vegetables and tubers), and lung cancer. Most studies showed decreased risk with increased intake of fruits and vegetables.¹²⁷⁻¹⁴³ In addition to an overall inverse association with fruit intake, the results of this evaluation show evidence for a significant inverse association between vegetable consumption and lung cancer incidence in smokers.^{131,134} The risk of squamous cell carcinomas specifically for current smokers was reduced with increasing fruit and vegetable consumption.¹²⁷ The data are similar for carotenoid intake from dietary sources (not supplements), demonstrating that dietary carotenoid intake, including higher serum levels of carotenoids, was associated with a lower risk of lung cancer.^{137,138} In the β -Carotene and Retinol Efficacy Trial (CARET), another large chemoprevention trial of 18,000 smokers, former smokers, and workers exposed to asbestos, β -carotene and vitamin A supplementation again was associated with a higher risk of lung cancer (see also Szabo et al,¹⁸ “Chemoprevention of Lung Cancer,” in the ACCP Lung Cancer Guidelines).¹⁴⁴ Interestingly, subanalyses revealed that intake of fruits and vegetables from a dietary source was associated with a reduced lung cancer risk in the placebo arm. The association was strongest with rosaceae fruit (eg, apples, pears, peaches, cherries, plums, apricots, raspberries, strawberries, and so forth) or cruciferae vegetables (cabbage, Brussels sprouts, broccoli, cauliflower, kale, arugula, radish, and so forth).¹³⁸ Epidemiologic studies (cohort and case control) have demonstrated that a higher intake of cruciferous vegetables was associated with a lower risk of lung cancer,^{136,138-140,143,145} after carefully controlling for cigarette smoking,¹³⁶ demonstrating this association beyond the confounding effects of smoking. More recent studies examining the mechanism of action have shown that these protective effects may be influenced by individual genetic variations (polymorphisms) in the metabolism and elimination of isothiocyanates from the body.^{139,145}

Evidence on the role of nutrition in lung cancer prevention comes predominantly from observational studies. There is a lack of RCTs, but the risks and burdens to patients are low.

Another common question is, “Does consumption of red meat and processed meat increase the risk of lung cancer?” Cohort and case-control studies have shown an association between increased red meat and processed meat intake and increased lung cancer risk.¹⁴⁶⁻¹⁴⁸ However, more recent studies^{149,150} failed to observe this association, although a reduced risk was observed with increased fish intake.¹⁴⁹ When red meats or processed meats are cooked at high temperatures, they contain heterocyclic amines and polycyclic aromatic hydrocarbons. Similarly, processed meats contain N-nitroso compounds, which are suspected mutagens and carcinogens. Many processed meats also contain high levels of salt and nitrites. A prospective study reported that individuals in the highest quartile of processed meat intake had a 16% elevated risk of lung cancer.¹⁴⁸ However, red meats are also an excellent source of heme iron, the most bioavailable form of iron, critical to prevent the consequences of iron-deficiency anemia. Based on the evidence, there is uncertainty in estimating the risks and burden; benefits, risk, and burden may be closely balanced.

2.6.2 Nutrition and Lung Cancer Treatment: PICO question: In patients with lung cancer, does nutritional intake of protein-energy-dense foods beneficially affect nutritional status compared with usual care?

RCTs evaluating the beneficial effects of nutritional supplementation during the treatment of lung cancer are limited. Research studies in other cancers have demonstrated the benefits of supplementation with protein and caloric-dense oral or parenteral supplements to improve markers of nutritional status. The average caloric deficit in weight-losing patients on cancer treatment is approximately 250 to 400 kcal/day. The average supplementation of 1-calorie/mL supplements has not been shown to improve the nutritional status of patients on chemotherapy.^{151,152} However, studies using a more calorie-dense (1.5 kcal/mL) and higher-protein supplementation have suggested that weight stabilization at least can be achieved,¹⁵³ although improvements in lean body mass have not been observed in these studies. Yin et al¹⁵⁴ examined the effect of amino acid (250 mL, 500 mL vs placebo) supplementation via the parenteral route on serum tryptophan and melatonin in 72 patients with NSCLC receiving chemotherapy. Although the concentrations of serum tryptophan and melatonin decreased after chemotherapy in all three arms of the study, the group administered 500 mL/d of amino acids demonstrated significantly higher ($P < .05$) levels compared with the lower-dose and placebo arms. To date, clinical trials pertaining to nutritional interventions during lung cancer treatment are sparse. The studies are also limited when it comes to measuring the extent

of change in intermediate end point biomarkers of nutritional status observed, in addition to markers of safety. However, based on studies of other populations of patients with cancer who share the symptoms observed in patients with lung cancer, where weight loss, anorexia, and cancer cachexia are cardinal symptoms, the benefits of supplementing patients with calorie-protein-dense supplements clearly outweigh the risk and burdens.

PICO question: In patients with lung cancer who have sarcopenia, does oral nutritional supplementation with n-3 fatty acids beneficially affect nutritional status compared with usual care with other nutritional supplements?

Fifty percent of patients with newly diagnosed advanced lung cancer have sarcopenia (severe muscle wasting)/cachexia. Plasma omega-3 fatty acids have been shown to be depleted in patients with cancer with sarcopenia, which may contribute to accelerated rates of muscle loss in this patient population.¹² Eicosapentaenoic acid (EPA) is an n-3 fatty acid and an essential fatty acid and polyunsaturated fat that is present in fish oils such as cod liver, sardine, and salmon oil. Evidence from laboratory and clinical studies has demonstrated that EPA has antitumor and anticachectic effects.^{155,156} A pilot trial of 36 subjects with cancer cachexia shows that 6 weeks of supplementation with 4 g per day omega-3 fatty acid led to a statistically significant increase in serum albumin level ($P < .0001$) and a moderately significant increase in serum transferrin ($P < .07$).¹¹ In a multicentered double-blinded RCT of 518 weight-losing patients with cancer, administration of pure EPA at 2 or 4 g daily for 8 weeks resulted in a borderline, nonsignificant weight gain.¹⁵⁷ In another RCT, 40 patients with stage III NSCLC were randomly assigned to receive two cans/day of a protein- and energy-dense oral nutritional supplement containing (omega-3) fatty acids or an isocaloric control supplement. The intervention group had better weight maintenance, better fat-free mass, reduced resting energy expenditure, and a higher energy and protein intake than the control group.¹⁵⁸ Although more well-powered RCTs are needed to confirm the preliminary findings in these studies, the benefits of omega-3 fatty acid supplementation in ameliorating sarcopenia in patients with NSCLC during and after treatment with single or multimodal therapies to treat cancer appear to outweigh the risks and burdens.

2.6.3 Recommendations

2.6.3.1. In people who might develop lung cancer a diet rich in non-starchy vegetables and fruits is suggested to reduce the risk of lung cancer (Grade 2C).

2.6.3.2. In people who might develop lung cancer, limiting the consumption of a large amount of red meat and processed meat is suggested; lower meat consumption may reduce the risk of lung cancer (Grade 2C).

2.6.3.3. In patients undergoing treatment of lung cancer who have experienced weight loss, the addition of high calorie and protein supplements (1.5 kcal/mL) as a nutritional adjunct is suggested to achieve weight stabilization (Grade 2C).

2.6.3.4. In patients with lung cancer who have sarcopenia oral nutritional supplementation with n-3 fatty acids is suggested in order to improve the nutritional status (Grade 2C).

2.6.4 Nutrition in Lung Cancer Survivors: As the number of cancer survivors continues to grow, so does the need to develop unique evidence-based guidelines to improve nutritional and functional status and QOL for this population. Survivorship should become a distinct phase of care and should include the provision of a care plan to recover from the consequences of cancer treatments and to prolong length of life and QOL. Nutritional status is a predictor of survival in the long term, independent of tumor extension and staging, in the population of patients with lung cancer. However, RCTs of nutritional interventions in lung cancer survivors after treatment are unavailable at this time. There is not enough evidence to make any recommendation on this issue.

3.0 CONCLUSION

Integrative medicine therapies are used widely by patients with lung cancer. Use of these therapies usually indicates underlying unmet needs of the patients. Health-care professionals should inquire about the use of complementary therapies and explore the reasons for their usage. Patients should be counseled on the nature of complementary therapies and their potential benefits and risks, so they can have realistic expectations when using them.

Regarding specific therapies, mind-body modalities are recommended as part of a multidisciplinary approach to reduce anxiety, mood disturbance, sleep disturbance, pain, and anticipatory chemotherapy-induced nausea and vomiting, and to improve QOL. The addition of massage therapy by trained professionals is recommended as a multimodality supportive care program for patients whose anxiety or pain is not adequately controlled by usual care. Supervised aerobic training or inpatient exercise-based multidisciplinary rehabilitation is suggested for patients awaiting surgical resection of lung cancer and after their surgery to

improve cardiorespiratory fitness and patient-reported outcomes. They are also suggested for select patients with lung cancer with inoperable disease, to improve exercise tolerance and functional capacity. Acupuncture is suggested as an adjunct treatment option in patients with chemotherapy- or radiotherapy-induced nausea and vomiting or cancer-related pain that is poorly controlled by usual care, and as part of a comprehensive smoking-cessation program. A diet rich in nonstarchy fruits and vegetables and low in red meat and processed meat is suggested for its potential benefit in the prevention of lung cancer. A protein- and energy-dense diet is suggested for patients undergoing active treatment of lung cancer. There is not enough evidence to support the routine use of dietary supplements for lung cancer prevention or for reducing side effects and improving therapeutic outcome during lung cancer treatment.

In general, clinical trials of complementary therapies suffer from limitations in the design and implementation of the studies. Therefore, there is no 1A recommendation in this article. More high-quality clinical trials need to be conducted to strengthen the evidence base of complementary therapies.

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Dr Deng: contributed to the decisions as to the content of the manuscript, the writing of individual section(s) of the manuscript, and the editing of the complete manuscript draft.

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