

## INTEGRATIVE MEDICINE FOR CANCER CARE

A therapeutic outline

This therapeutic outline provides an introduction to a variety of integrative medicine therapies that have been used and researched in the management of cancer symptoms and treatment side effects. This includes treatments with either nutraceuticals<sup>1</sup> or herbal medicine monotherapies<sup>2</sup> or where these are used adjunctively with conventional medical treatments.(1) Mind-body, manual, lifestyle, and other traditional therapies are also reviewed.

The outline has been drafted by experts in the field. However, it is not an exhaustive review of scientific evidence, such as a systematic review or meta-analysis, which is not its purpose. This outline provides a brief narrative review of the emerging evidence considered by the researchers at NICM Health Research Institute (NICM HRI) to be important in the area of integrative medicine for the management of cancer symptoms and treatment side effects.

# Why people use integrative medicine for cancer symptoms and treatment side effects

Complementary medicine (CM) is used in Australia and internationally to treat the symptoms of cancer and the side effects of treatment, such as anxiety, nausea, vomiting, peripheral neuropathy, and pain. An integrative approach to CM may improve patient outcomes by improving the effectiveness of conventional treatments through positive adjuvant effects and managing side effects, thereby improving tolerance of and compliance with chemotherapy and radiotherapy.(2)

The prevalence of CM use by people with cancer living in Australia increased from 22 per cent in 1996 to 65 per cent in 2008.(3, 4) CM is typically used as an adjuvant<sup>3</sup> to conventional treatment rather than an alternative. CM users tend to be mostly women, with breast and gynaecological cancers, have higher education and socioeconomic status, more advanced disease and younger or cultural groups where traditional health systems are part of usual mainstream care.(5) CM use is very high in women with breast cancer with 87 per cent reporting use.(6) Data is inconsistent on prevalence of use of CM use for particular tumour types. A nationwide survey in Japan found the prevalence of CM use was the highest in people with lung cancer (53 per cent).(7) In contrast, a European survey reported greater CM use among those diagnosed with pancreatic, liver, bone/spinal, and brain cancers.(8) In China, traditional Chinese medicine (TCM) is used to both treat cancer – often in synergy with conventional cancer therapies – as well as the symptoms of cancer and side effects of treatment within their standard healthcare system. In Australia, while the provision of CM by hospitals in Australia appears to have doubled over the past six years, services are limited and available in only 26 per cent of healthcare organisations.(9)





<sup>&</sup>lt;sup>1</sup> Nutraceuticals are nutrient-based natural products which are produced via pharmaceutical good manufacturing practice, standardised and optimised.

<sup>&</sup>lt;sup>2</sup> A monotherapy describes a treatment that has only a single active ingredient. The single active ingredient could be a medicine or a vitamin or a single herbal ingredient.

<sup>&</sup>lt;sup>3</sup> An adjuvant is a substance that is used in addition to usual treatment.

## Safety and evidence of integrative medicine in cancer care

CM studies in cancer care have generally been conducted in small population sample sizes which limits the strength and certainty of evidence for use. However, where there is indication of a favourable benefit it may be appropriate to adopt the use of a specific CM where safety of a particular CM has been determined and there is no adverse impact on the effectiveness of the conventional cancer treatment. For herbal medicines or dietary supplements, use may be contraindicated when a patient is undergoing cancer treatment but considered safe when treatment is completed. Therapies such as meditation, acupuncture, relaxation therapy, passive music therapy<sup>4</sup>, massage or yoga, pose relatively little risk and may have a positive impact on symptoms.(10, 11)

For traditional Chinese medicine (TCM), there were over 5834 randomised controlled trials (RCTs) conducted between 1985 and 2017.(12) The majority of these studies (4,752) combined TCM with conventional treatment such as chemotherapy or radiotherapy, while 1,082 used TCM only primarily to address symptoms and side effects. Most studies were in herbal medicine, with 1082 examining acupoint stimulation. The majority of RCTs (4051; 69.44 per cent) concluded there were beneficial effects using either TCM alone or TCM plus conventional treatment compared with conventional treatment. For the use of acupuncture alone, a bibliometric analysis of all acupuncture-related research articles including clinical and animal studies found research into cancer was the second most researched area after pain, and that research into this area is increasing.(13)

The use of CM should always be discussed with the treating cancer care team. In integrative oncology, patients and their cancer treatment teams work together to find appropriate conventional and complementary therapies that have been shown to be safe and effective. The following therapeutic outline is designed to provide a brief indication of where there may be support for an intervention to treat a particular symptom or side effect of cancer treatment. It is beyond the scope of this review to provide definitive summary of the evidence in support or otherwise any particular intervention.

# Effectiveness of integrative medicine in patients with cancer

The following summary provides an overview of potential clinical areas of benefit from the use of integrative medicine as a therapeutic tool. An overview of reviews was undertaken, including a systematic search of Pubmed/Medline and Cochrane Collaboration publications to end 2021 limited to English language papers. However, this summary is not an exhaustive systematic review of all scientific evidence in the field, but rather provides a brief narrative review of the emerging evidence in key clinical areas as understood by expert researchers in the field.

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<sup>&</sup>lt;sup>4</sup> Music Therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program. Music therapy can be passive, for example listening to music, or active, that is creating, singing, or moving to music (<a href="https://www.musictherapy.org/about/musictherapy/">https://www.musictherapy.org/about/musictherapy/</a> - accessed April 2018).

The Society of Integrative Oncology, a multi-disciplinary professional organisation for integrative oncology, is developing guidelines in conjunction with the American Society for Clinical Oncology (ASCO) on fatigue, anxiety, and depression<sup>5</sup>. These will complement the 2022 Integrative Medicine for Pain Management in Oncology: Society for Integrative Oncology – ASCO Guideline and the 2017 ASCO endorsed guideline for integrative oncology for breast cancer. NICM HRI has commenced a series of reviews of the evidence for biologically based therapies, mind-body therapies, and acupuncture in the treatment of a range of other side effects and symptoms.

People with cancer experience a range of symptoms and side effects of treatment, often in 'symptom clusters'. The careful selection of one therapy may address several symptoms simultaneously. This outline covers key applications and research of nutraceuticals, herbal medicines, and mind-body therapies for some of these symptoms and side effects.

### Nutraceuticals and herbal medicines in cancer care

## Chemotherapy-induced nausea and vomiting (CINV) - Treatment with nutraceuticals and herbal medicines

- Cannabis and cannabinoids for CINV A systematic review and meta-analysis published in 2015 identified 29 studies investigating efficacy of cannabinoids in the treatment of CINV (14 for nabilone; three for dronabinol; one for nabiximols; six for Tetrahydocannabinol; four for levonantradol). While findings were suggestive of increased risk of short-term adverse effects associated with cannabinoids, all studies demonstrated a greater benefit of cannabinoids compared with comparators or placebo but statistical significance was not achieved in all reviewed studies.(14) Furthermore, conclusions drawn by the National Academies of Science, Engineering and Medicine review suggest that there is conclusive evidence that oral cannabinoids are effective antiemetics in the treatment of CINV, however, that there is a lack of good quality randomised trials investigating the use of botanically derived cannabis despite an abundance of anecdotal reports.(15) Due to the complexity of botanical cannabis phytochemistry and obstacles to researching the plant due to Drug Scheduling laws internationally, this is a knowledge gap that should be a future research priority.(14-16)
  - Current recommendations and guidance In Australia, federal government guidance documents recommend that high-tetrahydrocannabinol (THC) medicinal cannabis products can sometimes be effective for nausea and vomiting but should only be prescribed after newer standard approved treatments have failed.(17) The Cancer Council of Australia and the Clinical Oncology Society of Australia joint position statement on the medical use of cannabis(18) suggests that there is some evidence that cannabis and cannabinoids in controlled delivery may have a benefit to people with cancer where conventional treatments are unsuccessful, such as in providing relief in CINV. Conversely, the American Society for Clinical Oncology suggests that the "evidence remains insufficient for a recommendation regarding treatment with



<sup>&</sup>lt;sup>5</sup> https://integrativeonc.org/practice-guidelines/announcements/208-announcement-of-sio-asco-collaboration-on-two-more-evidence-based-guidelines-in-2021-22.

medical marijuana for the prevention of nausea and vomiting in patients with cancer who receive chemotherapy or radiation therapy." Although approved cannabinoids – dronabinol and nabilone - are recommended for the treatment of CINV.

- Chinese herbal medicine for CINV in people with advanced non-small cell lung cancer (NSCLC) undergoing chemotherapy A meta-analysis published in 2013 compared adjunctive use of Chinese herbal medicine with usual care chemotherapy in people undergoing treatment for advanced NSCLC and found adjunctive use of Chinese herbal medicine to be effective in reducing nausea and vomiting at toxicity grade of III-IV (RR = 0.24, 95 per cent CI = 0.12-0.50, p = 0.0001).(22) The five RCTs included in this meta-analysis used different herbal formulations which makes it difficult to make a specific recommendation on Chinese herbal medicine for CINV.(23-27)
- Ginger for CINV in women with breast cancer undergoing chemotherapy Ginger can be considered as an addition to antiemetic drugs to control nausea and vomiting experienced by women with breast cancer undergoing chemotherapy,(10, 28) but the evidence on its use with other cancer types is not as strong.(29) As such, the American Society of Clinical Oncology guidelines on antiemetics state that evidence remains insufficient for a recommendation for or against the use of ginger for the prevention of nausea and vomiting in patients with cancer. In another systematic review of ginger in different cancer types a statistically significant effect of ginger tea consumption was found on overall CINV severity. However, the certainty in this effect was very low.(31)
  - <u>Current recommendation</u> Ginger can be considered as an addition to antiemetic drugs to control nausea and vomiting during chemotherapy in women with breast cancer (Grade C<sup>6</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### • Glutamine for CINV

 <u>Current recommendation</u> - Glutamine should not be recommended for improving nausea and vomiting during chemotherapy in women with breast cancer according to the Society of Integrative Oncology (Grade D<sup>7</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

## Chemotherapy-induced peripheral neuropathy (CIPN) - Treatment with nutraceuticals and herbal medicines

<u>Cannabis or cannabinoids for CIPN</u> – Results from a small-scale pilot study (n-18) investigating
 Sativex – a botanically derived standardised cannabis extract – for the treatment of
 chemotherapy-induced neuropathic pain found there was no statistically significant
 difference between the treatment and placebo groups in terms of pain outcomes. However,

 $<sup>^7</sup>$  A  $\underline{\text{Grade D}}$  recommendation of the Society of Integrative Oncology indicates no demonstrated effect.





<sup>&</sup>lt;sup>6</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

there appeared to be responders suggesting a larger, more statistically powered fully randomised, placebo-controlled trial is warranted.(32, 33)

- Nutritional supplements for CIPN A systematic review of 24 studies concluded that currently no nutritional supplement has shown solid beneficial evidence to be recommended for the treatment or prophylaxis of CIPN.(34)
  - o Acetyl-L-carnitine is not recommended for the prevention of CIPN.(10, 28, 35, 36)
  - o Acetyl-L-carnitine may be a treatment option for paclitaxel and cisplatin induced CIPN.(37, 38)
  - o Calcium and magnesium infusion (CaMg) is not recommended for the prevention of CIPN in patients receiving oxaliplatin-based chemotherapy.(35)
  - Glutathione is not recommended for the prevention of CIPN in patients receiving paclitaxel/carboplatin chemotherapy.(35)
  - o Omega-3 fatty acids may be beneficial for patients undergoing chemotherapy, according to one systematic review.(39) In another meta-analysis of three studies, the omega-3 PUFA group had significantly reduced the likelihood of developing CIPN compared to the control group.(21) But subsequent trials are needed to replicate and confirm these findings before a recommendation can be made.(1)
  - o <u>Vitamin E</u> is not recommended for the prevention of CIPN in patients with cancer undergoing treatment with neurotoxic agents.(35)
  - o No recommendations can be made on the use of N-acetylcysteine, glutamine or glutathione for patients receiving cisplatin or oxaliplatin-based chemotherapy for the prevention of CIPN at this time.(35)
  - o No recommendations can be made on the use of go-sha-jinki-gan, Jinlongshe granules or Xiao-Ai-Tong decoction for the prevention of CIPN at this time.(35, 40)

#### Fatigue - Treatment with nutraceuticals and herbal medicines

Fatigue is experienced by most patients undergoing cancer treatment and some people continue to experience fatigue after treatment has finished. The fatigue can become debilitating and is referred to as 'cancer-related fatigue'. Supportive care<sup>8</sup> can aid in reducing the severity of fatigue.(43)

- Acetyl-L-carnitine Should not be recommended for improving fatigue during treatment in women with breast cancer according to the Society of Integrative Oncology (Grade D9).(10, 44) This recommendation is endorsed by the American Society of Clinical Oncology.(28)
- <u>Astragalus</u> <sup>10</sup> May be helpful in advanced cancer in the form of Astragalus polysaccharides (PG2), a processed form of Astragalus.(45-47)

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<sup>8</sup> Supportive care for cancer patients refers to the prevention and management of adverse effects of cancer and its treatment42. Berman R. Davies A, Cooksley T, Gralla R, Carter L, Darlington E, et al. Supportive Care: An Indispensable Component of Modern Oncology. Clin Oncol (R Coll Radiol), 2020;32(11);781-8.

A Grade D recommendation of the Society of Integrative Oncology indicates no demonstrated effect.

<sup>10</sup> The roots of Astragalus membranaceous also known as milk vetch or huangqi, is one of the most commonly used herbs in Traditional Chinese Medicine (TCM). In the context of Western medicine, it is claimed to have immune modulating effects, anticancer actions, and support quality of life for people with cancer. Astragalus is often used in combination with other herbs, however three meta-analyses and six randomized controlled trials have evaluated Astragalus as a single herb for cancer outcomes.

- Chinese herbal medicines for fatigue Some Chinese herbal medicines may be useful for cancer-related fatigue. An example is American Ginseng, which has been found to be helpful for fatigue in patients with breast cancer.(48) Other specific Chinese herbs may be considered but should not be used concurrently with other treatments, such as chemotherapy, as the trials done in this space to date are methodologically weak.(49, 50)
- <u>Ginseng</u> Can be considered for improving fatigue during treatment in women with breast cancer according to the Society for Integrative Oncology (Grade C<sup>11</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28, 51) In a systematic review of ginseng, all three types of ginseng were tolerated well with few low-grade adverse events. American ginseng, for up to eight-weeks significantly reduced fatigue. Asian ginseng, symptoms of fatigue at the dosage of 400 mg/day in the majority of patients with CRF. Korean ginseng, consumed at the dosage of 3000 mg/day for 12-weeks, decreased symptoms of CRF. But the number of studies are not adequate to adopt ginseng as a standard treatment for CRF in all cancer types.(52)
- <u>Guarana</u> Should not be recommended for improving fatigue during treatment in women with breast cancer according to the Society of Integrative Oncology (Grade D<sup>12</sup>).(10, 44) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### Hot flushes - Treatment with nutraceuticals and herbal medicines

- <u>Black cohosh for hot flushes</u> There is not enough evidence to recommend black cohosh for hot flushes.(28)
- <u>Herbal medicines for hot flushes</u> There is insufficient evidence currently on effectiveness of herbal medicine treatments for hot flushes resulting from endocrine therapy for breast cancer so no recommendation can be made in this area.(53)
- <u>Soy for hot flushes</u> Soy is not recommended for hot flushes in patients with breast cancer due to lack of effect in women with breast cancer according to the Society of Integrative Oncology (Grade D<sup>13</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

 $<sup>^{13}</sup>$  A <u>Grade D</u> recommendation of the Society of Integrative Oncology indicates no demonstrated effect.





<sup>&</sup>lt;sup>11</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

<sup>&</sup>lt;sup>12</sup> A <u>Grade D</u> recommendation of the Society of Integrative Oncology indicates no demonstrated effect.

#### Mucositis<sup>14</sup> - Treatment with nutraceuticals and herbal medicines

- <u>Aloe vera for mucositis</u> There is mixed evidence on the efficacy of aloe vera for the prevention and treatment of radiation induced mucositis.(54, 55)
- <u>Calendula officinalis for mucositis</u> A small RCT (n=40 participants) assessing the efficacy of
  two per cent calendula extract mouthwash (as oral gel) in reducing radiation induced
  oropharyngeal mucositis (OM) in patients with head and neck cancer undergoing treatment
  found that calenda extract gel was effective in decreasing the intensity of radiotherapyinduced OM.(56, 57)
- <u>Glutamine for mucositis</u> Parenteral glutamine for mucositis is not recommended but oral glutamine is recommended, based on two RCTs showing that a glutamine dose from 10 to 30 g daily during RT-CT, may prevent mucositis.(58)
- <u>Honey for mucositis</u> Honey, applied topically and administered systemically, has been suggested for prevention in patients with head and neck cancer who received either RT or RT-CT. Some of the RCTs had a mixed patient population (RT and RT-CT), small sample size, and different sources for the honey; therefore, only a suggestion was possible.(58)
- Turmeric for mucositis Curcumin is an anti-inflammatory and an antioxidant. Curcumin may be helpful in reducing severity and redness of mucositis when used as a topical application.(59) In another RCT, the prophylactic use of curcumin delayed the incidence and severity of mucositis in those patients with head and neck cancer receiving radiotherapy.(60) Topical therapies preparations using 500 gm of fresh curcumin powder were effective, as was a turmeric gargle of a 400 mg turmeric capsule.
- Zinc for mucositis Supplementation was reported to reduce the incidence and severity of
  mucositis in leukaemia patients undergoing chemotherapy(61); and in patients receiving
  radiation therapy.(62) However, the Multinational Association for Supportive Care in Cancer
  has reviewed recent evidence and concluded that no guideline recommendation is possible
  either way currently.(58)

#### Pain - Treatment with nutraceuticals and herbal medicines

• Chinese herbal medicines for pain relief in people with cancer – A systematic review and metaanalysis published in 2016 found adjunctive use of Chinese herbal medicine for pain relief in patients with a variety of different kinds of advanced cancers resulted in significantly reduced pain (three studies; weighted mean difference in pain score of -0.90; 95 per cent CI: -1.69 to -0.11).(63-66) However, all of these studies provided limited information regarding risk of bias, and further to this, the three RCTs included in this meta-analysis used different herbal formulations which makes it difficult to make a specific recommendation on Chinese herbal medicine for pain.

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<sup>&</sup>lt;sup>14</sup> Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer.

- Cannabis and cannabinoids for pain relief in people with cancer A multicentre, double-blind, randomised placebo-controlled study by Johnson and colleagues demonstrated that a standardised tetrahydrocannabinol:cannabidiol extract (THC:CBD) was efficacious as an analgesic in patients with intractable cancer related pain that was not controlled by opioid medication.(67) Further, Sativex a botanically derived standardised cannabis extract was found to be a useful add-on analgesic for patients with opioid refractory cancer pain in a randomised, placebo-controlled graded-dose trial.(68) And a systematic review by Whiting et al. found that analyses across seven trials that assessed nabiximols (i.e. Sativex) and one examining inhaled cannabis was suggestive that plant-derived cannabinoids increase the odds for improvement of pain by approximately 40 per cent vs the control condition (OR, 1.41; 95 per cent CI=0.99-2.00; eight trials).(14, 69)
  - <u>Current recommendations and guidance</u> In Australia, federal government guidance documents have only specifically addressed chronic non-cancer pain (CNCP).(17) The Cancer Council of Australia and the Clinical Oncology Society of Australia joint position statement on the medical use of cannabis suggests that there is some evidence that cannabis and cannabinoids in controlled delivery may have a benefit to people with cancer where conventional treatments are unsuccessful, such as in providing relief as an adjunctive analgesic in patients with moderate to severe pain.(18)

#### Sleep - Treatment with nutraceuticals and herbal medicines

Melatonin - In RCT among people with breast cancer who took 5 mg of melatonin at bedtime
there were improved measures of sleep quality.(70) A systematic review of melatonin,
dosage minimum and maximum of 3 mg and 20 mg, showed a significant effect on sleep
quality and insomnia in four studies in people with cancer. Melatonin was found comparable
to zolpidem in affecting sleep duration, latency, efficiency, and disturbance in colorectal
cancer patients undergoing chemotherapy.(71)

## Mind-body therapies in cancer care

#### Chemotherapy-induced nausea and vomiting (CINV)

- <u>Relaxation</u> The evidence as it currently stands is limited with regard to the use of relaxation
  in the management of CINV in women with breast cancer, but there is sufficient evidence to
  suggest relaxation can be considered as an addition to antiemetics for the control of acute
  CINV in women.(73, 74)
  - Current recommendation Relaxation can be considered as additions to antiemetic drugs to control nausea and vomiting during chemotherapy in women with breast





cancer (Grade C<sup>15</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### Chemotherapy-induced cognitive change

Mindfulness-based approaches to reducing cancer-related cognitive impairment may be effective. A meta-analysis of four RCTs found a significant difference in subjective cognitive function and mental health quality of life. The limited number of studies require further research to confirm these findings.(75) Further research is also needed to optimise timing, duration and content.(76)

#### **Fatigue**

- <u>Mindfulness</u> Mindfulness is effective at reducing fatigue severity in cancer.(43, 77-79)
- Relaxation techniques Research shows relaxation techniques such as progressive muscle relaxation and guided imagery are effective at improving fatigue symptoms/ cancer-related fatigue.(43, 80)
- <u>Yoga</u> Yoga has been shown to be effective in reducing fatigue in women with breast cancer when compared with no other intervention.(78, 81, 82)
  - <u>Current recommendation</u> Yoga can be considered for improving post-treatment fatigue in women with breast cancer according to the Society of Integrative Oncology (Grade C<sup>16</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)
- Qigong The first randomised controlled trial completed that was large enough to detect an
  effect found that medical qigong is an effective treatment for fatigue in people with cancer
  (83) As a result of this study, the American Society of Clinical Oncology notes that qigong
  may offer some benefit to people with cancer experiencing fatigue but calls for additional
  research.(78, 84)

#### Mood disturbance, stress, and quality of life

<u>Mindfulness</u>-based interventions are associated with reduced anxiety and depression.(85) Specific interventions such as the <u>Mindfulness Based Stress Reduction (MBSR) programs</u> have been found to benefit the mental health (quality of life, mood stress, anxiety, depression) of patients with

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<sup>&</sup>lt;sup>15</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

<sup>&</sup>lt;sup>16</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

cancer.(86-89) Mindfulness-based interventions are varied in length and type, effects are variable, suggesting the need for research to optimise the dose of the intervention.

<u>Yoga</u> – of various types – has been found to be effective in reducing anxiety, depressive symptoms and other mood disturbances in people with cancer(90); this is in line with research that shows yoga reduces salivary cortisol levels(94, 95), with investigators reporting a dose-response relationship.(96) <u>Relaxation therapy</u>, such as <u>guided visualisation</u> or <u>Progressive Muscle Relaxation</u> (<u>PMR</u>), is effective for improving tension, anxiety, and mood and decreasing hostility, BP, pulse rate, nausea, sleep disturbance, and pain.(97) Relaxation is recommended for improving mood disturbance and depressive symptoms.(98)

Passive music therapy is recommended to reduce anxiety during radiation therapy, chemotherapy sessions, and post-surgery in women with breast cancer, with interventions found to reduce sedation requirements during radiation therapy. Culturally appropriate music therapy interventions for psychological distress is associated with improvements.(103)

#### Pain

- <u>Music Therapy</u> There is limited evidence suggesting a benefit on pain of music therapy.(125, 126)
  - o <u>Current recommendations</u> Music therapy can be considered for the management of pain in women with breast cancer according to the Society of Integrative Oncology (Grade C<sup>17</sup>).(10) Music therapy may be offered to patients experiencing surgical pain from cancer surgery, but evidence is low due to the quality of the studies.(1)

Guided imagery with progressive muscle relaxation may be offered to patients experiencing general pain from cancer treatment.(1)

#### Sleep disturbance

- <u>Yoga</u> Gentle yoga can be considered for improving sleep in women with breast cancer.(81, 127-131)
  - <u>Current recommendation</u> Gentle yoga can be considered for improving sleep in women with breast cancer according to the Society of Clinical Oncology (Grade C<sup>18</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)
- <u>Relaxation training</u> Relaxation training has been shown to be effective for improving sleep quality in people with cancer.(97)

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<sup>&</sup>lt;sup>17</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

<sup>&</sup>lt;sup>18</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

## Manual therapies in cancer care

#### Mucositis<sup>19</sup>

Low level laser therapy (LLLT) for mucositis – The Multinational Association of Supportive
Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) Clinical Practice
Guidelines for the management of mucositis provide specific protocols for the prevention of
oral mucositis using low level laser therapy (also referred to as photobiomodulation
(PBM).(58) PBM is recommended for prevention of mucositis in patients with head and neck
cancer receiving radiotherapy or chemotherapy based on recent evidence.

#### **Fatigue**

 <u>Massage for cancer related fatigue</u> - There is weak evidence that massage therapy has a weak short-term effect on cancer related fatigue.(10, 135-137)

#### Lymphoedema

- Manual lymphatic drainage and compression bandaging for lymphoedema There is limited evidence for the use of manual lymphatic drainage(138-145) or compression bandaging(140, 142) to treat arm lymphedema related to breast cancer. Despite this, either therapy can be considered as a treatment option for lymphedema, with manual lymphatic drainage being considered for those who have sensitivity to bandaging.
  - <u>Current recommendation</u> Manual lymphatic drainage and compression bandaging can be considered for improving lymphedema in women with breast cancer according to the Society of Integrative Oncology (Grade C<sup>20</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### Pain

Massage for pain relief - Massage provides immediate pain relief to people with a variety of
different cancers, including those with advanced cancer and those having undergone surgery
for cancer(136, 146). A recent systematic review and meta-analysis to evaluate the effects of
massage therapy in all cancer types found that massage therapy largely reduced pain in
patients and that foot reflexology appeared to be more effective than body or aroma
massage.(147) The 2022 American Society of Integrative Oncology pain guidelines
recommend massage of patients experiencing pain during palliative or hospice care; and for

<sup>&</sup>lt;sup>20</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.





<sup>&</sup>lt;sup>19</sup> Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer.

chronic pain in survivors of adult cancers. There is evidence that perioperative patients may benefit from massage used in conjunction with acupuncture in addition to usual care.(149, 150)

## Lifestyle therapies in cancer care

#### **Exercise**

- Exercise during and after cancer treatment Evidence strongly suggests that exercise is not only safe and feasible both during and after cancer treatment, but specific doses of aerobic, combined aerobic and resistance training; and/or resistance training can improve care-related health outcomes such as anxiety, depression, fatigue, physical functioning and quality of life.(155) The Clinical Oncology Society of Australia recommends people with cancer avoid inactivity and progress towards at least 150 minutes of moderate intensity aerobic exercise and two to three moderate intensity resistance exercise sessions each week.(156)
- Exercise to reduce cancer risk and reduce risk of cancer recurrence There is strong evidence that physical activity reduces the risk of cancers of the breast, colon, endometrium, bladder, stomach, oesophagus (adenocarcinoma) and kidney, and moderate evidence for an association with lung cancer risk. There is limited evidence that physical activity is associated with reduced risk for prostate cancer overall.(159, 160) Exercise has a favourable effect on mortality and recurrence in people with cancer.(160)

## Traditional therapies in cancer care

#### Chemotherapy-induced nausea and vomiting (CINV)

- Acupuncture for nausea and vomiting related to chemotherapy or radiation treatment –
  Reviews of studies using acupuncture of various types in cancer care electroacupuncture,
  manual acupuncture, acupressure, surface electrodes, or magnets show that acupuncture
  can be considered as an addition to antiemetics to help control nausea and vomiting when
  people undergo chemotherapy or radiation treatment.(161-165)
  - <u>Current recommendation</u> Acupressure and electroacupuncture can be considered as an addition to antiemetic drugs to control nausea and vomiting during chemotherapy in women with breast cancer according to the Society of Integrative Oncology (Grade B<sup>21</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

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<sup>&</sup>lt;sup>21</sup> A <u>Grade B</u> recommendation of the Society of Integrative Oncology indicates there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

#### Chemotherapy-induced peripheral neuropathy (CIPN)

- <u>Acupuncture for CIPN</u> A systematic review and meta-analysis published in 2022 assessed
  the efficacy of acupuncture for the treatment of CIPN. This study included nine RCTs with a
  total of 582 participants. Meta-analysis showed that acupuncture led to significant
  improvements in pain scores and nervous system symptoms, acupuncture may effectively
  relieve CIPN pain and functional limitation.(166, 167)
  - o <u>Current recommendation</u> Acupuncture may be offered to patients experiencing chemotherapy-induced peripheral neuropathy from cancer treatment.(1)

#### Dysphagia

Acupuncture for dysphagia caused by chemotherapy treatment for head and neck cancers –
There are some studies that indicate acupuncture may be useful in the treatment of dysphagia
caused by chemotherapy treatment for head and neck cancers, but sample sizes are small,
interventions variable, larger studies are needed.(168-170)

#### **Fatigue**

- Acupuncture for fatigue post cancer treatment Acupuncture can be considered as a treatment for patients, particularly for fatigue that lingers after cancer treatment has finished, noting the evidence suggests the net benefit is likely to be small.(10, 78, 171)
  - <u>Current recommendation</u> Acupuncture can be considered for improving posttreatment fatigue according to the Society of Integrative Oncology in women with breast cancer (Grade C<sup>22</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### **Hot flushes**

Acupuncture for hot flushes in women with breast cancer - Data from randomised trials suggest that acupuncture might be an efficacious option for the treatment of hot flashes in breast cancer survivors receiving adjuvant endocrine therapy. The effect duration of acupuncture appears to persist after treatment completion. Acupuncture could be considered for reducing hot flushes in women with breast cancer, with reported similar or better efficacy then venlafaxine and gabapentin.(172-175) Whenever available, this intervention could be considered for breast cancer survivors because it has very few side-effects and is associated

<sup>&</sup>lt;sup>22</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.



with additional benefits in other potential target symptoms, such as cancer-related fatigue and joint pain.(176)

 <u>Current recommendation</u> - Acupuncture can be considered for improving hot flushes in women with breast cancer according to the Society of Integrative Oncology (Grade C<sup>23</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)

#### Lymphoedema

Acupuncture for breast cancer treatment related lymphoedema - In a review of 14 RCTs with
758 participants of acupuncture and moxibustion arm circumference (compared to routine
care), range of motion and adduction (compared to oral diosmin) all significantly improved.
(177) Acupuncture and moxibustion appears safe for people with breast cancer treatment
related lymphoedema.(166, 178-181) However, studies are still required to confirm these
findings.

#### Mood disturbance, stress, and quality of life

Acupuncture may be effective in the management of anxiety and for stress in women with breast cancer.(182-185)

#### Pain

- Acupuncture for arthralgia induced by aromatase inhibitors (AI) Acupuncture can be
  recommended for arthralgia induced by aromatase inhibitors used for the treatment of breast
  cancer demonstrating similar results to medication with fewer side effects, but evidence
  suggests the net benefit is likely small.(161, 187-189).
  - <u>Current recommendations</u> Acupuncture should be offered to patients experiencing Al-related joint pain in breast cancer.(1)
- Acupuncture for cancer related pain A systematic review of 17 RCTs (and meta-analysis of 14 of these trials) published in 2019 found that acupuncture and/or acupressure was significantly associated with reduced cancer pain and decreased use of analgesics, although the evidence quality was moderate.(190) Acupuncture is suggested as an adjunct treatment when there is inadequate control of symptoms, particularly malignancy-related and surgery-induced pain.(11, 191-194) Studies were positive for pain post-operative for chronic pain or dysfunction as a result of neck dissection and breast cancer.(195, 196)

 $<sup>^{23}</sup>$  A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.



- <u>Current recommendations</u> Acupuncture can be considered for the management of pain in women with breast cancer according to the Society for Integrative Oncology (Grade C<sup>24</sup>).(10) This recommendation is endorsed by the American Society of Clinical Oncology.(28)
- Acupuncture may be offered to patients experiencing general pain or musculoskeletal pain from cancer. This recommendation is endorsed by the American Society of Clinical Oncology.(1)
- Acupressure for pain during treatment.
  - <u>Current recommendations</u> Reflexology or acupressure may be offered to patients experiencing pain during systemic therapy for cancer treatment.

#### Sleep disturbance

Acupuncture for cancer related insomnia – Few rigorous trials have tested the effects of
acupuncture for the management of cancer-related insomnia to date.(161) However, a
systemic review published in 2017 including six RCTs and a total of 475 people with a variety
of different cancers concluded there is a low level of evidence that acupuncture may be
superior to sham acupuncture, drugs or hormone therapy for the management of cancerrelated insomnia. Effect sizes were found to be very small and therefore of uncertain clinical
significance.(197, 198)

#### Xerostomia<sup>25</sup>

- Acupuncture for xerostomia related to cancer treatment There are some studies that indicate acupuncture may be useful in the treatment of xerostomia mostly in the area of head and neck cancer but sample sizes were small and larger studies are needed.(40, 195, 199-205) A 2020 meta-analysis and systematic review suggests that acupuncture is effective at improving xerostomia symptoms in people with cancer but not at objective salivary flow measurements.(206)
  - <u>Current recommendations</u> The Multinational Association of Supportive Care in Cancer (MASCC) and ASCO recommend acupuncture be offered during radiation therapy for head and neck cancer to reduce the risk of developing xerostomia; and after radiation therapy for improving xerostomia.(207)
- There is also a weak recommendation that transcutaneous electrostimulation or acupuncturelike transcutaneous electrostimulation of the salivary glands be offered after radiation therapy

<sup>&</sup>lt;sup>25</sup> Xerostomia is defined as dry mouth resulting from reduced or absent saliva flow and may occur after radiation treatment to the head and/or neck region.





<sup>&</sup>lt;sup>24</sup> A <u>Grade C</u> recommendation of the Society of Integrative Oncology indicates that the evidence is equivocal or that there is at least moderate certainty that the net benefit is small.

in patients with head and neck cancer for improvement of salivary gland hypofunction and xerostomia.(207)

# Other potential benefits of integrative medicine in cancer care

- Yoga to improve quality of life in patients with breast cancer Few yoga studies have shown preliminary efficacy in improving QOL of life in patients with breast cancer including those newly diagnosed, those undergoing treatment, and longer-term survivors.(10, 93, 129, 208-212)
  - <u>Current recommendations</u> Yoga is recommended for improving quality of life in women with breast cancer by the Society of Clinical Oncology (Grade B<sup>26</sup>).(10) This recommendation is endorsed by the American Society for Clinical Oncology.(28)
- <u>Massage for immune system function and neuroendocrine system function</u> Massage may improve immune and neuroendocrine functions.(30, 119)
- <u>Acupuncture for chemotherapy induced immune system impacts</u> There are some small studies of variable quality suggesting acupuncture may be beneficial for chemotherapy induced leukopenia<sup>27</sup> and neutropenia<sup>28</sup> but further study is needed.(213, 214)
- Chinese herbal medicine for as an adjunctive treatment to cancer treatment Chinese herbal medicine has been used as an adjunct to chemotherapy for people undergoing treatment for a variety of different cancers in China, including advanced non-small cell lung cancer,(22) inoperable pancreatic cancer,(215) nasopharyngeal cancer(216) and breast cancer.(217) It has also been used for cancer palliative care.(218) However, this body of work needs further investigation in Western countries before any recommendations relevant to this context can be made.

### References

- 1. Mao JJ, Ismaila N, Bao T, Barton D, Ben-Arye E, Garland EL, et al. Integrative Medicine for Pain Management in Oncology: Society for Integrative Oncology-ASCO Guideline. Journal of Clinical Oncology. 2022:JCO.22.01357.
- 2. Frenkel M, Cohen L, Peterson N, Palmer JL, Swint K, Bruera E. Integrative medicine consultation service in a comprehensive cancer center: findings and outcomes. Integrative cancer therapies. 2010;9(3):276-83.
- 3. Oh B, Butow P, Mullan B, Beale P, Pavlakis N, Rosenthal D, et al. The use and perceived benefits resulting from the use of complementary and alternative medicine by cancer patients in Australia. Asia-Pacific journal of clinical oncology. 2010;6(4):342-9.



<sup>&</sup>lt;sup>26</sup> A <u>Grade B</u> recommendation of the Society of Integrative Oncology indicates there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

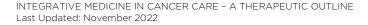
- 4. Begbie SD, Kerestes ZL, Bell DR. Patterns of alternative medicine use by cancer patients. The Medical journal of Australia. 1996;165(10):545-8.
- 5. Leis A, Millard J. Complementary and alternative medicine (CAM) and supportive care in cancer: a synopsis of research perspectives and contributions by an interdisciplinary team. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2007;15(8):909-12.
- 6. Kremser T, Evans A, Moore A, Luxford K, Begbie S, Bensoussan A, et al. Use of complementary therapies by Australian women with breast cancer. Breast (Edinburgh, Scotland). 2008;17(4):387-94.
- 7. Hyodo I, Amano N, Eguchi K, Narabayashi M, Imanishi J, Hirai M, et al. Nationwide survey on complementary and alternative medicine in cancer patients in Japan. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2005;23(12):2645-54.
- 8. Molassiotis A, Fernadez-Ortega P, Pud D, Ozden G, Scott JA, Panteli V, et al. Use of complementary and alternative medicine in cancer patients: a European survey. Annals of oncology: official journal of the European Society for Medical Oncology. 2005;16(4):655-63.
- 9. Smith CA, Hunter J, Ussher JM, Delaney G, Grant S, Templeman K, et al. Integrative Oncology in Australia 2016: Mapping Service Provision and Exploring Unmet Needs. Penrith (NSW): Western Sydney University; 2017.
- 10. Greenlee H, DuPont-Reyes MJ, Balneaves LG, Carlson LE, Cohen MR, Deng G, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA: a cancer journal for clinicians. 2017;67(3):194-232.
- 11. Deng GE, Rausch SM, Jones LW, Gulati A, Kumar NB, Greenlee H, et al. 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. Chest. 2013;143(5 Suppl):e420S-e36S.
- 12. Lu C-L, Li X, Zhou H-M, Zhang C, Yang Y-Y, Feng R-L, et al. Traditional Chinese Medicine in Cancer Care: An Overview of 5834 Randomized Controlled Trials Published in Chinese. Integrative Cancer Therapies. 2021;20:15347354211031650.
- 13. Ma Y, Dong M, Zhou K, Mita C, Liu J, Wayne PM. Publication Trends in Acupuncture Research: A 20-Year Bibliometric Analysis Based on PubMed. PloS one. 2016;11(12):e0168123.
- 14. Whiting PF, Wolff RF, Deshpande S, Di Nisio M, Duffy S, Hernandez AV, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. Jama. 2015;313(24):2456-73.
- 15. National Academies of Sciences Engineering and Medicine. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington DC: National Academies Press; 2017.
- 16. Smith LA, Azariah F, Lavender VT, Stoner NS, Bettiol S. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy. Cochrane Database Syst Rev. 2015;2015(11):Cd009464.
- 17. TGA. Guidance for the use of medicinal cannabis for the prevention or management of nausea and vomiting in Australia (Version 1). Woden: Therapeutic Goods Administration (Department of Health); 2017.
- 18. Cancer Council Australia and Clinical Oncology Society of Australia. Medical use of Cannabis (Joint Position Statement) [Available from: <a href="https://wiki.cancer.org.au/policy/Position\_statement">https://wiki.cancer.org.au/policy/Position\_statement</a> Medical use of cannabis.
- 19. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2017;35(28):3240-61.
- 20. Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, et al. Antiemetics: ASCO Guideline Update. Journal of Clinical Oncology. 2020;38(24):2782-97.
- 21. Lam CN, Watt AE, Isenring EA, de van der Schueren MAE, van der Meij BS. The effect of oral omega-3 polyunsaturated fatty acid supplementation on muscle maintenance and quality of life in patients with cancer: A systematic review and meta-analysis. Clinical Nutrition. 2021;40(6):3815-26.
- 22. Li SG, Chen HY, Ou-Yang CS, Wang XX, Yang ZJ, Tong Y, et al. The efficacy of Chinese herbal medicine as an adjunctive therapy for advanced non-small cell lung cancer: a systematic review and meta-analysis. PloS one. 2013;8(2):e57604.
- 23. Lu XA, Wei YR. Therapeutic effect of combination of Shenmai injection and radio-chemotherapy on advanced non-small cell lung cancer [Chinese language]. Hebei J Tradit Chin Med. 2009;31:597-9.
- 24. Huang YL, Hou AJ, Hu Y, Zhou L, Gao HF. The clinical effect of Yi Qi Yang Yin Chinese medicine combined with GP chemotherapy to the advanced non-small cell lung cancer patients [Chinese language]. J New Chin Med. 2011;43:47-9.
- 25. Huang YL, Hou AJ, Zhou L, Hu Y, Shen XY. Clinical study on non-small cell lung cancer treated by Zi Yin Qin Re herbs combined with chemotherapy [Chinese language]. Liaoning Tradit Chin Med J. 2012;2:53.
- 26. Xu ZY, Jin CJ, Shen DY. Clinical study on treatment of advanced non-small-cell lung cancer with Chinese herbal medicine in different stages combined with chemotherapy [Chinese language]. Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi = Chinese journal of integrated traditional and Western medicine. 2007:27(10):874-8.
- 27. Zheng QH LX, Wang Y Thirty cases of docetaxel plus cisplatin with Shenmai injection in treatment of advanced non-small cell lung cancer [Chinese language]. Jiangxi J Tradit Chin Med 2010;57-58.
- 28. Lyman GH, Bohlke K, Cohen L. Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline Summary. Journal of oncology practice. 2018;14(8):495-9.



- 29. Lee J. Oh H. Ginger as an antiemetic modality for chemotherapy-induced nausea and vomiting: a systematic review and meta-analysis. Oncology nursing forum. 2013;40(2):163-70.
- 30. Hernandez-Reif M, Field T, Ironson G, Beutler J, Vera Y, Hurley J, et al. Natural killer cells and lymphocytes increase in women with breast cancer following massage therapy. The International journal of neuroscience. 2005;115(4):495-510.
- 31. Gala D, Wright HH, Zigori B, Marshall S, Crichton M. Dietary strategies for chemotherapy-induced nausea and vomiting: A systematic review. Clinical Nutrition. 2022;41(10):2147-55.
- 32. Lynch ME, Cesar-Rittenberg P, Hohmann AG. A double-blind, placebo-controlled, crossover pilot trial with extension using an oral mucosal cannabinoid extract for treatment of chemotherapy-induced neuropathic pain. Journal of pain and symptom management. 2014;47(1):166-73.
- 33. Waissengrin B, Mirelman D, Pelles S, Bukstein F, Blumenthal DT, Wolf I, et al. Effect of cannabis on oxaliplatininduced peripheral neuropathy among oncology patients: a retrospective analysis. Therapeutic Advances in Medical Oncology. 2021;13:1758835921990203.
- 34. Schloss JM, Colosimo M, Airey C, Masci PP, Linnane AW, Vitetta L. Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): a systematic review. Clinical nutrition (Edinburgh, Scotland). 2013;32(6):888-93.
- 35. Hershman DL, Lacchetti C, Dworkin RH, Lavoie Smith EM, Bleeker J, Cavaletti G, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2014;32(18):1941-67.
- 36. Hershman DL, Unger JM, Crew KD, Till C, Greenlee H, Minasian LM, et al. Two-Year Trends of Taxane-Induced Neuropathy in Women Enrolled in a Randomized Trial of Acetyl-L-Carnitine (SWOG S0715). J Natl Cancer Inst. 2018;110(6):669-76.
- 37. Bianchi G, Vitali G, Caraceni A, Ravaglia S, Capri G, Cundari S, et al. Symptomatic and neurophysiological responses of paclitaxel- or cisplatin-induced neuropathy to oral acetyl-L-carnitine. European journal of cancer (Oxford, England: 1990). 2005;41(12):1746-50.
- 38. Maestri A, De Pasquale Ceratti A, Cundari S, Zanna C, Cortesi E, Crino L. A pilot study on the effect of acetyl-Lcarnitine in paclitaxel- and cisplatin-induced peripheral neuropathy. Tumori. 2005;91(2):135-8.
- 39. de Aguiar Pastore Silva J, Emilia de Souza Fabre M, Waitzberg DL. Omega-3 supplements for patients in chemotherapy and/or radiotherapy: A systematic review. Clinical nutrition (Edinburgh, Scotland). 2015;34(3):359-66.
- 40. Blom M, Dawidson I, Fernberg JO, Johnson G, Angmar-Mansson B. Acupuncture treatment of patients with radiation-induced xerostomia. European journal of cancer Part B, Oral oncology. 1996;32B(3):182-90.
- Ghoreishi Z, Esfahani A, Djazayeri A, Djalali M, Golestan B, Ayromlou H, et al. Omega-3 fatty acids are protective against paclitaxel-induced peripheral neuropathy: a randomized double-blind placebo controlled trial. BMC cancer. 2012;12:355.
- 42. Berman R, Davies A, Cooksley T, Gralla R, Carter L, Darlington E, et al. Supportive Care: An Indispensable Component of Modern Oncology. Clin Oncol (R Coll Radiol). 2020;32(11):781-8.
- 43. Duong N, Davis H, Robinson PD, Oberoi S, Cataudella D, Culos-Reed SN, et al. Mind and body practices for fatigue reduction in patients with cancer and hematopoietic stem cell transplant recipients: A systematic review and meta-analysis. Critical reviews in oncology/hematology. 2017;120:210-6.
- 44. Palma CG, Lera AT, Lerner T, de Oliveira MM, de Borta TM, Barbosa RP, et al. Guarana (Paullinia cupana) Improves Anorexia in Patients with Advanced Cancer. J Diet Suppl. 2016;13(2):221-31.
- 45. Chen HW, Lin IH, Chen YJ, Chang KH, Wu MH, Su WH, et al. A novel infusible botanically-derived drug, PG2, for cancer-related fatigue: a phase II double-blind, randomized placebo-controlled study. Clin Invest Med. 2012;35(1):E1-11.
- 46. Guo L, Bai SP, Zhao L, Wang XH. Astragalus polysaccharide injection integrated with vinorelbine and cisplatin for patients with advanced non-small cell lung cancer: effects on quality of life and survival. Med Oncol. 2012;29(3):1656-62.
- 47. Huang WC, Kuo KT, Bamodu OA, Lin YK, Wang CH, Lee KY, et al. Astragalus polysaccharide (PG2) Ameliorates Cancer Symptom Clusters, as well as Improves Quality of Life in Patients with Metastatic Disease, through Modulation of the Inflammatory Cascade. Cancers (Basel). 2019;11(8).
- 48. Barton DL, Liu H, Dakhil SR, Linquist B, Sloan JA, Nichols CR, et al. Wisconsin Ginseng (Panax quinquefolius) to improve cancer-related fatigue: a randomized, double-blind trial, NO7C2. Journal of the National Cancer Institute. 2013;105(16):1230-8.
- 49. Su CX, Wang LQ, Grant SJ, Liu JP. Chinese herbal medicine for cancer-related fatigue: a systematic review of randomized clinical trials. Complementary therapies in medicine. 2014;22(3):567-79.
- 50. Kwon CY, Lee B, Kong M, Lee SH, Jung HJ, Kim KI, et al. Effectiveness and safety of herbal medicine for cancer - related fatigue in lung cancer survivors: A systematic review and meta - analysis. Phytotherapy Research, 2021;35(2):751-70.
- Yennurajalingam S, Tannir NM, Williams JL, Lu Z, Hess KR, Frisbee-Hume S, et al. A Double-Blind, Randomized, Placebo-Controlled Trial of Panax Ginseng for Cancer-Related Fatigue in Patients With Advanced Cancer. J Natl Compr Canc Netw. 2017;15(9):1111-20.

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- 52. Sadeghian M, Rahmani S, Zendehdel M, Hosseini SA, Zare Javid A. Ginseng and Cancer-Related Fatigue: A Systematic Review of Clinical Trials. Nutrition and Cancer. 2021;73(8):1270-81.
- 53. Li Y, Zhu X, Bensussan A, Li P, Moylan E, Delaney G, et al. Herbal Medicine for Hot Flushes Induced by Endocrine Therapy in Women with Breast Cancer: A Systematic Review and Meta-Analysis. Evidence-based complementary and alternative medicine: eCAM. 2016;2016(Article ID 1327251).
- 54. Aghamohamamdi A, Hosseinimehr SJ. Natural Products for Management of Oral Mucositis Induced by Radiotherapy and Chemotherapy. Integrative cancer therapies. 2016;15(1):60-8.
- 55. Lima ICGdS, de Fátima Souto Maior L, Gueiros LAM, Leão JC, Higino JS, Carvalho AAT. Clinical applicability of natural products for prevention and treatment of oral mucositis: a systematic review and meta-analysis. Clinical Oral Investigations. 2021;25(6):4115-24.
- 56. Babaee N, Moslemi D, Khalilpour M, Vejdani F, Moghadamnia Y, Bijani A, et al. Antioxidant capacity of calendula officinalis flowers extract and prevention of radiation induced oropharyngeal mucositis in patients with head and neck cancers: a randomized controlled clinical study. Daru. 2013;21(1):18.
- 57. Marucci L, Farneti A, Di Ridolfi P, Pinnaro P, Pellini R, Giannarelli D, et al. Double-blind randomized phase III study comparing a mixture of natural agents versus placebo in the prevention of acute mucositis during chemoradiotherapy for head and neck cancer. Head Neck. 2017;39(9):1761-9.
- 58. Elad S, Cheng KKF, Lalla RV, Yarom N, Hong C, Logan RM, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2020;126(19):4423-31.
- 59. Normando AGC, de Menêses AG, de Toledo IP, Borges G, de Lima CL, Dos Reis PED, et al. Effects of turmeric and curcumin on oral mucositis: A systematic review. Phytother Res. 2019;33(5):1318-29.
- 60. Dharman S, G M, Shanmugasundaram K, Sampath RK. A Systematic Review and Meta-Analysis on the Efficacy of Curcumin/Turmeric for the Prevention and Amelioration of Radiotherapy/Radiochemotherapy Induced Oral Mucositis in Head and Neck Cancer Patients. Asian Pac J Cancer Prev. 2021;22(6):1671-84.
- 61. Rambod M, Pasyar N, Ramzi M. The effect of zinc sulfate on prevention, incidence, and severity of mucositis in leukemia patients undergoing chemotherapy. European journal of oncology nursing: the official journal of European Oncology Nursing Society. 2018;33:14-21.
- 62. Yarom N, Ariyawardana A, Hovan A, Barasch A, Jarvis V, Jensen SB, et al. Systematic review of natural agents for the management of oral mucositis in cancer patients. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2013;21(11):3209-21.
- 63. Ju SB, Zou YH. Effectiveness on Jia-Wei-Xiang-Sha-Liu-Jun-Zi decoction plus Fentanyl Transdermal Patch for cancer related pain in 60 advance cancer patients [Ariticle in Chinese]. New J Trad Chin Med. 2006;38:55-6.
- 64. Chung VC, Wu X, Lu P, Hui EP, Zhang Y, Zhang AL, et al. Chinese Herbal Medicine for Symptom Management in Cancer Palliative Care: Systematic Review And Meta-analysis. Medicine. 2016;95(7):e2793.
- 65. Jiang GS. The combination of traditional Chinese medicine and Western medicine for advanced colorectal cancer. Chin J Experiment Trad Med Formulae 2013;9:323-5.
- 66. Wu XD, Zheng NY, Xu LQ, al. e. Clinical observation on the combination of Gui-Dan-San-Zi-San-Re-Wei and Hyperthermia, radiotherapy for treating pain in cancer patients with bone metastases [Article in Chinese]. J New Chin Med. 2011;43:102–3.
- 67. Johnson JR, Burnell-Nugent M, Lossignol D, Ganae-Motan ED, Potts R, Fallon MT. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain. Journal of pain and symptom management. 2010;39(2):167-79.
- 68. Portenoy RK, Ganae-Motan ED, Allende S, Yanagihara R, Shaiova L, Weinstein S, et al. Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain: a randomized, placebo-controlled, graded-dose trial. The journal of pain: official journal of the American Pain Society. 2012;13(5):438-49.
- 69. Campbell G, Hall WD, Peacock A, Lintzeris N, Bruno R, Larance B, et al. Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study. Lancet Public Health. 2018;3(7):e341-e50.
- 70. Innominato PF, Lim AS, Palesh O, Clemons M, Trudeau M, Eisen A, et al. The effect of melatonin on sleep and quality of life in patients with advanced breast cancer. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2016;24(3):1097-105.
- 71. Shahrokhi M, Ghaeli P, Arya P, Shakiba A, Noormandi A, Soleimani M, et al. Comparing the Effects of Melatonin and Zolpidem on Sleep Quality, Depression, and Anxiety in PatientsWithColorectalCancerUndergoingChemotherapy. Basic and clinical neuroscience. 2021;12(1):105-14.
- 72. Jafari-Koulaee A, Bagheri-Nesami M. The effect of melatonin on sleep quality and insomnia in patients with cancer: a systematic review study. Sleep Med. 2021;82:96-103.
- 73. Molassiotis A, Yung HP, Yam BM, Chan FY, Mok TS. The effectiveness of progressive muscle relaxation training in managing chemotherapy-induced nausea and vomiting in Chinese breast cancer patients: a randomised controlled trial. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2002;10(3):237-46.
- 74. Yoo HJ, Ahn SH, Kim SB, Kim WK, Han OS. Efficacy of progressive muscle relaxation training and guided imagery in reducing chemotherapy side effects in patients with breast cancer and in improving their quality of



- life. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2005;13(10):826-33.
- 75. Zhang Y, Luo Y, Zeng Y. Meta-analysis of meditative/relaxation-based interventions for cognitive impairment in cancer patient. International Journal of Nursing Sciences. 2017;4(3):322-7.
- 76. Cifu G, Power MC, Shomstein S, Arem H. Mindfulness-based interventions and cognitive function among breast cancer survivors; a systematic review. BMC cancer. 2018;18(1):1163.
- 77. Haller H, Winkler MM, Klose P, Dobos G, Kummel S, Cramer H. Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. Acta oncologica (Stockholm, Sweden). 2017;56(12):1665-76.
- 78. Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2014;32(17):1840-50.
- 79. Johns SA, Von Ah D, Brown LF, Beck-Coon K, Talib TL, Alyea JM, et al. Randomized controlled pilot trial of mindfulness-based stress reduction for breast and colorectal cancer survivors: effects on cancer-related cognitive impairment. J Cancer Surviv. 2016;10(3):437-48.
- 80. Hilfiker R, Meichtry A, Eicher M, Nilsson Balfe L, Knols RH, Verra ML, et al. Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: a systematic review incorporating an indirect-comparisons meta-analysis. British journal of sports medicine. 2018;52(10):651-8.
- 81. Cramer H, Lauche R, Klose P, Lange S, Langhorst J, Dobos GJ. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. The Cochrane database of systematic reviews. 2017;1:Cd010802.
- 82. Zetzl T, Renner A, Pittig A, Jentschke E, Roch C, van Oorschot B. Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. Support Care Cancer. 2021;29(6):2973-82.
- 83. Oh B, Butow P, Mullan B, Clarke S, Beale P, Pavlakis N, et al. Impact of medical Qigong on quality of life, fatigue, mood and inflammation in cancer patients: a randomized controlled trial. Annals of oncology: official journal of the European Society for Medical Oncology. 2010;21(3):608-14.
- 84. BrintzenhofeSzoc K, Caicedo L, Zabora J, Campos C, Blinka M, Gonzalez F, et al. Impact of nueva vida's service model on quality of life, distress levels and self-efficacy in Latinas with breast cancer. Psycho-Oncology. 2012:1):44-5.
- 85. Oberoi S, Yang J, Woodgate RL, Niraula S, Banerji S, Israels SJ, et al. Association of Mindfulness-Based Interventions With Anxiety Severity in Adults With Cancer: A Systematic Review and Meta-analysis. JAMA Network Open. 2020;3(8):e2012598-e.
- 86. Shennan C, Payne S, Fenlon D. What is the evidence for the use of mindfulness-based interventions in cancer care? A review. Psycho-oncology. 2011;20(7):681-97.
- 87. Ledesma D, Kumano H. Mindfulness-based stress reduction and cancer: a meta-analysis. Psycho-oncology. 2009;18(6):571-9.
- 88. Matchim Y, Armer JM. Measuring the psychological impact of mindfulness meditation on health among patients with cancer: a literature review. Oncology nursing forum. 2007;34(5):1059-66.
- 89. Smith JE, Richardson J, Hoffman C, Pilkington K. Mindfulness-Based Stress Reduction as supportive therapy in cancer care: systematic review. Journal of advanced nursing. 2005;52(3):315-27.
- 90. Gonzalez M, Pascoe MC, Yang G, de Manincor M, Grant S, Lacey J, et al. Yoga for depression and anxiety symptoms in people with cancer: A systematic review and meta-analysis. Psycho-Oncology. 2021;30(8):1196-208.
- 91. Lin KY, Hu YT, Chang KJ, Lin HF, Tsauo JY. Effects of yoga on psychological health, quality of life, and physical health of patients with cancer: a meta-analysis. Evidence-based complementary and alternative medicine: eCAM. 2011;2011:659876.
- 92. Smith KB, Pukall CF. An evidence-based review of yoga as a complementary intervention for patients with cancer. Psycho-oncology. 2009;18(5):465-75.
- 93. Dhruva A, Miaskowski C, Abrams D, Acree M, Cooper B, Goodman S, et al. Yoga breathing for cancer chemotherapy-associated symptoms and quality of life: results of a pilot randomized controlled trial. Journal of alternative and complementary medicine (New York, NY). 2012;18(5):473-9.
- 94. Banasik J, Williams H, Haberman M, Blank SE, Bendel R. Effect of lyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors. Journal of the American Academy of Nurse Practitioners. 2011;23(3):135-42.
- 95. Vadiraja HS, Raghavendra RM, Nagarathna R, Nagendra HR, Rekha M, Vanitha N, et al. Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial. Integrative cancer therapies. 2009;8(1):37-46.
- 96. Carson JW, Carson KM, Porter LS, Keefe FJ, Shaw H, Miller JM. Yoga for women with metastatic breast cancer: results from a pilot study. Journal of pain and symptom management. 2007;33(3):331-41.
- 97. Kwekkeboom KL, Cherwin CH, Lee JW, Wanta B. Mind-body treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer. Journal of pain and symptom management. 2010;39(1):126-38.



- 98. Lyman GH. Greenlee H. Bohlke K. Bao T. DeMichele AM. Deng GE, et al. Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline. Journal of Clinical Oncology. 2018:JCO. 2018.79. 721.
- 99. Binns-Turner PG, Wilson LL, Pryor ER, Boyd GL, Prickett CA. Perioperative music and its effects on anxiety, hemodynamics, and pain in women undergoing mastectomy. AANA journal. 2011;79(4 Suppl):S21-7.
- 100. Bulfone T. Quattrin R. Zanotti R. Regattin L. Brusaferro S. Effectiveness of music therapy for anxiety reduction in women with breast cancer in chemotherapy treatment. Holistic nursing practice. 2009;23(4):238-42.
- 101. Li XM, Zhou KN, Yan H, Wang DL, Zhang YP. Effects of music therapy on anxiety of patients with breast cancer after radical mastectomy: a randomized clinical trial. Journal of advanced nursing. 2012;68(5):1145-55.
- 102. Zhou K, Li X, Li J, Liu M, Dang S, Wang D, et al. A clinical randomized controlled trial of music therapy and progressive muscle relaxation training in female breast cancer patients after radical mastectomy: results on depression, anxiety and length of hospital stay. European journal of oncology nursing: the official journal of European Oncology Nursing Society. 2015;19(1):54-9.
- 103. Sheikh-Wu SF, Kauffman MA, Anglade D, Shamsaldeen F, Ahn S, Downs CA. Effectiveness of different music interventions on managing symptoms in cancer survivors: A meta-analysis. European Journal of Oncology Nursing. 2021;52:101968.
- 104. Greenlee H, Balneaves LG, Carlson LE, Cohen M, Deng G, Hershman D, et al. Clinical practice guidelines on the use of integrative therapies as supportive care in patients treated for breast cancer. Journal of the National Cancer Institute Monographs. 2014;2014(50):346-58.
- 105. Lengacher CA, Johnson-Mallard V, Post-White J, Moscoso MS, Jacobsen PB, Klein TW, et al. Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. Psycho-oncology. 2009;18(12):1261-72.
- 106. Wurtzen H, Dalton SO, Elsass P, Sumbundu AD, Steding-Jensen M, Karlsen RV, et al. Mindfulness significantly reduces self-reported levels of anxiety and depression: results of a randomised controlled trial among 336 Danish women treated for stage I-III breast cancer. European journal of cancer (Oxford, England: 1990). 2013;49(6):1365-73.
- 107. Piet J, Wurtzen H, Zachariae R. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and meta-analysis. Journal of consulting and clinical psychology. 2012;80(6):1007-20.
- 108. Zainal NZ, Booth S, Huppert FA. The efficacy of mindfulness-based stress reduction on mental health of breast cancer patients: a meta-analysis. Psycho-oncology. 2013;22(7):1457-65.
- 109. Casellas-Grau A, Font A, Vives J. Positive psychology interventions in breast cancer. A systematic review. Psycho-oncology. 2014;23(1):9-19.
- 110. Kim YH, Kim HJ, Ahn SD, Seo YJ, Kim SH. Effects of meditation on anxiety, depression, fatigue, and quality of life of women undergoing radiation therapy for breast cancer. Complementary therapies in medicine. 2013:21(4):379-87.
- 111. Hidderley M, Holt M. A pilot randomized trial assessing the effects of autogenic training in early stage cancer patients in relation to psychological status and immune system responses. European journal of oncology nursing: the official journal of European Oncology Nursing Society. 2004;8(1):61-5.
- 112. Nunes DF, Rodriguez AL, da Silva Hoffmann F, Luz C, Braga Filho AP, Muller MC, et al. Relaxation and guided imagery program in patients with breast cancer undergoing radiotherapy is not associated with neuroimmunomodulatory effects. Journal of psychosomatic research. 2007;63(6):647-55.
- 113. Walker LG, Walker MB, Ogston K, Heys SD, Ah-See AK, Miller ID, et al. Psychological, clinical and pathological effects of relaxation training and guided imagery during primary chemotherapy. British journal of cancer. 1999;80(1-2):262-8.
- 114. Gudenkauf LM, Antoni MH, Stagl JM, Lechner SC, Jutagir DR, Bouchard LC, et al. Brief cognitive-behavioral and relaxation training interventions for breast cancer: A randomized controlled trial. Journal of consulting and clinical psychology. 2015;83(4):677-88.
- 115. Carlson LE, Doll R, Stephen J, Faris P, Tamagawa R, Drysdale E, et al. Randomized controlled trial of Mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2013;31(25):3119-26.
- 116. Crane-Okada R, Kiger H, Sugerman F, Uman GC, Shapiro SL, Wyman-McGinty W, et al. Mindful movement program for older breast cancer survivors: a pilot study. Cancer nursing. 2012;35(4):E1-13.
- 117. Maratos AS, Gold C, Wang X, Crawford MJ. Music therapy for depression. The Cochrane database of systematic reviews. 2008(1):Cd004517.
- 118. Kutner JS, Smith MC, Corbin L, Hemphill L, Benton K, Mellis BK, et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. Annals of internal medicine. 2008:149(6):369-79.
- 119. Hernandez-Reif M, Ironson G, Field T, Hurley J, Katz G, Diego M, et al. Breast cancer patients have improved immune and neuroendocrine functions following massage therapy. Journal of psychosomatic research. 2004;57(1):45-52.





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- 120. Listing M, Krohn M, Liezmann C, Kim I, Reisshauer A, Peters E, et al. The efficacy of classical massage on stress perception and cortisol following primary treatment of breast cancer. Archives of women's mental health. 2010:13(2):165-73.
- 121. Wilkinson SM, Love SB, Westcombe AM, Gambles MA, Burgess CC, Cargill A, et al. Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer: a multicenter randomized controlled trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2007;25(5):532-9.
- 122. Krohn M, Listing M, Tjahjono G, Reisshauer A, Peters E, Klapp BF, et al. Depression, mood, stress, and Th1/Th2 immune balance in primary breast cancer patients undergoing classical massage therapy. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2011;19(9):1303-11.
- 123. Listing M, Reisshauer A, Krohn M, Voigt B, Tjahono G, Becker J, et al. Massage therapy reduces physical discomfort and improves mood disturbances in women with breast cancer. Psychooncology. 2009;18(12):1290-
- 124. Fernandez-Lao C, Cantarero-Villanueva I, Diaz-Rodriguez L, Cuesta-Vargas AI, Fernandez-Delas-Penas C, Arroyo-Morales M. Attitudes towards massage modify effects of manual therapy in breast cancer survivors: a randomised clinical trial with crossover design. European journal of cancer care. 2012;21(2):233-41.
- 125. Hilliard RE. Music Therapy in Hospice and Palliative Care: a Review of the Empirical Data. Evidence-based complementary and alternative medicine: eCAM. 2005;2(2):173-8.
- 126. Nilsson U, Rawal N, Unosson M. A comparison of intra-operative or postoperative exposure to music--a controlled trial of the effects on postoperative pain. Anaesthesia. 2003;58(7):699-703.
- 127. Bower JE, Garet D, Sternlieb B, Ganz PA, Irwin MR, Olmstead R, et al. Yoga for persistent fatigue in breast cancer survivors: a randomized controlled trial. Cancer. 2012;118(15):3766-75.
- 128. Chandwani KD, Perkins G, Nagendra HR, Raghuram NV, Spelman A, Nagarathna R, et al. Randomized, controlled trial of yoga in women with breast cancer undergoing radiotherapy. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2014;32(10):1058-65.
- 129. Chandwani KD, Thornton B, Perkins GH, Arun B, Raghuram NV, Nagendra HR, et al. Yoga improves quality of life and benefit finding in women undergoing radiotherapy for breast cancer. Journal of the Society for Integrative Oncology. 2010;8(2):43-55.
- 130. Danhauer SC, Mihalko SL, Russell GB, Campbell CR, Felder L, Daley K, et al. Restorative yoga for women with breast cancer: findings from a randomized pilot study. Psycho-oncology. 2009;18(4):360-8.
- Mustian KM, Sprod LK, Janelsins M, Peppone LJ, Palesh OG, Chandwani K, et al. Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2013;31(26):3233-41.
- 132. Bensadoun RJ, Nair RG. Low-level laser therapy in the prevention and treatment of cancer therapy-induced mucositis: 2012 state of the art based on literature review and meta-analysis. Curr Opin Oncol. 2012;24(4):363-
- 133. He M, Zhang B, Shen N, Wu N, Sun J. A systematic review and meta-analysis of the effect of low-level laser therapy (LLLT) on chemotherapy-induced oral mucositis in pediatric and young patients. European Journal of Pediatrics. 2018;177(1):7-17.
- 134. Oberoi S, Zamperlini-Netto G, Beyene J, Treister NS, Sung L. Effect of Prophylactic Low Level Laser Therapy on Oral Mucositis: A Systematic Review and Meta-Analysis. PLOS ONE. 2014;9(9):e107418.
- 135. Kinkead B, Schettler PJ, Larson ER, Carroll D, Sharenko M, Nettles J, et al. Massage therapy decreases cancerrelated fatigue: Results from a randomized early phase trial. Cancer. 2018;124(3):546-54.
- 136. Lopez G, Liu W, Milbury K, Spelman A, Wei Q, Bruera E, et al. The effects of oncology massage on symptom self-report for cancer patients and their caregivers. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2017;25(12):3645-50.
- 137. Wang T, Zhai J, Liu X-L, Yao L-Q, Tan J-Y. Massage Therapy for Fatigue Management in Breast Cancer Survivors: A Systematic Review and Descriptive Analysis of Randomized Controlled Trials. Evidence-Based Complementary and Alternative Medicine. 2021;2021:9967574.
- 138. Andersen L, Hojris I, Erlandsen M, Andersen J. Treatment of breast-cancer-related lymphedema with or without manual lymphatic drainage--a randomized study. Acta oncologica (Stockholm, Sweden). 2000;39(3):399-405.
- 139. Devoogdt N, Christiaens MR, Geraerts I, Truijen S, Smeets A, Leunen K, et al. Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: randomised controlled trial. BMJ (Clinical research ed). 2011;343:d5326.
- 140. Gurdal SO, Kostanoglu A, Cavdar I, Ozbas A, Cabioglu N, Ozcinar B, et al. Comparison of intermittent pneumatic compression with manual lymphatic drainage for treatment of breast cancer-related lymphedema. Lymphatic research and biology. 2012;10(3):129-35.
- 141. Maher J, Refshauge K, Ward L, Paterson R, Kilbreath S. Change in extracellular fluid and arm volumes as a consequence of a single session of lymphatic massage followed by rest with or without compression. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2012;20(12):3079-86.



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- 142. McNeely ML, Magee DJ, Lees AW, Bagnall KM, Haykowsky M, Hanson J, The addition of manual lymph drainage to compression therapy for breast cancer related lymphedema: a randomized controlled trial. Breast cancer research and treatment. 2004:86(2):95-106.
- 143. Williams AF, Vadgama A, Franks PJ, Mortimer PS. A randomized controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. European journal of cancer care, 2002:11(4):254-61.
- 144. Dayes IS, Whelan TJ, Julian JA, Parpia S, Pritchard KI, D'Souza DP, et al. Randomized trial of decongestive lymphatic therapy for the treatment of lymphedema in women with breast cancer. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2013;31(30):3758-63.
- 145. Thompson B, Gaitatzis K, Janse de Jonge X, Blackwell R, Koelmeyer LA. Manual lymphatic drainage treatment for lymphedema: a systematic review of the literature. Journal of Cancer Survivorship. 2021;15(2):244-58.
- 146. Gentile D, Boselli D, O'Neill G, Yaguda S, Bailey-Dorton C, Eaton TA. Cancer Pain Relief After Healing Touch and Massage. Journal of alternative and complementary medicine (New York, NY). 2018;24(9-10):968-73.
- 147. Lee SH, Kim JY, Yeo S, Kim SH, Lim S. Meta-Analysis of Massage Therapy on Cancer Pain. Integrative cancer therapies. 2015;14(4):297-304.
- 148. Paice JA, Portenoy R, Lacchetti C, Campbell T, Cheville A, Citron M, et al. Management of Chronic Pain in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2016;34(27):3325-45.
- 149. Mehling WE, Jacobs B, Acree M, Wilson L, Bostrom A, West J, et al. Symptom management with massage and acupuncture in postoperative cancer patients; a randomized controlled trial. Journal of pain and symptom management, 2007;33(3):258-66.
- 150. Izgu N, Metin ZG, Karadas C, Ozdemir L, Çetin N, Demirci U. Prevention of chemotherapy-induced peripheral neuropathy with classical massage in breast cancer patients receiving paclitaxel: An assessor-blinded randomized controlled trial. Eur J Oncol Nurs. 2019;40:36-43.
- 151. Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, et al. Nutrition and physical activity guidelines for cancer survivors. CA: a cancer journal for clinicians. 2012;62(4):243-74.
- 152. Meneses-Echávez JF, González-Jiménez E, Ramírez-Vélez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC cancer. 2015;15:77.
- 153. Tomlinson D, Diorio C, Beyene J, Sung L. Effect of exercise on cancer-related fatigue: a meta-analysis. Am J Phys Med Rehabil. 2014;93(8):675-86.
- 154. Hilfiker R, Meichtry A, Eicher M, Nilsson Balfe L, Knols RH, Verra ML, et al. Exercise and other nonpharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: a systematic review incorporating an indirect-comparisons meta-analysis. British Journal of Sports Medicine. 2018;52(10):651.
- 155. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc. 2019;51(11):2375-90.
- 156. Cormie P, Atkinson M, Bucci L, Cust A, Eakin E, Hayes S, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. Medical Journal of Australia. 2018;209(4):184-7.
- 157. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Medicine and science in sports and exercise. 2010;42(7):1409-26.
- 158. Cormie P, Zopf EM, Zhang X, Schmitz KH. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. Epidemiologic reviews. 2017;39(1):71-92.
- 159. McTiernan A, Friedenreich CM, Katzmarzyk PT, Powell KE, Macko R, Buchner D, et al. Physical Activity in Cancer Prevention and Survival: A Systematic Review. Medicine and science in sports and exercise. 2019;51(6):1252-61.
- 160. Morishita S, Hamaue Y, Fukushima T, Tanaka T, Fu JB, Nakano J. Effect of Exercise on Mortality and Recurrence in Patients With Cancer: A Systematic Review and Meta-Analysis. Integrative cancer therapies. 2020;19:1534735420917462.
- 161. Garcia MK, McQuade J, Haddad R, Patel S, Lee R, Yang P, et al. Systematic review of acupuncture in cancer care: a synthesis of the evidence. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2013;31(7):952-60.
- 162. Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, Issell BF, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. The Cochrane database of systematic reviews. 2006(2):Cd002285.
- 163. Dibble SL, Chapman J, Mack KA, Shih AS. Acupressure for nausea: results of a pilot study. Oncology nursing forum. 2000;27(1):41-7.
- 164. Dibble SL, Luce J, Cooper BA, Israel J, Cohen M, Nussey B, et al. Acupressure for chemotherapy-induced nausea and vomiting: a randomized clinical trial. Oncology nursing forum. 2007;34(4):813-20.
- 165. Molassiotis A, Helin AM, Dabbour R, Hummerston S. The effects of P6 acupressure in the prophylaxis of chemotherapy-related nausea and vomiting in breast cancer patients. Complementary therapies in medicine. 2007:15(1):3-12.
- 166. Chien TJ, Liu CY, Fang CJ. The Effect of Acupuncture in Breast Cancer-Related Lymphoedema (BCRL): A Systematic Review and Meta-Analysis. Integrative cancer therapies. 2019;18:1534735419866910.



- 167. Pei L-X, Yi Y, Guo J, Chen L, Zhou J-Y, Wu X-L, et al. The effectiveness and safety of acupuncture/electroacupuncture for chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. Acupuncture in medicine: journal of the British Medical Acupuncture Society. 2022;0(0):09645284221076512.
- 168. Lu W, Posner MR, Wayne P, Rosenthal DS, Haddad RI. Acupuncture for dysphagia after chemoradiation therapy in head and neck cancer; a case series report. Integrative cancer therapies, 2010;9(3):284-90.
- 169. Lu W, Wayne PM, Davis RB, Buring JE, Li H, Macklin EA, et al. Acupuncture for Chemoradiation Therapy-Related Dysphagia in Head and Neck Cancer: A Pilot Randomized Sham-Controlled Trial. The oncologist. 2016;21(12):1522-9.
- 170. Bonomo P, Stocchi G, Caini S, Desideri I, Santarlasci V, Becherini C, et al. Acupuncture for radiation-induced toxicity in head and neck squamous cell carcinoma: a systematic review based on PICO criteria. European Archives of Oto-Rhino-Laryngology. 2022;279(4):2083-97.
- 171. Cheng CS, Chen LY, Ning ZY, Zhang CY, Chen H, Chen Z, et al. Acupuncture for cancer-related fatigue in lung cancer patients: a randomized, double blind, placebo-controlled pilot trial. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2017;25(12):3807-14.
- 172. Hervik J, Mjaland O. Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial. Breast cancer research and treatment. 2009;116(2):311-6.
- 173. Walker EM, Rodriguez AI, Kohn B, Ball RM, Pegg J, Pocock JR, et al. Acupuncture versus venlafaxine for the management of vasomotor symptoms in patients with hormone receptor-positive breast cancer: a randomized controlled trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2010:28(4):634-40.
- 174. Garcia MK, Graham-Getty L, Haddad R, Li Y, McQuade J, Lee RT, et al. Systematic review of acupuncture to control hot flashes in cancer patients. Cancer. 2015;121(22):3948-58.
- 175. Johns C, Seav SM, Dominick SA, Gorman JR, Li H, Natarajan L, et al. Informing hot flash treatment decisions for breast cancer survivors: a systematic review of randomized trials comparing active interventions. Breast cancer research and treatment. 2016;156(3):415-26.
- 176. Franzoi MA, Agostinetto E, Perachino M, Del Mastro L, de Azambuja E, Vaz-Luis I, et al. Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. The Lancet Oncology. 2021;22(7):e303-e13.
- 177. Gao Y, Ma T, Han M, Yu M, Wang X, Lv Y, et al. Effects of Acupuncture and Moxibustion on Breast Cancer-Related Lymphedema: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Integrative cancer therapies. 2021;20:15347354211044107.
- 178. Cassileth BR, Van Zee KJ, Chan Y, Coleton MI, Hudis CA, Cohen S, et al. A safety and efficacy pilot study of acupuncture for the treatment of chronic lymphoedema. Acupuncture in medicine: journal of the British Medical Acupuncture Society. 2011;29(3):170-2.
- 179. Cassileth BR, Van Zee KJ, Yeung KS, Coleton MI, Cohen S, Chan YH, et al. Acupuncture in the treatment of upper-limb lymphedema: results of a pilot study. Cancer. 2013;119(13):2455-61.
- 180. Bao T, Van Zee KJ, Cassileth BR, Coleton M, Li QS, Mehrara B, et al. Acupuncture for breast cancer related lymphedema: A randomized controlled trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2017;35(15\_suppl):e21706-e
- 181. Bao T, Iris Zhi W, Vertosick EA, Li QS, DeRito J, Vickers A, et al. Acupuncture for breast cancer-related lymphedema: a randomized controlled trial. Breast Cancer Research and Treatment. 2018;170(1):77-87.
- 182. Bao T, Cai L, Snyder C, Betts K, Tarpinian K, Gould J, et al. Patient-reported outcomes in women with breast cancer enrolled in a dual-center, double-blind, randomized controlled trial assessing the effect of acupuncture in reducing aromatase inhibitor-induced musculoskeletal symptoms. Cancer. 2014;120(3):381-9.
- 183. Mao JJ, Farrar JT, Bruner D, Zee J, Bowman M, Seluzicki C, et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. Cancer. 2014;120(23):3744-51.
- 184. Molassiotis A, Bardy J, Finnegan-John J, Mackereth P, Ryder DW, Filshie J, et al. Acupuncture for cancer-related fatigue in patients with breast cancer: a pragmatic randomized controlled trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2012;30(36):4470-6.
- 185. Mallory MJ, Croghan KA, Sandhu NP, Lemaine V, Degnim AC, Bauer BA, et al. Acupuncture in the postoperative setting for breast cancer patients: a feasibility study. The American journal of Chinese medicine. 2015;43(1):45-
- 186. Nedstrand E, Wijma K, Wyon Y, Hammar M. Vasomotor symptoms decrease in women with breast cancer randomized to treatment with applied relaxation or electro-acupuncture: a preliminary study. Climacteric: the journal of the International Menopause Society. 2005;8(3):243-50.
- 187. Hershman DL, Unger JM, Greenlee H, Capodice J, Lew DL, Kengla AT, et al. Abstract GS4-04: Randomized blinded sham- and waitlist-controlled trial of acupuncture for joint symptoms related to aromatase inhibitors in women with early stage breast cancer (S1200). Cancer Research. 2018;78(4).
- 188. Bao T, Cai L, Giles JT, Gould J, Tarpinian K, Betts K, et al. A dual-center randomized controlled double blind trial assessing the effect of acupuncture in reducing musculoskeletal symptoms in breast cancer patients taking aromatase inhibitors. Breast Cancer Res Treat. 2013;138(1):167-74.



W

- 189. Liu X, Lu J, Wang G, Chen X, Xv H, Huang J, et al. Acupuncture for Arthralgia Induced by Aromatase Inhibitors in Patients with Breast Cancer: A Systematic Review and Meta-analysis. Integrative Cancer Therapies. 2021;20:1534735420980811.
- 190. He Y, Guo X, May BH, Zhang AL, Liu Y, Lu C, et al. Clinical Evidence for Association of Acupuncture and Acupressure With Improved Cancer Pain: A Systematic Review and Meta-Analysis. JAMA oncology. 2019;6(2):271-8.
- 191. Chiu HY, Hsieh YJ, Tsai PS. Systematic review and meta analysis of acupuncture to reduce cancer related pain. European journal of cancer care. 2017;26(2).
- 192. Charlton JE. Cancer pain management. Cahiers d'anesthesiologie. 1993;41(6):621-4.
- 193. Wong RH, Lee TW, Sihoe AD, Wan IY, Ng CS, Chan SK, et al. Analgesic effect of electroacupuncture in postthoracotomy pain: a prospective randomized trial. The Annals of thoracic surgery. 2006;81(6):2031-6.
- 194. Choi TY, Lee MS, Kim TH, Zaslawski C, Ernst E. Acupuncture for the treatment of cancer pain: a systematic review of randomised clinical trials. Support Care Cancer. 2012;20(6):1147-58.
- 195. Pfister DG, Cassileth BR, Deng GE, Yeung KS, Lee JS, Garrity D, et al. Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2010;28(15):2565-70.
- 196. He JP, Friedrich M, Ertan AK, Muller K, Schmidt W. Pain-relief and movement improvement by acupuncture after ablation and axillary lymphadenectomy in patients with mammary cancer. Clinical and experimental obstetrics & gynecology. 1999;26(2):81-4.
- 197. Choi TY, Kim JI, Lim HJ, Lee MS. Acupuncture for Managing Cancer-Related Insomnia: A Systematic Review of Randomized Clinical Trials. Integrative cancer therapies. 2017;16(2):135-46.
- 198. Garland SN, Xie SX, DuHamel K, Bao T, Li Q, Barg FK, et al. Acupuncture Versus Cognitive Behavioral Therapy for Insomnia in Cancer Survivors: A Randomized Clinical Trial. J Natl Cancer Inst. 2019;111(12):1323-31.
- 199. Meng Z, Garcia MK, Hu C, Chiang J, Chambers M, Rosenthal DI, et al. Randomized controlled trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. Cancer. 2012;118(13):3337-44.
- 200. Meng Z, Kay Garcia M, Hu C, Chiang J, Chambers M, Rosenthal DI, et al. Sham-controlled, randomised, feasibility trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. European journal of cancer (Oxford, England: 1990). 2012;48(11):1692-9.
- 201. Braga FP, Lemos Junior CA, Alves FA, Migliari DA. Acupuncture for the prevention of radiation-induced xerostomia in patients with head and neck cancer. Brazilian oral research. 2011;25(2):180-5.
- 202. Simcock R, Fallowfield L, Monson K, Solis-Trapala I, Parlour L, Langridge C, et al. ARIX: a randomised trial of acupuncture v oral care sessions in patients with chronic xerostomia following treatment of head and neck cancer. Annals of oncology: official journal of the European Society for Medical Oncology / ESMO. 2013;24(3):776-83.
- 203. Cho JH, Chung WK, Kang W, Choi SM, Cho CK, Son CG. Manual acupuncture improved quality of life in cancer patients with radiation-induced xerostomia. Journal of alternative and complementary medicine (New York, NY). 2008;14(5):523-6.
- 204. Blom M, Lundeberg T. Long-term follow-up of patients treated with acupuncture for xerostomia and the influence of additional treatment. Oral diseases. 2000;6(1):15-24.
- 205. Garcia MK, Meng Z, Rosenthal DI, Shen Y, Chambers M, Yang P, et al. Effect of True and Sham Acupuncture on Radiation-Induced Xerostomia Among Patients With Head and Neck Cancer: A Randomized Clinical Trial. JAMA Netw Open. 2019;2(12):e1916910.
- 206. Ni X, Tian T, Chen D, Liu L, Li X, Li F, et al. Acupuncture for Radiation-Induced Xerostomia in Cancer Patients: A Systematic Review and Meta-Analysis. Integrative cancer therapies. 2020;19:1534735420980825.
- 207. Mercadante V, Jensen SB, Smith DK, Bohlke K, Bauman J, Brennan MT, et al. Salivary Gland Hypofunction and/or Xerostomia Induced by Nonsurgical Cancer Therapies: ISOO/MASCC/ASCO Guideline. Journal of Clinical Oncology. 2021;39(25):2825-43.
- 208. Raghavendra RM, Nagarathna R, Nagendra HR, Gopinath KS, Srinath BS, Ravi BD, et al. Effects of an integrated yoga programme on chemotherapy-induced nausea and emesis in breast cancer patients. European journal of cancer care. 2007;16(6):462-74.
- 209. Culos-Reed SN, Carlson LE, Daroux LM, Hately-Aldous S. A pilot study of yoga for breast cancer survivors: physical and psychological benefits. Psycho-oncology. 2006;15(10):891-7.
- 210. Moadel AB, Shah C, Wylie-Rosett J, Harris MS, Patel SR, Hall CB, et al. Randomized controlled trial of yoga among a multiethnic sample of breast cancer patients: effects on quality of life. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2007;25(28):4387-95.
- 211. Littman AJ, Bertram LC, Ceballos R, Ulrich CM, Ramaprasad J, McGregor B, et al. Randomized controlled pilot trial of yoga in overweight and obese breast cancer survivors: effects on quality of life and anthropometric measures. Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer. 2012;20(2):267-77.
- 212. Siedentopf F, Utz-Billing I, Gairing S, Schoenegg W, Kentenich H, Kollak I. Yoga for Patients with Early Breast Cancer and its Impact on Quality of Life a Randomized Controlled Trial. Geburtshilfe und Frauenheilkunde. 2013;73(4):311-7.



- 213. Lee JH, Jang E, H. JM, Ha K, Han C. Clinical effectiveness of acupuncture in the treatment of chemotherapy-induced leukopenia: A systematic review. European Journal of Integrative Medicine. 2016;8(5):802-8.
- 214. Fu H, Chen B, Hong S, Guo Y. Acupuncture Therapy for the Treatment of Myelosuppression after Chemotherapy: A Literature Review over the Past 10 Years. Journal of acupuncture and meridian studies. 2015;8(3):122-6.
- 215. Li B, Gan R, Yang Q, Huang J, Chen P, Wan L, et al. Chinese Herbal Medicines as an Adjunctive Therapy for Unresectable Pancreatic Cancer: A Systematic Review and Meta-Analysis. Evidence-based complementary and alternative medicine: eCAM. 2015;2015:350730.
- 216. Kim W, Lee WB, Lee J, Min Bl, Lee H, Cho SH. Traditional herbal medicine as adjunctive therapy for nasopharyngeal cancer: a systematic review and meta-analysis. Integrative cancer therapies. 2015;14(3):212-20.
- 217. Sun X, Zhang X, Nian JY, Guo J, Yin Y, Zhang GL, et al. Chinese Herbal Medicine as Adjunctive Therapy to Chemotherapy for Breast Cancer: A Systematic Review and Meta-Analysis. Evidence-based complementary and alternative medicine: eCAM. 2016;2016:3281968.
- 218. Chung VC, Wu X, Hui EP, Ziea ET, Ng BF, Ho RS, et al. Effectiveness of Chinese herbal medicine for cancer palliative care: overview of systematic reviews with meta-analyses. Scientific reports. 2015;5:18111.

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