

Joav Merrick

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Joav Merrick (Series Editor)



Pain Management Yearbook



2017



NOVA

DISABILITY STUDIES

PAIN MANAGEMENT YEARBOOK 2017

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JOAV MERRICK
EDITOR



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INTRODUCTION

Chapter 1

COMPLEXITY IN PSYCHOSOCIAL ONCOLOGY

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ABSTRACT

Initially the stigma and fear associated with just the word "cancer" and its automatic association with death and dying made it an unspeakable experience for many patients, families and health care providers dealing with the disease. People were left alone to deal with the illness and it took until the mid to late 1970s that the use of the term psycho-oncology emerged. Though psychosocial oncology is being described as a distinct discipline- clinicians involved in cancer care need to rely and work closely with the members of the psychosocial team to provide whole person care in a complex disease such as cancer. Promulgation of the idea that body, mind and spirit are to be considered

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as distinct and separate entities can only do a disservice to any attempt we make at providing health care.

INTRODUCTION

Cancer care spans the continuum of health-care issues from primary prevention through long-term survival and end-of-life care. The Canadian Cancer Society estimated 196,900 cases of new cancer and 78,000 deaths from cancer in Canada in 2015 (1).

The physical symptoms of cancer are complex and daunting, wherein even the basic treatment of the underlying disease can result in physical pain and discomfort. These symptoms are often addressed with medical treatment, such as the inclusion of palliative care earlier in the disease trajectory (2). However, it is the conjoined and often associated emotional impact of the disease that can be equally challenging for care providers, patients, family and friends alike, to deal with.

Initially the stigma and fear associated with just the word "cancer" and its automatic association with death and dying made it an unspeakable experience for many patients, families and health care providers dealing with the disease. People were left alone to deal with the illness and it took until the mid to late 1970s that the use of the term psycho-oncology even emerged (2).

As a disease and field of scholarship – the provision of cancer care is becoming increasingly complex, requiring a multi-disciplinary cadre of specialist in all aspects of holistic care to provide quality care (3). The undeniable link between the psychological and physiological elements to cancer treatment and survival are being looked into and researched through the field of psychoneuroimmunology- however component of holistic care, illustrated in figure 1, acknowledge the equal importance of mind, body and spirit as part of the care needs for patients and caregiver that forms the basis of an integrated approach to psychosocial oncology (3).

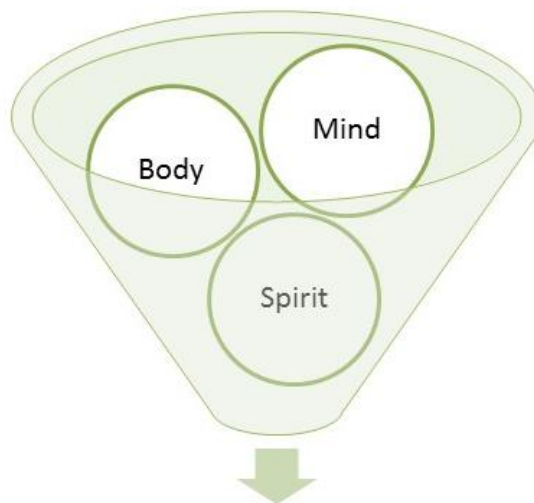


Figure 1. Integrated psychosocial oncology care.

WHY PSYCHOSOCIAL ONCOLOGY IS IMPORTANT

A significant proportion of cancer patients will suffer some form of social, emotional and psychological distress and challenges as a result of the disease and its treatment. Unattended, psychosocial issues can leave patients and families ill-equipped to cope and manage their cancer diagnosis and treatment, particularly if they are unfamiliar with the variety of supports and resources available to them.

Recent research into the psychosocial experience faced by patients identified the following significant themes experienced across a wide range of cancers: diminished sense of well-being, perceived role changes in intimate relationships, heightened awareness of limited time, a new order of priorities, taking things as they come and development of trust in health professionals. These themes indicate relevant areas of patients' well-being, which might be addressed through effective psychosocial support services (4).

We know that when psychosocial care is properly integrated into clinical care, it has direct impact on a patient's quality of life. In fact, new standards of quality cancer care, based on the 2007 Institute of Medicine of the National Academies of Sciences' provided evidenced-based support strategies to provide good care for the whole patient; mandating that psychosocial aspects must be integrated into routine cancer care. Suggesting that patients should be screened at their initial visit for psychosocial needs and survivors should have a treatment plan that includes attention to possible increased anxiety on completing treatment, development of posttraumatic stress symptoms, and mixed anxiety and depressive symptoms (5).

Table 1. Multiple factors along the cancer care continuum

Body	Mind	Spirit	Relational
Type of cancer	Developmental age	Religious beliefs	Family
Type of treatment	Mental health	Spiritual beliefs	Caregivers
Age	Life stage	Belief in alternative and complementary medicine	Age of children
Gender	Grief/Bereavement	Quality of life	Socio-economic factors
Sexuality	Health literacy	Hope	Insurance
Culture	Illness understanding		Trust in health care
Language	Survivorship or preparation for death		Community supports
Stage of illness			Access to palliative care
Goals of care			Heredity concerns
Research/Treatment			

CANCER CARE COMPLEXITY

We know that cancer affects the whole family and not just the patient (6) and that patient/family centered care is needed to effectively provide whole level care. Table 1 outlines a very preliminary listing of multiple factors that need to be considered along the cancer care continuum. An artificial separation of physical care from other holistic components will not affectively address the complex and changing needs. The need for multidisciplinary rounds and comprehensive tumor rounds illustrate the evolving complexity and care needs that extend well beyond the limits of just the doctor-patient relationship.

CONCLUSION

Though psychosocial oncology is being described as a distinct discipline- clinicians involved in cancer care need to rely and work closely with the members of the psychosocial team to provide whole person care in a complex disease such as cancer. Promulgation of the idea that body, mind and spirit are to be considered as distinct and separate entities can only do a disservice to any attempt we make at providing health care.

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**SECTION ONE: PSYCHOSOCIAL AND ETHICAL ISSUES
ALONG THE CANCER CARE CONTINUUM**

Chapter 2

FINDING A HOME (SOMEWHERE) FOR MEDICAL AID IN DYING

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ABSTRACT

Recent alterations to the criminal code following the passing of Bill C-14 have made Medical Aid in Dying (MAID) legal in Canada. With the new legislation in place, institutional questions arise concerning how MAID should be provided within the health care system. Alternatively, what are the limitations of conscientious objection to MAID? Palliative Care Units (PCUs) are in dire need of the answers to these questions, as they face contrary obligations towards patients requesting MAID. MAID seems to contradict some of the principle values of palliative care, while palliative care patients are also in a condition where they more likely to be eligible for MAID. Yet, examining some of these value contradictions more closely, there are more commonalities between MAID and palliative care than it would first seem. As a result, if PCUs conscientiously object to MAID as departments, then they are neglecting to fulfill their responsibility to honor their own missions and values. These commonalities in value between MAID and palliative care have clinical implications, as many of the patients who would prefer palliative care are also patients who would consider pursuing MAID concurrently. Three cases where patients could request both MAID and palliative care are outlined. They reveal a risk that a departmental conscientious objection to MAID in the PCU comes at the expense of patients receiving necessary palliative care.

Keywords: medical assistance in dying, palliative care, moral responsibility

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INTRODUCTION

Is it morally justifiable for palliative care units (PCU) as organizations to conscientiously object to providing medical aid in dying (MAID)? Sentiments in PCUs on MAID are divided, as they face contradictory obligations with regard to MAID. A worry of providing MAID in the PCU is that it conflicts with the missions and values of palliative care. In fact, MAID seems so contradictory to the purpose of palliative care that the Hospice Palliative Care of Ontario (HPCO) portrays requests for MAID as a failure of the health care system underutilizing and insufficiently delivering palliative services (1). Yet palliative care is an end-of-life service. As such, the PCU provides care to many of the people who would be expected to make a MAID request – intolerably suffering patients who have a naturally foreseeable death. While some patients are likely to request MAID in the community or as part of a freestanding hospice care program, patients requesting MAID within the hospital may not have access to care in the PCU. It would be inappropriate to abandon the patients who seek palliative care options on the basis of a MAID request.

There has been little legal and political guidance on whether PCUs can collectively conscientiously object to MAID. Following *Carter v Canada* (2015), where the Supreme Court of Canada decided that MAID is constitutional, concerns arose in the medical community about physicians' rights to conscientiously object, on an individual, and institutional basis (2). Modifications to the criminal code in light of the *Carter* decision, outlined in Bill C-14, guarantees the right of health care professionals to conscientiously object, with a proviso that effective referral is initiated to transfer care of patients to other health care providers who can meet their needs (3). Additionally, in Ontario, the Ministry of Health announced that hospitals may conscientiously object as institutions (4). Yet it does not speculate on the limitations of this right. If both individuals and institutions as a whole are able to conscientiously object, where does this leave health care departments?

Rather than examining the legal limitations of the PCU's right to conscientious objection, I will approach this issue morally by considering whether MAID and palliative care indeed have contrary missions and values that would justify conscientious objection. What I find is that MAID is highly compatible with palliative care values of avoiding hastening death, respecting autonomy, and encouraging compassion for suffering. As a result palliative care bears some responsibility to honor MAID requests, such that conscientious objections from PCUs fail to fulfill their own missions and values. Clinically, this responsibility to palliative care missions and values affects end-of-life patients, who are likely to pursue MAID and palliative care concurrently.

DISCUSSION

Internationally, federally, and provincially it seems as though, insofar as MAID intentionally causes the death of the patient, it cannot be part of palliative care. The World Health Organization (WHO), and the HPCO define palliative care as an “approach that improves the quality of life of patients and their families facing the problem[s] associated with life threatening illness[es]” (5). Among the intentions listed by the WHO, palliative care is to neither hasten nor postpone death (5). HPCO similarly claims that quality hospice palliative

care neither hastens death nor prolongs life (1), a claim echoed at the federal level by the Canadian department of justice (6). Naturally, this value directly conflicts with one of the primary goals of MAID, to intentionally end the patient's life. As a result, palliative care organizations such as the HPCO explicitly distinguish euthanasia and physician assisted dying as not being part of the practice of palliative care (1).

Clinically this interpretation of MAID is true; the treatments are meant to hasten the death of the patient. Yet it ignores the legal, social, and political factors which justify MAID as a charter right. In *Carter v Canada*, the Supreme Court ruled that access to MAID is protected by our section seven charter right to "life liberty and security of the person" (2). This is because, through gathering testimony from end of life patients, the Supreme Court discovered that denying MAID to patients encourages them to take their lives in anticipation of their further decline. After all, at the point where these patients would pursue MAID, they would be incapable of taking their lives on their own (2). MAID invokes the right to life by protecting patients from taking their lives prematurely, instead allowing them to end their lives when their condition is intolerable. To the extent that it does hasten death, MAID does so minimally. Since Bill C-14 outlines a reasonably foreseeable natural death as one of the eligibility requirements, patients who qualify for MAID are likely to die whether they pursue MAID or not.

Additionally, hastening death through MAID does not conflict with palliative care anymore than other end-of-life practices. In *Carter v. Canada*, MAID is likened to treatments that intentionally hasten death and are ethically acceptable: palliative sedation and the withholding or withdrawal of lifesaving or life-sustaining medical treatment (2). Consequentially, this resemblance could also mean that there is no ethical distinction between palliative care and MAID. For instance, the trial judge of the British Columbia Supreme Court referred to as Smith J. argues that, ethically, if the outcome is likely to be death there is little distinguishing MAID from end-of-life practices (2). Palliative care units regularly reconcile their mission not to hasten death with end-of-life practices which allow for a hastened death to occur. There is no reason to think MAID should be treated any differently.

There could be an important difference between these other end of life treatments and MAID which reveals a difference in priorities between palliative care values, and those which motivate MAID. Palliative care "deploys nurses, doctors, and social workers to help people with a fatal illness have the fullest possible life right now... focusing on objectives like freedom from pain and discomfort, or maintaining mental awareness for as long as possible, or getting out with family once and a while" (7). In contrast, the first priority of MAID is to end the patient's life. As a treatment which prioritizes the death of the patient, possibly the most grievous and irreversible harm, MAID has no place being part of palliative care.

Yet quality of life is influenced by more factors than harm avoidance, many of which motivate access to both MAID and palliative care. When patients could pursue aggressive treatment options which are more likely to cure them, what justifies their choice to pursue palliative care is that they have a right to dignity, which allows patients to decide what they value in their care. "People have concerns besides simply prolonging their lives and avoiding suffering" (7). For instance, patients surveyed in the US prioritized "being with family, having the touch of others, being mentally aware, and not becoming a burden to others" (7).

Deciding what the patient values in their care is likewise an important value of MAID. Outlined in Bill C-14, the Parliament of Canada recognizes the autonomy of persons (3): allowing patients to have control over the time and manner of their death. Gloria Taylor, an

appellant in *Carter v. Canada* (2015), recognizes the importance of autonomy in upholding a good quality of life when she explains that, as her condition progressed, she wanted independence and control over how she died (2). She did not want to “live in a bedridden state, stripped of dignity and independence...[or an] ugly death” (2). In Canada, “numerous polls indicate that a majority of Canadians believe medical aid in dying should be an option” (6). As Dr. Francine Lemire executive director and chief executive officer of the College of Family Physicians Canada, claims “we have a responsibility as health care providers... as decision makers and advisors, to listen to the public” (6).

Additionally pain management, one of the primary missions of palliative care according to the WHO, is also a principle motivator of MAID. After all, patients request MAID in order to end “suffering that is intolerable to the individual in the circumstances of his or her condition” (2). While, at face value, it may seem as though MAID has no place in palliative care, it is in fact compatible with the missions and values of palliative care in many ways. With these compatibilities, it is problematic for PCUs to conscientiously object to providing MAID, because it involves objecting to some of the fundamental values which drive palliative care. By extension, for the PCU to ignore these compatibilities is to ignore their responsibilities to patients.

Data collected in Oregon over a ten-year period reveals that this commonality between palliative care values and the values that drive MAID translates clinically, as patients often want to pursue palliative care and MAID concurrently. Oregon has a health care system and population which most closely resembles our own, yet it has one key difference. There, only physician assisted suicide (PAS), where the patient self-administers a lethal dose of medication is legal. Over 85 per cent of patients in Oregon who completed an assisted suicide treatment have been in a hospice (8), with the percentage of patients electing assisted suicide who were already enrolled in a hospice increasing in recent years (8). While these cases are typically completed in the community, and therefore avoid the complications arising in our PCUs, it reveals interesting values on behalf of patients. For most patients, palliative care and MAID are not treatments one chooses between, but treatments which are taken together (8). As part of end-of-life care, MAID is “a measure of last resort within palliative care, not... an alternative to it” (8).

Consider three clinical scenarios where a patient may make a MAID request, and concurrently require treatment from the PCU. One scenario is where a patient’s condition is so severe that they require palliative services up between the point where they make a MAID request, and the treatment is completed. At minimum, this may occur during the ten clear day waiting period; a required time period beginning the day after a patient makes a request for MAID which allows for reflection and coordination. The patient may require longer than ten days to arrange their preferred conditions of their death – including both personal and clinical factors.

Alternatively, some patients may initiate a MAID request, but may opt instead for palliative care as their circumstances change. Consider a patient who experiences grievous and irremediable suffering that they find intolerable. Yet the patient’s natural death is not reasonably foreseeable since the patient has an implanted device which supports heart function, and on which they are completely reliant. They are therefore ineligible for the treatment but they have thought about the process for many years. If the patient’s device were to be turned off, they could be eligible for a MAID treatment. Yet the prospect is risky. It is possible that, upon withdrawing the implanted device, their heart rate could return to a

minimal yet sustainable rate – worsening their suffering, and leaving them still unable to meet the criteria for MAID. Such a patient is likely better off in the PCU where they have better access to palliative sedation. A case which begins as a MAID request could at any time become a purely palliative case.

Patients may also be initiating a MAID request not as a means to end their lives immediately, but as a contingency. This way, if their condition worsens to a point they can no longer bare, they can have some control over when and how they die. Such patients may prefer palliative care treatments to MAID treatments. They may request MAID without the intention of ever having to complete the treatment. In fact, they may never complete the treatment that they requested. In Oregon, “the number of patients who request assisted death is quite small and the number who follow through with it is even smaller” (8). There, where there is a requirement for a six month waiting period between a request for MAID and the completion of the treatment, patients who have elected assisted suicide have lived well beyond that deadline before using the prescribed medication (8).

In each of these cases, a unit-wide conscientious objection to MAID could result in patients having to be transferred out of palliative care at the time that their request arises: a course of action that is unacceptable for most patients in end-of-life care. Unit-wide conscientious objection could additionally effect who would be eligible for palliative care, as patients may be refused transfer to the PCU. This course of action is irresponsible and negligent for two main reasons. Firstly, in each of these cases patients are in conditions which require, or are likely to require, palliative treatments. It is unfair to leverage an essential service for end-of-life patients on the condition that patients will not pursue MAID.

Secondly, in two of the three aforementioned scenarios, there is no certainty that the patient will ever complete their MAID treatment simply because they made a request. As a result, denying palliative care to patients is not done on the basis of conscientious objection to MAID, but a conscientious objection to the possibility that they could pursue a MAID treatment. This reasoning is insufficient to justify denying patients essential care.

CONCLUSION

In summary, the commonalities between the values motivating both MAID and palliative care reveal that a departmental conscientious objection on behalf of the PCU would be inappropriate. For the PCU to object to MAID would be, on some level to object to palliative care itself. Further, because of these commonalities in value, many of the patients who believe in palliative care values are likely to pursue both palliative care and MAID. In fact three common clinical scenarios can arise where a patient requires both MAID and palliative care treatments: the patient is either in need of palliative care during the waiting period between making a formal request and completion of the treatment, requires palliative care in case they lose eligibility for MAID, or is planning to use MAID as a contingency and primarily wishes to pursue palliative care. The patient in each scenario has a need for palliative care and a legitimate reason for transfer. Why should one’s objections to MAID treatments be prioritized above one’s duty to palliative care patients?

Allowing MAID to be offered in the PCU is an important step to furthering our responsibility of compassion towards patients, and to uphold the autonomy and longevity of

patients. To close, consider how embracing these values could improve both the quality and user-ship of the PCU. Based on data from Oregon the passage of the Oregon Death with Dignity Act in 1994, it is likely that the use of hospice facilities and the quality of hospice care will rise (8). Accessibility to MAID could also help advance palliative care services, so that fewer MAID treatments are necessary. Until patients in end-of-life care have the option to access MAID, we will not fully understand the limitations of palliative care (8). By understanding these limitations, we could have a tangible understanding of how palliative care might grow and advance.

CONFLICT OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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Chapter 3

THE USE OF VITAMINS, MINERALS, HERBAL SUPPLEMENTS, AND OTHER DIETARY SUPPLEMENTS AS COMPLEMENTARY AND ALTERNATIVE THERAPIES IN CANCER CARE: A LITERATURE REVIEW

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ABSTRACT

Complementary and alternative medicines have become increasingly popular among cancer patients over the past 45 to 55 years. Among the various types of complementary and alternative therapies, vitamins, minerals, and supplements appear to be most commonly used. This literature review aims to identify evidence related to the efficacy and safety of vitamins, minerals, herbal supplements, and any other dietary supplements (VMHD) as complementary and alternative therapies in the treatment of cancer. Methods: A literature search was conducted using Ovid MEDLINE, Embase, and Cochrane Central databases to identify any trials assessing the efficacy and safety of VMHD over the past 5 years. Results: Twenty studies were included in this review. Included studies investigated the use of VMHD as treatments for traditional medicine side effects, or as potential treatments for cancer. Goshajinkigan was reported to significantly reduce peripheral neurotoxicity in two independent studies. However, outcomes for other VHMD therapies were not reported across multiple studies, making comparison of findings challenging. Conclusions: Limited evidence supporting VHMD therapies for disease management and remedying the side-effects of traditional treatments

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is available from the past five years. Comparisons using recent trial evidence are challenging due to limited cases where multiple studies evaluate the same VHMD therapies for the same outcomes, and quality of evidence is limited by small sample sizes and drawbacks in study design. Future syntheses may benefit from inclusion of other study designs and peer-reviewed literature published prior to the year 2011.

Keywords: complementary, alternative, vitamins, minerals, herbal supplements, dietary supplements

INTRODUCTION

The National Center for Complementary and Integrative Health defines an alternative medicine or therapy as “a non-mainstream practice used in place of conventional medicine,” while, a complementary medicine or therapy is defined as “a non-mainstream practice used together with conventional medicine” (1).

Typical complementary health approaches among adults in the United States include natural products (herbs, vitamins, minerals, and probiotics), mind and body practices (yoga, chiropractic and osteopathic manipulation, meditation, massage therapy, acupuncture, relaxation techniques, tai chi, healing touch, hypnotherapy, movement therapies and qi gong), and other approaches including traditional Chinese medicine, homeopathy, naturopathy, ayurvedic medicine, and traditional healers (1). Some forms of alternative medicine, such as traditional Chinese medicine, date back over 3,000 years ago. Despite this, it was in the 1960s and 1970s that complementary and alternative medicine (CAM) first rose in visibility and availability (2-4). Since then, the use of CAM for diseases and disorders, including cancer, has increased significantly. A recent systematic review and meta-analysis of articles from 15 countries found the average proportion of cancer patients using CAM in the 1970s and 1980s to be 25% (5). This proportion increased significantly to 49% for investigations completed after the year 2000 (5).

Among types of complementary and alternative therapies, vitamins, minerals, and supplements seem to be most commonly used among cancer patients (6, 7). The 2007 National Health Interview Survey conducted in the United States found that among 1,785 respondents, vitamin/mineral supplementation were used by nearly 77% (7).

The purpose of this literature review is to discuss the efficacy and safety of vitamins, minerals, herbal supplements, and any other dietary supplements (VMHD) as complementary and alternative therapies in the treatment of cancer.

METHODS

A literature search was conducted using Ovid MEDLINE (2011 – August Week 31 2016), Embase (2011 – 2016 Week 31) and Cochrane Central (2011 – 2016 Week 31) databases. Search terms included: “vitamins,” “minerals,” “supplements,” “herbs,” “cancer or neoplasm,” “integrative therapy,” “alternative therapy” and “complementary therapy.”

Eligibility criteria

Articles were considered eligible if they: a) involved an experimental study design; b) involved a cancer patient population; and c) evaluated the effectiveness of orally-ingested VMHD therapies on cancer symptom outcomes. Other study designs, studies examining other patient populations, and studies evaluating VMHD therapies administered through other routes were excluded.

Selection process, data abstraction and analysis

Titles and abstracts from the literature search were screened for eligibility by a single reviewer. Potentially eligible titles and abstracts were retrieved as full-text articles and screened using the same *a priori* eligibility criteria by the reviewer. Data extraction was subsequently completed by the reviewer for studies deemed eligible for inclusion, and checked for accuracy by a second reviewer, with discrepancies resolved via discussion. Results were subsequently summarized qualitatively.

RESULTS

One hundred and eighteen articles were identified by the literature search using the three electronic databases. Following the removal of duplicates, titles and abstract screening yielded 40 potentially eligible hits, of which 20 were finally deemed eligible following full-text review (see Figure 1).

Of the 20 eligible studies, 15 evaluated herbal supplements (8-22), 4 evaluated dietary supplements (23-26), 2 evaluated vitamins (8, 27), and two evaluated minerals (in combination with herbal supplements) (13, 14) (see Table 1). Four enrolled patients from the United States of America (9, 10, 18, 23), 4 from Japan (8, 17, 20, 21), 3 from Iran (24-26), 2 from China (15, 22), 2 from Taiwan (12, 16) 1 from Egypt (14), 1 from Germany (27), 1 from India (13), 1 from Israel (19), and 1 from Malaysia (11).

Therapies treating side-effects

Two independent studies investigated the efficacy of Goshajinkigan (GJG), a traditional Japanese medicine, in treating chemotherapy-induced neurotoxicity and found promising results. Abe and colleagues compared GJG with Mecobalamin (vitamin B12) as treatments for peripheral neurotoxicity associated with docetaxel in breast cancer patients (8). It was found that there were significantly fewer incidences of neurotoxicity ($p < 0.01$) in patients given GJG compared to vitamin B12. In a study by Nishioka and colleagues, colorectal patients received the FOLFOX6 chemotherapy treatment regimen and received GJG or no therapy (17). Those given GJG experienced significantly less grade 3 peripheral neuropathy than those in the control group given placebo ($p < 0.01$). No significant differences were found between the two treatment arms in number of adverse events or tumor response to the

FOLFOX regimen (17). Another study by El-Ghiaty and colleagues examined the ability of cystone to reduce cisplatin-induced nephrotoxicity (14). Clearance and serum creatinine was found to be significantly better in those receiving cystone compared to baseline ($p < 0.05$), indicating some potential protective effects of cystone with regard to nephrotoxicity (14). Rostock and colleagues also investigated the efficacy of vitamin B1/B6 in treating chemotherapy-induced peripheral neuropathy, but found no significant difference across any assessment measures when compared to placebo (27).

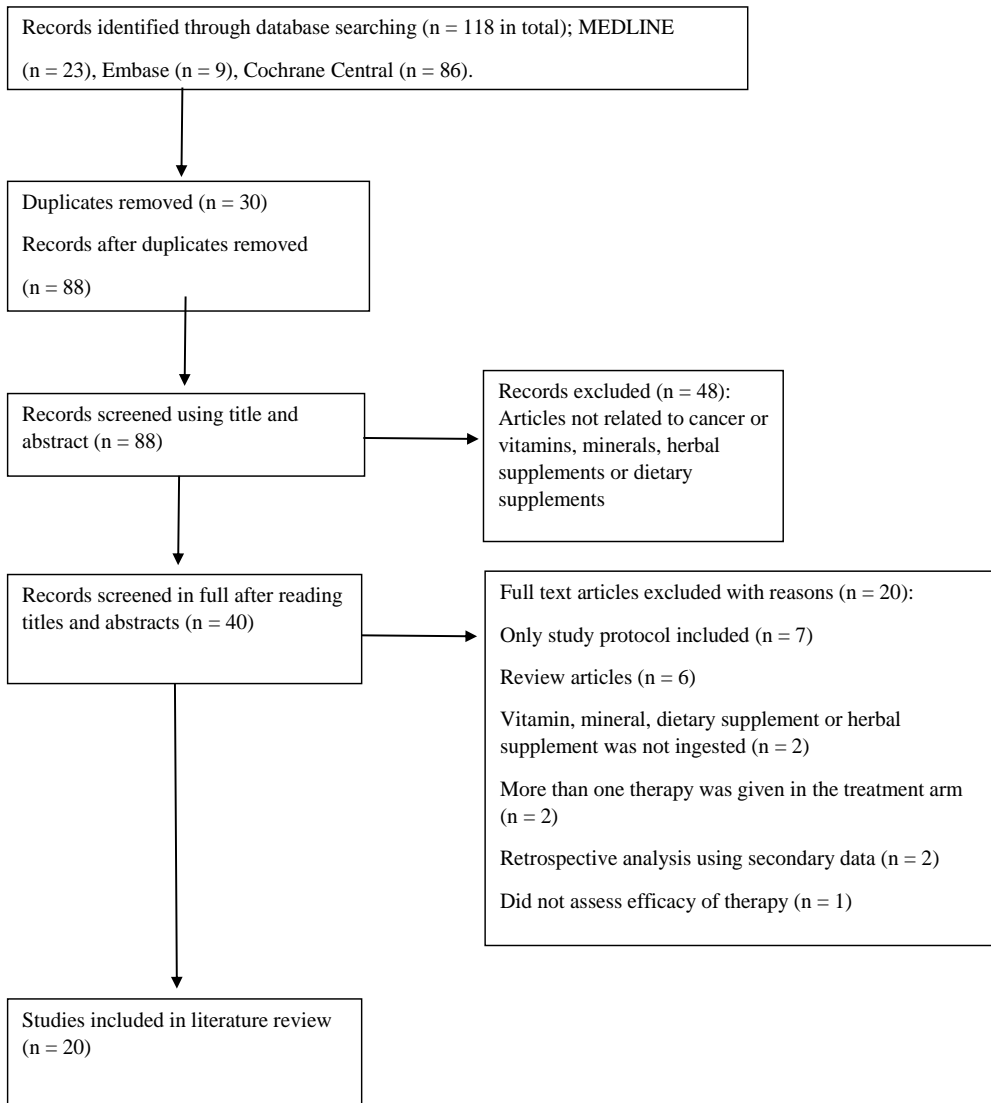


Figure 1. Identification of studies on vitamins, minerals, herbal supplements or dietary supplements as complementary or alternative therapies used in cancer patients.

Other studies have focused on chemotherapy-induced side effects and quality of life (QoL), and have discovered potential benefits for specific outcomes. Deshmukh and colleagues found the use of ayurvedic drugs MPP and MKD significantly increased patient Karnofsky Performance Status (KPS) ($p < 0.0001$) and decreased Eastern Cooperation Oncology Group (ECOG) scores ($p = 0.0022$) compared to placebo, when used for 6 months after treatment (13). Ryan and colleagues found significant reduction in average nausea ($p = 0.013$) and nausea at its worst ($p = 0.003$) when comparing ginger to control (18). However, no difference in QoL or vomiting symptoms were found (18). Some gastrointestinal adverse events were reported, including grade 2 heartburn, bruising/flushing and rashes (18). Yaal-Hahoshen and colleagues found significantly less severe anemia ($p < 0.01$), leukopenia ($p < 0.03$) and neutropenia ($p < 0.04$) in breast cancer patients treated with botanical compound mixture LCS101 (19).

The use of oral *Fructus bruceae* oil for radiotherapy-induced side effects in esophageal cancer patients was assessed by Shan and colleagues (15). The rate of complete and partial remission was reported to be significantly higher in the treatment arm compared to the control group with no treatment ($p < 0.05$) (15). A significant improvement in KPS, nausea and vomiting, and radiation esophagitis and pneumonitis was also seen ($p < 0.05$ for all) (15).

In addition to chemotherapy and radiotherapy, three studies investigated the use of herbal supplements on postoperative adverse effects and recovery. Yoshikawa and colleagues investigated the use of daikenchuto on gastrectomy and laparoscopic colectomy side effects and complications (20, 21). For those undergoing gastrectomy who were randomized to receive daikenchuto, the median time until first defecation and incidence of bowel movement disorder was significantly lower ($p = 0.05$ for both outcomes). No daikenchuto-related serious adverse events occurred. For those undergoing laparoscopic colorectal resection who received daikenchuto, a significantly shorter time until first flatus was seen when compared to control ($p = 0.02$) (20, 21). Zhong and colleagues administered Jianpi Huayu, a mixture of herbal extracts, to patients after hepatectomy (22). Significant differences favoring the treatment arm were seen in length of stay ($p = 0.034$), postoperative alanine aminotransferase (ALT) levels ($p = 0.042$), disease recurrence, number of singular recurrent lesions, and disease-free survival and overall survival at 1, 3 and 5 years follow-up (22).

Three studies assessed the efficacy of therapies on sleep and fatigue. Cruciani and colleagues found no significant difference between L-carnitine and placebo for the treatment of fatigue (23). Barton and colleagues did not provide data to support the efficacy of *Valeriana officinalis* on improving sleep, but an exploratory analysis found that use for fatigue may warrant further study (10). Biswal and colleagues found that the treatment arm given herbal supplement *Withania somnifera* produced significantly lower scores on the Piper's Fatigue Scale (PFS), Schwartz's Cancer Fatigue Scale (SCFS-6) and the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 quality of life questionnaire fatigue scale ($p < 0.001$, $p = 0.003$ and $p < 0.001$, respectively) (11).

Lastly, Madhavi and colleagues investigated conjugated linoleic acid (CLA) supplementation as a therapy for improving nutritional status, and symptoms of eating problems and dietary intake in patients with rectal cancer (24). In those receiving CLA, a significant decrease was seen in appetite loss, nausea, diarrhea, pain, and significant increase in dietary intake ($p < 0.05$ for all) (24).

Table 1. Overview of articles included in literature review, including author, complementary and alternative medicine (CAM) type, CAM, sample size, cancer type, current treatment being received, and the symptoms, diseases or conditions intended to be treated

Author	CAM Type	CAM	Sample Size (n)	Cancer Type	Current Treatment of patients enrolled	Dependent variable/Intent to treat
Abe H et al. (2013), Japan	Herbal supplement and Vitamin	Goshajinkigan, Vitamin B12	60	Breast cancer (stage I, IIA, IIB, or III)	Chemotherapy (Docetaxel)	Peripheral neuropathy/neurotoxicity
Azrad M et al. (2013), USA	Herbal supplement	Flaxseed	147	Prostate cancer	Awaiting Prostatectomy	Tumor cell proliferation
Barton DL et al. (2011), USA	Herbal supplement	Valeriana Officinalis	119	Any	Chemotherapy, Radiotherapy, Oral anti-tumor agents, or Endocrine therapy	Sleep
Biswal BM et al. (2012), Malaysia	Herbal supplement	Withania somnifera	100	Breast cancer	Chemotherapy	Chemotherapy-induced fatigue and Quality of Life
Chen WT-L et al.(2014), Taiwan	Herbal supplement	MB-6	72	Metastatic colorectal cancer	Chemotherapy (FOLFOX4)	Chemotherapy effectiveness
Cruciani RA et al. (2012), USA	Dietary supplement	L-cartinine	376	Any (invasive malignancies)	Any	Fatigue
Deshmukhq V et al. (2014), India	Herbal supplement and Mineral	Ayurvedic drugs (MPP, MKD)	67	Any	Chemotherapy	Chemotherapy side effects and toxicity
El-Ghiaty MA et al. (2014), Egypt	Herbal supplement and Mineral	Cystone	49	Any	Chemotherapy (Cisplatin)	Cisplatin-induced nephrotoxicity, cytotoxic activity of cisplatin.
Kuo W-H et al. (2012), Taiwan	Herbal supplement	Tien-hsein	44	Metastatic Breast cancer	None	Breast cancer
Mahdavi R et al. (2013), Iran	Dietary supplement	Linoleic acid	31	Rectal cancer (stage II or III)	Chemotherapy and Radiotherapy	Nutritional status, eating problems, and dietary intake

Author	CAM Type	CAM	Sample Size (n)	Cancer Type	Current Treatment of patients enrolled	Dependent variable/ Intent to treat
Mohammadzadeh M et al. (2013), Iran	Dietary supplement	Linoleic acid	32	Rectal cancer (stage II or III)	Chemotherapy and Radiotherapy	Inflammatory factors and matrix metalloproteinase (MMP) enzymes
Nishioka M et al. (2011), Japan	Herbal supplement	Goshajinkigan	45	Colorectal cancer	Chemotherapy (FOLFOX6)	Peripheral neuropathy
Ostradrahimi A et al. (2014), Iran	Dietary supplement	Beta glucan	30	Breast cancer (stage II or III)	Chemotherapy	White blood cell counts and serum levels of IL-4 and IL-12
Rostock M et al. (2013), Germany	Vitamin	Vitamin B1/B6	32	Any cancer (in remission)	Completed chemotherapy	Chemotherapy-induced peripheral neuropathy
Ryan JL et al. (2012), USA	Herbal supplement	Ginger	576	Any	Chemotherapy	Chemotherapy-induced nausea
Shan GY et al. (2011), China	Herbal supplement	Fructus bruceae Oil	80	Esophageal cancer (grade II or III)	Radiotherapy	Radiotherapy side effects
Yaal-Hahoshen N et al. (2011), Israel	Herbal supplement	LCS101	65	Breast cancer	Chemotherapy	Chemotherapy-induced Hematological toxicity
Yoshikawa K et al. (2015), Japan	Herbal supplement	Daikenchuto	195	Gastric cancer	Gastrectomy	Gastrectomy side effects
Yoshikawa K et al. (2012), Japan	Herbal supplement	Daikenchuto	30	Colorectal cancer	Laparoscopic Colectomy	Inflammatory response
Zhong C et al. (2014), China	Herbal supplement	Jianpi Huayu	120	Hepatocellular carcinoma	Hepatectomy	Postoperative recovery

CAM = Complementary and Alternative Medicine; MKD = Mauktikyukta Kamdudha; MPP = Mauktikyukta Praval Panchmrut.